CONTROVERSIES IN HYPERTENSION

Weight Loss and Blood Pressure Control (Pro)

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Overweight is an increasingly prevalent condition throughout the world. Current estimates, which are probably conservative, indicate that at least 500 000 000 people worldwide are overweight as defined by a body mass index (BMI) of between 25.0 and 29.9 and an additional 250 000 000 are obese with a BMI of 30.0 or higher. In the United States, recent data indicate that as much as 66% of the adult population is overweight or obese.

Overweight and obesity are established risk factors for cardiovascular disease (CVD), stroke, noninsulin dependent diabetes (NIDDM), certain cancers, and numerous other disorders. It is also a risk factor for hypertension.

Hypertension, defined as a systolic blood pressure in excess of 140 mm Hg or a diastolic blood pressure higher than 90 mm Hg, is also a globally increasing public health concern. Roughly 1 billion individuals worldwide are estimated to exhibit clinically significant elevated blood pressure with about 50 million of those residing in the United States. Hypertension, in turn, is associated with increased risk for CVD, stroke, renal disease, and all-cause mortality.

The JNC VII report defines Stage 1 hypertension as blood pressure levels between 140 and 159 mm Hg systolic and 90 and 99 diastolic. Additionally, the report establishes a category of Prehypertension (Systolic blood pressure between 120 and 140 mm Hg or diastolic between 80 and 89 mm Hg). These 2 blood pressure classifications are deemed to be appropriate primary targets for lifestyle modification interventions, including weight loss. Higher levels of blood pressure, or stage 1 hypertension that is maintained over a long period, should be addressed primarily with medications or other physician directed treatments.

There is a positive relationship between overweight or obesity and blood pressure and risk for hypertension. As early as the 1920s, a significant association between body weight and blood pressure was noted in men. In the intervening years, epidemiological studies have routinely confirmed this association. The Framingham Study found that hypertension is about twice as prevalent in the obese as the nonobese of both sexes. Stamler and colleagues noted an odds ratio for hypertension of obese relative to nonobese (BMI of less than 25) of 2.42 for younger adults and 1.54 for older ones. The Nurses Health Study compared women with BMIs of less than 22 with those above 29 and found a 2- to 6-fold greater prevalence of hypertension among the obese.

More recent data from the Framingham Study further support this relationship. Divided into BMI quintiles, Framingham participants of both sexes demonstrated increasing blood pressures with increased overweight. In this instance those in the highest BMI quintile exhibited 16 mm Hg higher systolic and 9 mm Hg higher diastolic blood pressures than those in the lowest quintile. For systolic blood pressure this translated into an increase of 4 mm Hg for each 4.5 kg of increased weight. In younger Canadian adults, Rabkin et al noted a 5-fold greater incidence of hypertension in individuals with BMIs of more than 30 relative to those less than 20 for both sexes.

The public health burden of hypertension is certainly enormous. Although perhaps impossible to tease out because of associations with other risk factors, including overweight, hypertension is clearly a major contributor to most categories of chronic disease. Diseases of the heart and cerebrovascular diseases are the 1st and 3rd major causes of mortality in the United States accounting for more than 1/3 of all deaths annually. Hypertension is one of the clearest risk factors for both of these causes of death. Therefore, reduction in hypertension constitutes a major health goal for the immediate future. The federal government through the Healthy People 2010 initiative proposes to increase to 50% those in the adult hypertensive population with controlled hypertension. This contrasts with the currently estimated figure of 34%.

Blood pressure control, the return of blood pressure to normotensive status, would have significant impact on mortality from heart and cerebrovascular diseases. In clinical trials antihypertensive therapy can result in reductions of incidence of stroke, myocardial infarction, and heart failure of between 20% and 50%. Ogden et al estimate that a 12-mm Hg decline in systolic blood pressure maintained over a period of 10 years in a population with initial stage 1 hypertension will reduce incident mortality by between 9%
and 11%. A population wide reduction of 5.5 mm Hg systolic or 3.0 mm Hg diastolic would result in an estimated 15% decline in incident coronary heart disease and a 27% decline in stroke.24,25

The challenge, therefore, is how to accomplish this goal. Numerous treatments have proved efficacious, at least in the short term, in clinically significantly reducing blood pressure levels.8 Of these, weight loss offers a number of attractive features. We will consider the evidence for weight loss mediated reductions in blood pressure accomplished through the more traditional means of caloric restriction and other lifestyle modification strategies. We will not review the data associated with weight loss resulting from pharmacological or surgical interventions except as it may relate to maintenance of weight loss.

