Journal of Public Health | Vol. 39, No. 3, pp. e95–e102 | doi:10.1093/pubmed/fdw077 | Advance Access Publication August 13, 2016

How much excess weight loss can reduce the risk of hypertension?

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ABSTRACT

Background A 25% relative reduction in the prevalence of hypertension is a global target. This meta-analysis estimated the effect of excess weight loss on hypertension.

Methods We searched PubMed, Web of Science and Scopus until January 2016. We included prospective cohort studies addressing the association between overweight/obesity and hypertension. We expressed the strength of association using risk ratio and the excess risk using attributable risk fraction with 95% CI based on the random-effects model.

Results We found 7617 references and included 10 studies with 173 828 participants. Compared with normal weight, the risk ratio of hypertension was 1.52 (1.37, 1.67; 9 studies, $I^2 = 82.4\%$) for overweight and 2.17 (1.84, 2.50; 9 studies, $I^2 = 88.9\%$) for obesity. The excess risk of hypertension attributable to overweight was 32% (24%, 40%; 8 studies, $I^2 = 85.5\%$) and that attributable to obesity was 47% (40%, 54%; 8 studies, $I^2 = 88.2\%$). That means, excess weight loss may reduce the risk of hypertension by between 24% and 40% in people who are overweight and by between 40% and 54% in people who are obese.

Conclusions Excess weight loss is a vital strategy for controlling hypertension and is sufficient for achieving the global target, particularly if it is accompanied with other preventive measures.

Keywords hypertension, meta-analysis, obesity, overweight

Introduction

Raised blood pressure is a major health problem worldwide.[1] Uncontrolled blood pressure is associated with coronary heart diseases and cerebrovascular diseases.[2] A 25% relative reduction in the prevalence of raised blood pressure is one of the nine voluntary global targets that are defined for the prevention and control of non-communicable diseases.[3] Based on current evidence, a blood pressure reduction of 10 mm Hg systolic or 5 mm Hg diastolic is associated with 22% reduction in coronary heart disease events and a 41% reduction in stroke.[4]

The main risk factors for raised blood pressure are now well-studied and understood. This gives policymakers an immediate advantage to take action. Harmful use of alcohol, smoking, high dietary salt intake, excess body weight, physical inactivity and hypercholesterolemia is among the main risk factors for raised blood pressure.[3,5–7]

Excess weight is a growing health problem worldwide.[5] Overweight and obesity kill at least 2.8 million people every year.[8] Obesity is strongly associated with major cardiovascular risk factors such as hypertension, diabetes and hyperlipidemias.[5,6] In order to achieve the global target of 25% relative reduction in the prevalence of raised blood pressure, we need to implement prevention program to reduce the level of risk factors associated with high blood pressure, including overweight and obesity. However, we also need to know how much excess weight loss may help reduce the risk of hypertension. The relative risk (RR) is a measure of the strength of the association. It is an important index for deriving a causal inference in etiologic studies, but it is not

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useful for public health policy. Therefore, another index is required to indicate the impact of excess weight loss on blood pressure. Attributable risk fraction (ARF) is a measure that can indicate how much of the relative prevalence of raised blood pressure will reduce per specified weight loss. Therefore, the ARF has major applications in health policy.[9]

To date, no meta-analysis has been performed yet to answer this question that how much excess weight loss may help reduce the risk of hypertension. In this meta-analysis, we reviewed the prospective cohort studies, conducted in different settings, to estimate the effect of overweight and obesity on the risk of raised blood pressure and to estimate the amount of relative reduction in the incidence of hypertension that may occur if excess body weight is controlled.

Materials and methods

This systematic review was approved and funded by the Vice Chancellor of Research and Technology, Hamadan University of Medical Sciences.

Eligibility criteria

We included prospective cohort studies, addressing the association between overweight and obesity and high blood pressure, irrespective of language, date of publication, nationality, race, age and gender. We excluded the prospective cohort studies that did not distinguish between overweight and obesity or categorized body mass index (BMI) other than what we considered for this meta-analysis. We exclusively included prospective cohort studies, which is the 'gold standard' of observational studies,[10] and excluded the retrospective cohort studies in order to minimize the potential for recall and other bias in assessing the exposure and to have greater validity of the exposure assessments.[9] In addition, we excluded other observational studies, including case-control and cross-sectional studies, because ARF can only be obtained from cohort studies.

The exposure of interest was overweight and obesity. Overweight refers to a BMI between 25 and 29.9 kg/m^2. Obesity refers to a BMI equal to or >30 kg/m^2.[11] The outcome of interest was high blood pressure so called hypertension. Hypertension refers to a mean systolic/diastolic blood pressure at or above 140/90 mm Hg.[12]

Information sources and search

We searched PubMed, Web of Science and Scopus until January 2016. We also scanned the reference lists of all retrieved studies to identify additional studies.

