Obesity and Hypertension: A Review

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Hypertension has been recognized as the single most potent, common, and remediable risk factor for cardiovascular morbidity and mortality. While obesity has been associated with an increased risk for cardiovascular diseases, this increased risk has been attributed to the increased incidence of hypertension, glucose intolerance, and hyperlipidemia. In this review we discuss the relationship of hypertension and obesity, focusing on the epidemiological data which support such a relationship, as well as the pathophysiological and hemodynamic changes which occur in obese hypertensive patients.

Epidemiology of Obesity and Hypertension

The association between hypertension and obesity has been well documented by numerous clinical and epidemiological studies (1-8). Data from the Framingham study (9) showed that subjects who were overweight at the start of the study later developed hypertension more often than subjects who were not overweight (10). In the Evans County, Georgia, study (2), a weight gain over a six-year period was clearly associated with twice the likelihood that hypertension would develop. Moreover, obesity at the start of the study with no further weight gain was also associated with a fivefold greater chance of reaching hypertensive levels of blood pressure, and the relative risk of hypertension was eight times greater in those who were both overweight at the outset and who also gained weight during the six-year study. The Evans County study also showed that the rate of remission of "hypertensive" blood pressure into the normal range was twice as great for subjects who lost 4.5 kg (10 lb) or more over six years as for those who gained 4.5 kg (10 lb) or more during the same interval. Data from a study done on former students of Catholic University of America who graduated in 1968 showed that 60% of the participants were more than 20% above ideal body weight (13) in contrast to 24% and 14% of all American women and men, respectively (14).

Much evidence exists regarding the beneficial effect of weight reduction on blood pressure. Weight reduction often reduces arterial pressure in both normotensive and hypertensive individuals (15). In obese hypertensive persons, blood pressures fall before normal weight is achieved. This fall in blood pressure in normotensive as well as hypertensive subjects contrasts with other interventions designed to affect blood pressure (16). For example, a marked reduction in sodium intake has little or no effect on persons with normal blood pressure yet will return blood pressure to normal levels rapidly in persons with salt-sensitive hypertension (17). A weight loss of 7 kg (15 lb) in untreated obese hypertensive patients was associated with a 13/10 mm Hg fall in blood pressure (18) and a loss of 9 kg (20 lb) was associated with a 19/18 mm Hg fall in blood pressure (19). In patients treated with antihypertensive drugs, blood pressure fell by 23/15 mm Hg with a 6 kg (13 lb) weight loss (5) and by 30/21 mm Hg with a 9 kg (20 lb) weight loss (6). This blood pressure-lowering effect of weight loss appears to be independent of salt intake (6) and appears to be maintained for at least one year (5).

In all of these studies, special, large-sized blood pressure cuffs were used to avoid the erroneously high readings that may result from using standard-sized cuffs on obese patients (19).
The national health and nutrition examination survey (NHANES) (20) defined obesity or "overweight" in statistical terms as a body mass index (weight/height) exceeding the 85th percentile. Overweight, as defined by an elevated body mass index, was differentiated from excess fat by measuring the thickness of the triceps and the subscapular skinfold. Interestingly, hypertension was approximately 2.5 times more prevalent in patients with an elevated body mass index than in those with a normal body mass index and excess body fat. In contrast, subjects with excess body fat but normal weight had no higher prevalence of hypertension (21). Thus it appears that increased body mass index rather than excess body fat may be linked to hypertension (22). Other studies demonstrated that blood pressure correlates positively with the waist-to-hip ratio (23,24). This relationship remained significant even for systolic pressure when the body mass index and skinfold thickness were taken into account (23,24). Similarly, a pattern of fat distribution, predominantly in the trunk, was related to elevated systolic pressure (25,26). Therefore, abdominal obesity more than gynoid obesity appears to increase the risk for hypertension.

In addition to the strong association between hypertension and obesity, obesity is also associated with hypercholesterolemia and impaired glucose tolerance (27), both of which are important risk factors of cardiovascular disease. Obesity, particularly of abdominal distribution, is possibly a risk factor for coronary artery disease, independent of other major risk factors (27).