Blood pressure alteration is theorized to be positively associated with weight change. Although a number of studies have examined this from a perspective of weight loss and reduction in blood pressure, there are little data in humans to inform directly the idea that increase in weight relates to increased blood pressure at the individual level. Animal studies have been the principle source of this information. Rocchini et al26 noted significant increases in blood pressure accompanying weight gain from overfeeding in dogs. Hall et al27 have confirmed this relationship.

On the other hand, numerous clinical interventions in humans have examined the relationship of weight loss to blood pressure change. Haynes28 reviewed 6 clinical trials available to that time relating weight loss and blood pressure, noting that 3 of them showed a significant impact of weight loss whereas the other 3 did not demonstrate a clear impact. More recently, a meta-analysis of 25 studies on this topic was performed by Neter et al.29 The authors concluded that a 1-kg loss of body weight was associated with an approximate 1-mm Hg drop in blood pressure. Further this blood pressure reduction was accomplished without the necessity of also attaining normal weight status. The Trial of Hypertension Prevention (TOHP), one of the largest of these studies, included a weight loss intervention arm.30 In this instance, a 2-kg loss in weight over a 6-month period resulted in a decline of 3.7 mm Hg in systolic and 2.7 mm Hg in diastolic blood pressure. In addition, a 42% decline in the instance of hypertension was noted on this sample.31

Another analysis of multiple clinical trials of blood pressure reduction was conducted by Ebrahim and Smith.32 In this report, 8 trials were examined for the effects of weight loss on blood pressure and concluded that weight gain was associated with increased blood pressure whereas weight loss resulted in reduced blood pressure. Blood pressure reductions were on the order of 5.2 mm Hg both systolic and diastolic for varying degrees of weight reduction.

Given the established association between weight change and blood pressure status, the question arises as to how this interaction functions physiologically. Rocchini33 identifies numerous potential biological mechanisms by which weight loss or fat loss might lead to parallel declines in blood pressure. Among them are reductions in insulin resistance, enhanced sodium retention, alterations in vascular structure and function, changes in ion transport, enhanced stimulation of the renin-aldosterone-angiotensin system, increased activation of sympathetic nervous system, and changes in natriuretic peptide. The wide range of potential mechanisms also may be a major factor in accounting for the apparent heterogeneity in blood pressure response to any treatment. Weight loss may variably and simultaneously impact one or more of these proposed routes of action. Because weight status itself is a result of multiple causes, the fashion in which it induces blood pressure change would not surprisingly be variable.

Examination of these possible mechanisms raises one important caveat about recommending weight loss for blood pressure control. This is the possibility that the effects of weight loss are mediated through some other system and that weight loss might not be an independent influence on blood pressure status.

Because most weight loss is accomplished through dietary manipulation, it is possible that some aspects of diet, when altered, are the true determinants of blood pressure reduction. Chief among perceived dietary influences on blood pressure is sodium consumption. A large literature supports the notion that decreasing sodium consumption below that typical in Western society will result in a decline of blood pressure. Numerous epidemiological studies have demonstrated this relationship.24,34,35,36 Reductions in sodium intake on the order of 75 mmol/d or less have been associated with a decline in blood pressure of about 1.9 mm Hg systolic and 1.1 diastolic.37 The previously mentioned Trial of Hypertension Prevention found that a decrease of 44 mmol/d of sodium led to a 38% reduction in the incidence of hypertension in one of its treatment arms.38 The previously cited group analysis by Ebrahim and Smith32 found a pooled reduction of 2.9 and 2.1 mm Hg blood pressure level with varying degrees of sodium restriction. The Dietary Alterations to Stop Hypertension Study (DASH-Na) found a maximum reduction of about 6.7 mm Hg systolic and 3.5 diastolic in blood pressure with an approximate 100-mmol/d reduction in sodium intake in those with elevated blood pressure on a typical American diet. An approximate 50 mmol/d reduction in sodium consumption led to a blood pressure decline of 2.1 and 1.1 mm Hg systolic and diastolic.39 These findings were produced in the absence of weight loss.

