Obesity, Insulin Resistance, and Nocturnal Systolic Blood Pressure

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An increasing prevalence of obesity is observed in all age and ethnicity groups and is increasingly being recognized as a serious health problem in children and adolescents.[1–4] Obesity is associated with a number of metabolic abnormalities, as well as increased risk for cardiovascular disease (CVD).[3,4] In this issue of *Hypertension*, Lurbe et al[5] reported a relationship between insulin resistance, determined by the homeostatic model assessment technique, and nocturnal elevations of systolic blood pressure and heart rate in a large cohort of overweight and obese European children and adolescents. This relationship was present even after adjustment for age, sex, and height. Furthermore, waist circumference was strongly associated with insulin resistance, and both waist circumference and insulin resistance were associated with elevated nocturnal, but not daytime, blood pressures. These are important observations despite some limitations as to the methodology that the investigators used. One limitation of this report is the fact that sleep was not well documented, which limited the ability to strongly relate the nocturnal blood pressures and heart rate to circadian rhythmicity. Another potential limitation of this study relates to the fact that the children were recruited from an obesity clinic; therefore, the data may not be representative of the general population of children and adolescents. Finally, the results of this study are limited by the fact that it was a cross-sectional rather than a prospective longitudinal investigation. Nevertheless, the observations in this study are in concert with previous reports of a positive relationship between insulin resistance and hypertension in children and adolescents.[6,7] As noted by the authors, the results of this cross-sectional study need to be validated in prospective longitudinal investigations in this population. Furthermore, the impact of weight reduction and other strategies to improve insulin sensitivity on elevated nocturnal blood pressures would be a potentially important avenue of investigation. Because both nocturnal elevation of blood pressure and insulin resistance are predictive of renal disease,[8,9] as well as CVD, the impact of insulin resistance and elevated nocturnal systolic blood pressure in children on blood pressure temporal trends, as well as the impact on development of CVD and renal disease in adulthood, needs to be assessed in future prospective studies.

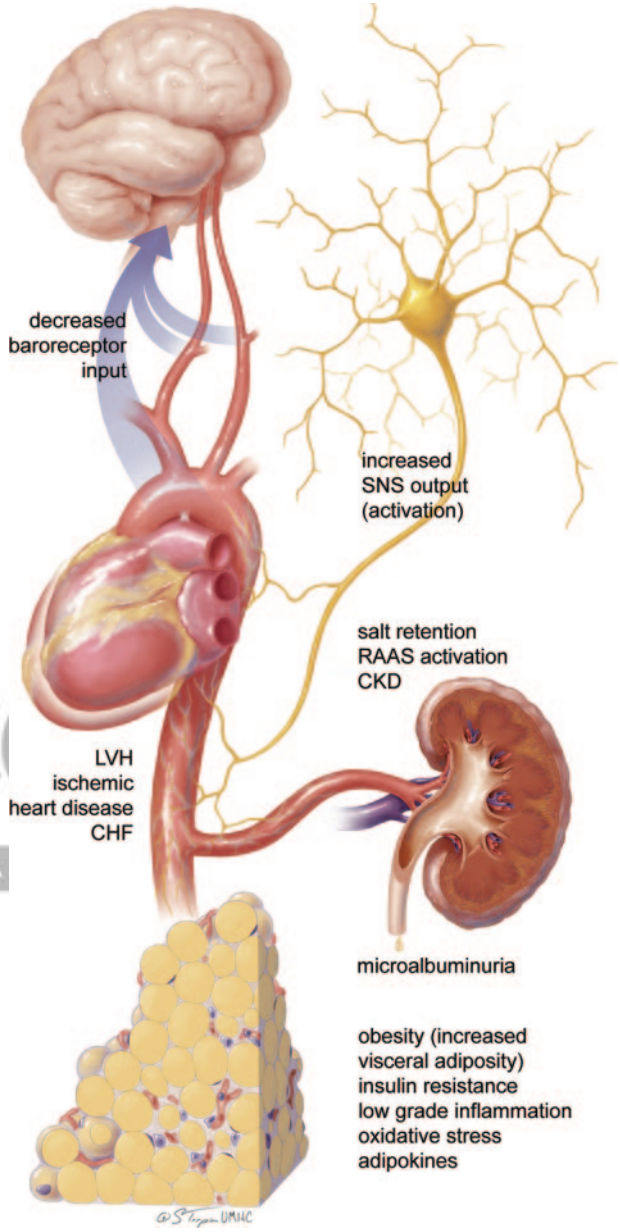

Figure. Depicts the relationship among nocturnal nondipping, visceral adiposity, and insulin resistance, as mediated by inflammation, oxidative stress, and altered sympathetic nervous system (SNS) output. The presence of nocturnal nondipping is associated with renal (eg, salt retention, microalbuminuria, renin-angiotensin-aldosterone system [RAAS], and chronic kidney disease) and cardiovascular end-organ damage (eg, left ventricular hypertrophy [LVH], ischemic heart disease, and congestive heart failure [CHF]) and increased risk of CVD event.

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A loss of the normal 24-hour circadian blood pressure and heart rate pattern has been reported in those with autonomic nervous abnormalities accompanying obesity and insulin resistance.[8–11] A nondipping pattern may be promoted by increases in inflammation, oxidative stress, endothelial dysfunction, and early renal disease, as manifested by the presence of microalbuminuria (Figure).[8–11] Obesity and insulin resistance contribute to endothelial dysfunction, increased sympathetic nervous system activity, increased cardiovascular and renal oxidative stress, and inflammation (Figure).[4] There is increasing evidence suggesting that adipose tissue, especially central fat, is a major source of production of inflammatory cytokines.[4] These inflammatory molecules, in turn, may contribute to insulin resistance, endothelial dysfunction, and activation of the sympathetic nervous system, as well as the renin-angiotensin-aldosterone system.[12] Collectively, these metabolic and vascular abnormalities are associated with loss of the normal circadian rhythm of blood pressure (Figure).[8–11] There are substantial data indicating that the presence of nocturnal nondipping is an important harbinger for CVD and chronic kidney disease in the adult population; the current investigation by Lurbe et al[5] highlights the importance of this emerging biomarker for CVD and early renal disease[9] in the adolescent population. Therefore, determining its presence and development of strategies to correct this abnormality may be very important in the future management of obesity and insulin resistance in children. This approach could potentially be a preventative measure for the development of CVD and chronic kidney disease in adulthood. Hopefully, publication of this cross-sectional study will lead to prospective studies evaluating the relationship between isolated nocturnal elevations of systolic blood pressure and heart rate and the development of sustained daytime hypertension, as well as biomarkers of CVD and chronic kidney disease during adolescence and early adulthood. Prospective longitudinal studies are also needed to ascertain the impact of weight reduction, exercise, and other hygienic measures in children to determine whether restoration of normal insulin sensitivity and circadian rhythm of blood pressure and heart rate is contemporaneously associated with reductions of albuminuria and other biomarkers of early renal disease and CVD in young adults.

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