Pathophysiology of Obesity Hypertension

Despite the clinical and epidemiologic evidence, pathogenic mechanisms of the relationship between hypertension and obesity are not fully understood. We will try to elucidate such mechanisms in the following discussion of the pathophysiological characteristics of obesity hypertension.

Increased cardiac output

Obese people usually have an increased cardiac output. The cardiac output is believed to be increased (28) in response to elevated metabolic requirements in obese subjects (29,30). The high cardiac output is produced mainly by increased stroke volume which in turn results from an expanded intravascular volume (29,31). Whyte (32) suggested that obesity hypertension occurs because the increased cardiac output is disproportionately high for the size of the aorta into which it is ejected. Mujais et al (33) found that the cardiac output of obese hypertensive men was significantly higher than that of nonobese hypertensive men but not higher than that of normotensive obese men.

Sodium retention and increased blood volume

Sodium retention was thought to play an important role in the pathogenesis of hypertension in obese patients. In 1958, Dahl and associates (34) suggested that the hypertension of obesity is salt-dependent because "in the process of overeating, higher than the usual amounts of sodium would be ingested" and that obese patients who had salt and calorie restriction had an im-
excess leading to hypertension and changes in internal cation ever, insulin has been shown to have a stimulatory effect on the independent of any induced changes in hemodynamic or adrenal renal sympathetic nerve stimulation cause sodium reabsorption caloric restriction. Conversely, catecholamine administration or which may contribute to the blood pressure-lowering effect of renin secretion and angiotensin-II production (42), obesity, and the caloric reduction probably decreases the pressor and heart rate response to physical stress via its effects on sympathetic nervous system activity (42).

The decrease in catecholamines in response to weight reduc­tion reduces renin secretion and angiotensin-II production (42), which may contribute to the blood pressure-lowering effect of caloric restriction. Conversely, catecholamine administration or renal sympathetic nerve stimulation cause sodium reabsorption independent of any induced changes in hemodynamic or adrenal steroid secretion. Thus, catecholamine response to overfeeding (46) may contribute to sodium retention and blood pressure elevation (47).

Role of opiates
Opioid peptides may play a role in blood pressure control (48-50). Einhorn et al (51) reported that the fall in blood pressure found with fasting in spontaneously hypertensive rats could be reversed by the administration of naltrexone (opiate antagonist). Thus, fasting results in opiate stimulation which may have a blood pressure-lowering effect.

Hyperinsulinemia
Hyperinsulinemia has been reported to be common in obese subjects and also in hypertensive patients (52). Hyperinsulinemia and tissue insulin resistance in obesity may play a role in the pathogenesis of obesity hypertension by altering internal sodium and potassium distribution in a direction that is presumably associated with increased peripheral vascular resistance (53-55). Modan et al (52) observed increased erythrocyte sodium, reduced erythrocyte potassium, and increased plasma potassium in obese subjects, hypertensive patients, and patients with abnormal glucose tolerance. However, insulin has been shown to have a stimulatory effect on the sympathetic nervous system, with its attendant catecholamine excess leading to hypertension and changes in internal cation distribution (56-58). This effect might be important because obesity is associated with both catecholamine excess and hyperinsulinemia.

Role of thyroid hormones
Overfeeding increases thyroxin (T4) deiodination to triiodothyronine (T3) while carbohydrate restriction and weight reduction reduce serum T3. The increase of serum T3 in obese patients, with the onset of their obesity in adolescence or later in life, may be a contributing factor to the development of hypertension because T3 increases the beta-adrenergic receptor number and thus may increase sensitivity to pressor mechanisms (47). Table 1 summarizes the etiological factors in the pathogenesis of hypertension in obese subjects.