The jury of scientific opinion is still out on the degree to which weight loss or sodium restriction make independent contributions to blood pressure reduction. An early study, Dahl et al40 found sodium restriction in low calorie diets to be the primary cause of blood pressure reduction. This is also the finding of Fagerberg et al.41 Several more recent studies have sided with weight loss as having an independent effect on blood pressure reduction. Reisen et al42 found blood pressure reductions on the order of 3 mm Hg for each kg of weight loss in a sample of hypertensive men with no sodium restriction. Tuck et al43 and Maxwell et al44 additionally reported sodium independent effects of weight loss in a sample of hypertensive men as well.

Other dietary constituents have been implicated in the control of blood pressure as well. Vegetarian diets are widely associated with lower blood pressure levels.45 The Dietary Approaches to Stop Hypertension Trial25 demonstrated that a
diet high in fruit, vegetable, and low-fat dairy servings could reduce blood pressure by 5.3 and 3.0 mm Hg systolic and diastolic blood pressure, respectively, in the absence of either weight loss or sodium restriction. Raben et al. found that significantly increased sucrose consumption led to noteworthy increases in both weight and fat mass as well as increases in blood pressure on the order of 4 mm Hg.

Likewise, physical activity has been shown to influence blood pressure levels and is additionally a part of the recommended regimen of weight loss strategies. Bouchard et al. examined the pertinent studies to that time and concluded that approximately 1 hour per day of low to moderate level physical activity could support weight loss but that such a program would require several years to be completely effective. Ebrahim and Smith studied 8 clinical trials in which exercise was a primary component in blood pressure reduction. They found modest impacts on blood pressure reduction of 0.8 to 3.7 and 0.2 to 1.0 mm Hg resulting from primarily low levels of physical activity. A meta-analysis of the effects of physical activity on blood pressure conducted by Kelley et al. led the authors to predict a decline in systolic blood pressure of 3 to 5 mm Hg associated with moderate physical activity. Whelton et al. reported a meta-analysis of normo-tensive with significant reductions in blood pressure attendant to a variety of types of physical activity. Interestingly, although there appears to be consensus among these investigators that increased physical activity drives somewhat larger declines in blood pressure, the nature of this relationship is unclear. Although there might be a dose response relationship in the largest sense, most of these studies examine the impact of low to moderate physical activity and therefore have a cap on the degree they are capable of examining the full impact of exercise on blood pressure.

Because weight loss cannot be accomplished in the absence of some combination of dietary or physical activity behaviors, separating independent effects of each component on blood pressure is extremely challenging. It is clear, however, that weight loss, regardless of how obtained, is associated with clinically significant reductions in blood pressure.

Another issue is the extent to which maintained weight loss continues to influence blood pressure status. The majority of studies linking weight loss to blood pressure reduction do so only in the short term, usually examining impacts on a scale of less than 1 year. The effect of longer term weight loss has predictably been much less examined. A number of clinical trials have examined the issue on the scale of more than 1 year.

The Premier Trial followed 810 individuals with initial elevated blood pressure or stage 1 hypertension for 18 months after randomization to control or either of 2 putatively heart healthy active interventions. Both active interventions counseled an increase in physical activity, and either a reduced fat and calorie diet, or a diet high in fruits, vegetables, and low fat dairy servings using the DASH dietary model. Both active interventions also counseled reduction in sodium intake. Weight and blood pressure change were observed at baseline, at interim periods, and at the end of 18 months of intervention. At the end of the trial both active interventions saw sustained weight loss and blood pressure reduction. The active intervention without the DASH diet resulted in an average weight loss of 3.8 kg, that with the DASH diet of 4.3 kg. Mean blood pressure reductions (systolic/diastolic) were 8.6/6.0 and 9.5/6.2 mm Hg for the same intervention arms, respectively. Urinary sodium reductions were 18.4 and 24.5 mmol/d, respectively, for each group as well.