We used the following search terms individually and in combination: (obesity or obese or overweight or BMI or body size or BMI) or (hypertension or hypertensive or blood pressure) and (cohort stud* or prospective stud* or follow-up stud* or follow-up stud* or longitudinal stud*).

Study selection

We merged search results using EndNote reference manager software, and removed duplicate records of the same report. Then, we (E.H., M.B., P.A.) screened titles and abstracts in separate to remove obviously irrelevant reports. We resolved any disagreements through discussion. We retrieved the full text of the potentially relevant reports and examined full-text reports in order to identify the studies that would meet the inclusion criteria of this review. In cases where there were multiple reports of the same study, we used the last published report.

Data extraction

We entered the extracted data in an electronic data sheet prepared in Stata software. The data collection form included the following information: first author's name, year of publication, country, age mean, gender, BMI (obesity, overweight), type of effect size (risk ratio, ARF), follow-up period, sample size, effect estimate and its associated 95% confidence intervals (CIs).

Methodological quality

We assessed the quality of reporting of the included studies using Newcastle Ottawa Statement (NOS) Manual.[13] The NOS scale is a quality assessment tool for assessing non-randomized studies with their design and content. This scale consists of a set of items, allocating a maximum of nine stars to the following domains: selection, comparability, exposure and outcome. In this meta-analysis, the studies with seven star-items or more were considered high-quality and those with six star-items or less were considered low-quality.

Heterogeneity and reporting biases

We considered the χ^2 test at the 5% significance level to explore statistical heterogeneity.[14] We also quantified inconsistency across the results of the studies using I^2 statistic.[15] We explored the possibility of publication bias using the Egger's[16] and Begg's[17] tests.

Summary measures

We expressed the strength of the association between overweight and obesity and hypertension using RR. We also estimated the excess risk hypertension attributable to overweight and obesity using ARF with 95% CIs. Wherever

reported, we used full adjusted forms of RR controlled for one or more potential confounding factors. We uses Stata software, version 11 (StataCorp, College Station, TX, USA) for data analysis. We analyzed data using a random-effects model with 95% CI.[18]

Results

Description of studies

We found a total of 7617 references, including 6543 articles through searching the databases until January 2016 and 1074 articles through screening the reference list of the included studies. We excluded 991 duplicates and 6473 ineligible studies through reading titles and abstracts and retrieved 153 references for further assessment. We excluded 143 references because they did not meet the inclusion criteria of this meta-analysis. Finally, 10 prospective cohort studies remained for meta-analysis (Fig. 1) involving 173 828 participants[19–28] (Table 1).

Exposure-outcome association

The strength of association between overweight and obesity and hypertension is given in Fig. 2. This figure shows that, in comparison with normal weight, overweight can increase the risk of hypertension by 1.52 fold (95% CI: 1.37, 1.67) and obesity by 2.17 fold (95% CI: 1.84, 2.50). There was an evidence of moderate to high heterogeneity across studies exploring the association between overweight and obesity and hypertension (I^2 = 82.4% and I^2 = 88.9%, respectively).

We excluded the study conducted by Tsujimoto *et al.*[27] from the meta-analysis in order to establish relative homogeneity among the studies addressing the effect of overweight and obesity on hypertension. Based on the results of this study, the RR of hypertension was 1.58 (95% CI: 1.54, 1.63) for people who were overweight and 2.23 (95% CI: 2.04, 2.42) for those who were obese. When we included this study in the meta-analysis, the overall estimate of RR changed to 1.53 (95% CI: 1.39, 1.66; 10 studies, I^2 = 91.9%) for people who were overweight and 2.18 (95% CI: 1.87, 2.48; 10 studies, I^2 = 91.1%) for the obese. As we see, the overall estimates of RR did not change significantly, but the heterogeneity across studies increased considerably.

The excess risk of hypertension attributable to overweight and obesity is given in Fig. 3. Based on this figure, the excess risk of hypertension was 32% (95% CI: 24%, 40%) for overweight and 47% (95% CI: 40%, 54%) for obesity. That means, excess weight loss may reduce the risk of hypertension 24–40% in people were overweight and 40–54% in people who were obese. There was a moderate to high heterogeneity among studies estimating the excess risk of hypertension attributed to overweight (I^2 = 85.5%) and obesity (I^2 = 88.2%).