Hemodynamic Changes in Obesity and Hypertension
The hallmark of essential hypertension is increased peripheral vascular resistance (59). With progression of hypertensive cardiovascular disease, cardiac output begins to fall and total peripheral vascular resistance becomes more elevated (60). As total peripheral vascular resistance increases progressively, intravascular volume becomes contracted progressively (61, 62). With progression of hypertension, renal blood flow falls and renal vascular resistance increases progressively (63-65). Conversely, any increase in body mass requires a higher cardiac output and expanded intravascular volume to meet the elevated metabolic requirements (66). Thus, obesity corresponds to a mild volume overload state (67-69). Provided that blood pressure remains unchanged, an elevated cardiac output will result in a fall in total peripheral vascular resistance in obese patients. Therefore, for any level of blood pressure, cardiac output is higher and systemic vascular resistance is lower in obese patients than in lean patients (66).

As the stroke volume and thus the cardiac output increases, the left ventricular filling pressure and end-diastolic volume also become elevated, which in turn increases preload which gives rise to chamber dilatation (70). The dilated left ventricle adapts to these stresses, if they persist, by an increase in muscle mass. Obesity therefore produces predominantly left ventricular hypertrophy and dilatation, or eccentric hypertrophy, regardless of the blood pressure level (66). Actually, body weight and body surface area are the most powerful determinants of left ventricular chamber size, wall thickness, and muscle mass (71).

Obese patients who have distinct eccentric left ventricular hypertrophy on echocardiogram but who lack electrocardiographic evidence of left ventricular hypertrophy have a markedly increased prevalence and complexity of ventricular ectopy compared to those without left ventricular hypertrophy or to slender patients (72). This is in accordance with data from the Framingham study which identify obesity as an independent risk factor for sudden death and other cardiovascular morbidity and mortality (73). However, hypertension alone causes left ventricular hypertrophy without chamber dilatation or concentric hypertrophy (74-76). Hypertensive patients who have left ventricular hypertrophy on electrocardiography have 40 to 50 times more frequent and more complex ventricular ectopy than patients with normal or less hypertrophic myocardium (77). When obesity and hypertension occur in the same patient, both preload and afterload are elevated, thus presenting a double burden to the left ventricle. Congestive heart failure, sudden death, and coronary artery disease are common sequelae of obesity hypertension (69). Table 2 summarizes the hemodynamic changes in obesity and hypertension states.

Management of Obesity Hypertension
Weight reduction and caloric and salt restriction should be the main therapeutic interventions in treating obese hypertensive
patients. Weight reduction, regardless of sodium intake, is commonly associated with a drop in blood pressure (3-6), and the maximum fall in blood pressure frequently occurs before normal weight is achieved (6,78). Decreased blood pressure in response to weight loss has been attributed to several factors including reduced sodium intake (34), contraction of total blood volume, redistribution of the cardiopulmonary volume to the periphery (79), attenuated sympathetic drive to the cardiovascular system (39,80), decreased basal and stress-stimulated sympathetic nervous system activity (19,81), increased opioid peptides activity (55), and decreased plasma renin activity and aldosterone levels (42,81). Hypertension is a serious risk factor in obese patients who often have other risk factors such as glucose intolerance and hyperlipidemia. Consequently, therapy with dietary (caloric and salt) restriction and antihypertensive drugs should be started immediately. The progress of the treatment should be checked with blood pressure readings obtained by using a large-sized cuff. If the diet succeeds on a long-term basis, the patient will experience a gratifying reduction in blood pressure without annoying side effects. Control of blood pressure will probably be possible with fewer medications or by using smaller doses of drugs or the dmg treatment may even be stopped (19). Antihypertensive drugs should not be withheld while waiting for the beneficial effects of weight reduction. Hypertension should be controlled with antihypertensive drugs, thus removing the strain on the heart and arteries and thereby protecting them. Then a long-term weight loss regimen can be attempted. Sodium intake should be restricted to about 70 mmol/day (70 mEq/24 hr) (19). This modest salt restriction permits diuretics, beta blockers, angiotensin-converting enzyme inhibitors, and other antihypertensive agents to work more effectively in lowering blood pressure. Patient compliance (82) is the major problem in an effective weight reduction program. Strong motivation from the patient and a close patient-physician relationship are required for a successful weight reduction program.

References
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