The Trial of Hypertension Prevention examined 181 participants for weight loss or sodium reduction and blood pressure for 7 years of follow-up. The sample was randomly assigned to a nontreated control, a sodium reduction, or a weight loss arm. The active component of the intervention lasted 18 months but individuals were further monitored for blood pressure, weight, and dietary status for 7 years. Incident hypertension was the outcome variable of interest. The weight loss group in the absence of sodium restriction, which had an average reduction of 5 kg in weight at 18 months, demonstrated an incidence of hypertension of 18.9% after 7 years. This contrasts with the sodium reduction in the absence of weight loss group which found an incidence of hypertension of 22.4% over the same period. These results were found in spite of the fact that much of the weight in the weight loss group had been regained at year 7.

The Hypertension Prevention Trial followed 841 individuals for up to 3 years in caloric restriction/weight loss, sodium reduction, caloric restriction and sodium reduction, and sodium reduction and increased potassium intervention arms. At 3 years of follow-up, the caloric restriction group had maintained weight loss about 4% of baseline and demonstrated a 5.1/2.4 mm Hg reduction in blood pressure. The other dietary interventions resulted in smaller amounts of blood pressure reduction. The authors recommend caloric restriction and accompanying weight loss as the strategy of choice in influencing blood pressure.

Most recently the Weight Loss Maintenance program has released its findings. In this instance, 1083 participants who had previously lost 8.5 kg or more were enrolled in a self-directed control or 1 of 2 treatment arms for study of weight status over a 30-month period. Although all 3 groups exhibited some regain over this time, all maintained at least about 3 kg of weight loss. One arm, a monthly personal contact group, maintained a larger 4.5-kg weight loss. All levels of maintained weight loss would result in significant reductions in blood pressure in the general population.

Several other smaller scale studies have documented a positive association between weight loss maintained for periods of up to 2 years and reduced blood pressure. In sum, it is clear that weight loss reduces blood pressure reduction and that the blood pressure benefits are retained over at least the short to midperiod, particularly in those who maintain the weight loss.

The effects over longer time frames are less clear. Sjostrom et al. report 8 years of follow-up on the relationship of weight loss to blood pressure in a group 1157 obese participants who received gastric bypass surgery to induce weight loss. Initial weight losses of 18% of presurgical body weight were associated with a decline in blood pressure of about 12 mm Hg systolic and 8 mm Hg diastolic. Over a 6-
8-year period, weights increased only very slightly in this group whereas blood pressure levels rebounded and, at the end of the study, were similar to or higher than untreated controls. The authors themselves, however, are skeptical that this is a generalizable finding pointing to methodological and analytic inconsistencies in their sample.66 It remains for other research examining maintained weight loss.

Taken in its totality, it is clear that weight loss is associated with a decline in blood pressure at least in the short and midterm. These findings extend even to those initially in the normotensive range and hold for both genders and all ethnic groups examined. This conclusion is endorsed by the JNC VII expert panel and has become a part of the suggested lifestyle armamentarium in combating hypertension.8 Undoubtedly, much of the attractiveness of suggesting weight loss stems from its multipurpose healthy nature. Not only is weight reduction associated with improved blood pressure control but it confers benefits in the management of many other disorders including Type II diabetes, musculo-skeletal disorders, some cancers, and other health concerns including all cause mortality.3,4,5,6,7

Nevertheless, using weight loss as sole means of accomplishing blood pressure control is not without problems. Chief among these is the difficulty involved with achieving and maintaining optimal weight. Most who attempt weight loss achieve little in this regard, and most who are initially successful rebound to their early status or higher.57,58,59 In the grimmest scenarios, the net result is not only a population at increased biomedical risk but also suffering from a number of psycho-social insults resulting from these failures.60 Nevertheless, weight loss is successfully accomplished and is maintained by a significant percentage of those who attempt using only lifestyle modifications.61 The methods and strategies used are still developing and, if careful attention is paid to refining them, the result will undoubtedly be improvement in those achieving weight loss and a decline in recidivism.62 Maintenance of weight loss remains the challenge. Wing and Phelan63 report that approximately 20% of those attempting weight reduction via lifestyle modification are successful at achieving weight (BMI < 25.0). Smaller decrements of weight loss clearly are of clinical significance in controlling blood pressure levels. Likewise, complete maintenance of weight loss is not necessary in this regard. Some recidivism in weight loss is normal but, as long as weight is still below baseline level, there can be impact on blood pressure.31

An additional issue, alluded to earlier, is the degree to which weight loss may be identified as an independent influence on blood pressure status. As noted weight loss, at least via traditional approaches, can only be accomplished through some combination of diet and physical activity changes. Numerous dietary components have been identified as potentially impacting blood pressure, most notably sodium intake. But increased fruit and vegetable consumption is clearly pertinent as are numerous other macro and micronutrients.25 Physical activity, likewise, is associated with decreases in blood pressure level. The result is a situation in which it is not practicable to sort out independent causal effects. The argument then might emerge as to whether dietary or physical activity is a more desirable target for blood pressure control. In these cases, however, data on recidivism are not much more encouraging.62 Adoption of the entire package of lifestyle changes, appropriate eating, physical activity, and attention to weight management, yields the greatest likelihood of success.48,61 Overweight and obesity are best seen in this light as an ongoing major risk factor for hypertension, requiring life-long surveillance for both and immediate treatment as indicated by physician review.

And, at least in the case for blood pressure management, the bar may not be so high as for overall success in weight loss. Data clearly show that modest reductions in weight can have an impact on blood pressure,20,29,63 Weight loss in the range of 2 to 4 kg are associated with systolic blood pressure declines in the range of 3 to 8 mm Hg, a clinically significant impact.30,31,32,48,49 Additionally, these impacts are felt rapidly as weight is lost usually within a few weeks48 and appear to be maintained, with corresponding maintenance of weight loss, for periods of at least 18 months to 3 years.49 Data on long term maintenance of weight loss are still to be produced. Such studies are, clearly, both expensive and, by definition, time consuming. Emerging information from such programs as the Weight Loss Maintenance study,51 however, yield some confidence that, through appropriate treatment including lifestyle modification, weight can be lost and kept off.

Perhaps the largest problem with weight reduction as the primary mechanism for blood pressure control is that it is ethically appropriate only for those with stage 1 hypertension or less. Clinical considerations require drug or other more intensive interventions in those with more elevated blood pressures. Nevertheless, those in the prehypertensive and stage 1 hypertensive range constitute about 95 to 100 million Americans, about 40% of the adult population.64 This demographic is a very large target for weight loss intervention, and one that has the potential for considerable public health impact.

In conclusion, weight loss is clearly associated with a decrease in blood pressure as well as numerous other improvements in biomedical status. Its accomplishment is done successfully as the major component of a spectrum of appropriate lifestyle modifications. Strategies for achieving long-term weight loss are emerging, and the proportion of those who are successful is growing. As a major public health issue, the management of overweight is of the highest priority and is receiving major support from the federal government and other institutions. Successfully accomplishing national goals for weight management can supply additional benefits in the reduction of blood pressure and the associated biomedical burden of risk for CVD and stroke.

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None.
References

Response to Weight Loss and Blood Pressure Control: The Pro Side

Allyn L. Mark

Harsha and Bray argue that diet and behavioral modification produce significant and sustained weight loss and that this modest diet-induced weight loss diet is effective in treating mild hypertension. I remain unconvinced and deeply skeptical on both points. I refer the reader to my companion article in this issue and to my recent article “Weight reduction for treatment of obesity-associated hypertension: nuances and challenges” in Current Hypertension Reports (2007;9:368–372). Harsha and Bray highlight the recent Weight Loss Maintenance trial. I’m unimpressed. Like previous trials, it shows weight regain with only modest residual weight loss. The duration of the trial was not long enough to establish sustained weight loss, and there was no measurement of blood pressure. Further, there are questions about the pragmatism of long-term widespread lifestyle modification in the “real world.” In addition, although even modest weight loss produces an early reduction in blood pressure, the long-term reductions in blood pressure are much less impressive than the short term reductions. One more nail in the coffin of the idea that weight loss is the answer to hypertension in obesity is the following. In patients undergoing bariatric surgery for morbid obesity, although blood pressure decreases initially, it returns to control levels after 6 to 8 years despite substantial and sustained decreases in body weight. In summary, chronic blood pressure reduction during dieting and weight loss is not as sustained or pronounced as generally assumed.
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