We excluded a studies conducted by Radi[28] and Tsujimoto[27] from the meta-analysis in order to achieve homogeneity across the studies addressing the association between overweight and hypertension and the studies conducted by Radi[28] and Ford[20] in order to achieve homogeneity across the studies addressing the association between obesity and hypertension. When we included these studies in the meta-analysis, the overall estimate of ARF increased to

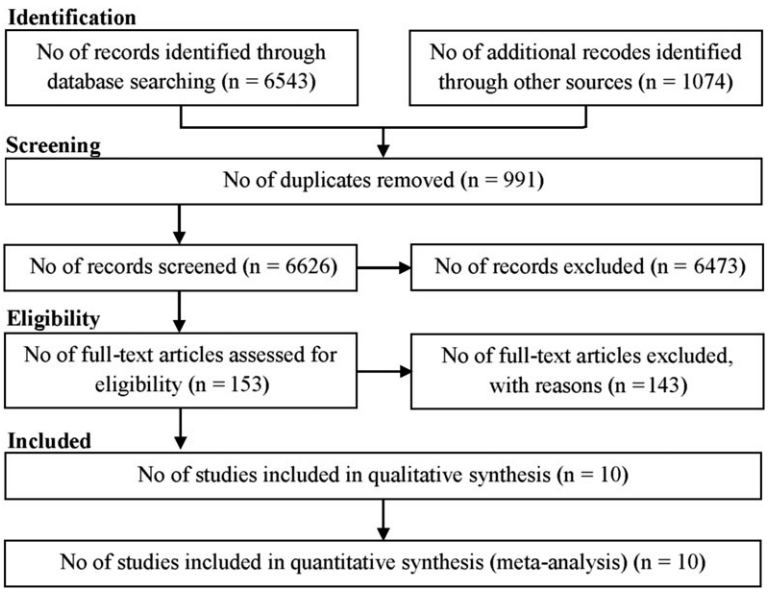

Fig. 1 Flow of information through the different phases of the systematic review.

Table 1 Summary of study results.

First author, year	*Country*	*Age mean (year)*	*Gender*	*BMI*	*Effect estimate*	*Control for confounding*	*Follow-up (year)*	*Sample*	*NOS score*	*Quality*
Banda *et al.*, 2010	The USA	44.0	Male	Overweight and obesity	RR, ARF	Unadjusted	11	14 568	9	High
Ford *et al.*, 2008	The USA	15.4	Both	Overweight and obesity	RR, ARF	Unadjusted	7	14 322	8	High
Hu *et al.*, 2004	Finland	43.1	Both	Overweight and obesity	RR, ARF	Unadjusted	11	17 441	9	High
Malekzadeh *et al.*, 2013	Iran	61.2	Both	Overweight and obesity	RR, ARF	Unadjusted	5	21 350	8	High
Moliner-Urdiales *et al.*, 2014	The USA	47.6	Female	Overweight and obesity	RR	Adjusted	9	10 309	9	High
Pereira *et al.*, 2012	Portugal	47.8	Both	Overweight and obesity	RR	Adjusted	3	2485	8	High
Radi *et al.*, 2004	France	38.5	Both	Overweight and obesity	RR, ARF	Adjusted	1	21 566	8	High
Shihab *et al.*, 2012	The USA	23.1	Male	Overweight and obesity	RR, ARF	Adjusted	46	1132	9	High
Talaei *et al.*, 2014	Iran	47.3	Both	Overweight and obesity	RR, ARF	Adjusted	7	2450	8	High
Tsujimoto *et al.*, 2012	Japan	58.1	Both	Overweight and obesity	RR	Unadjusted	4	68 205	8	High

RR, risk ratio; ARF, attributable risk fraction.

36% (95% CI: 29%, 42%; 10 studies, $I^2 = 94.0\%$) for overweight and to 54% (95% CI: 43%, 65%; 10 studies, $I^2 = 97.5\%$) for obesity. These studies had a substantial effect not only the overall estimates of ARF, but also on the heterogeneity across studies.

Risk of bias

We assessed the publication bias using Begg's and Egger's tests. Based on these statistical tests, there was no evidence of publication bias among studies exploring the association between overweight and hypertension ($P = 0.436$ and $P = 0.088$) and obesity and hypertension ($P = 0.475$ and $P = 0.945$), respectively.

The quality of the included studies was explored using NOS scale. According to this scale, the score of the studies was between 8 and 9, therefore, the quality of all included studies was high.

Discussion

Main finding of this study

The results of this meta-analysis indicated that excess body weight plays an important role in the incidence risk of raised blood pressure. Our findings also revealed that weight loss may reduce the risk of hypertension by between 24% and 40% among people who are overweight and by between 40% and 54% among people who are obese. That means, excess weight loss is effective in reduction of hypertension and it is sufficient enough for achieving a 25% relative reduction in the prevalence of raised blood pressure, which is one of the nine voluntary global targets for the prevention and control of noncommunicable diseases.[3]

In this meta-analysis, we reported both the RR and the ARF. The RR is a measure of the strength of the association. It is an important consideration in deriving a causal inference in etiologic studies, whereas the ARF is a measure of how much of the disease risk (hypertension) is attributable to a certain exposure (overweight/obesity). Indeed, the ARF has major applications in clinical practice and public health.[9] Consequently, the ARF is useful in answering the question of how much the incidence rate of hypertension will be reduced if people, who are overweight or obese, reduce their excess body weight to a normal level. According to our findings, excess weight loss by itself is sufficient for prevention and control of raised blood pressure; however, other

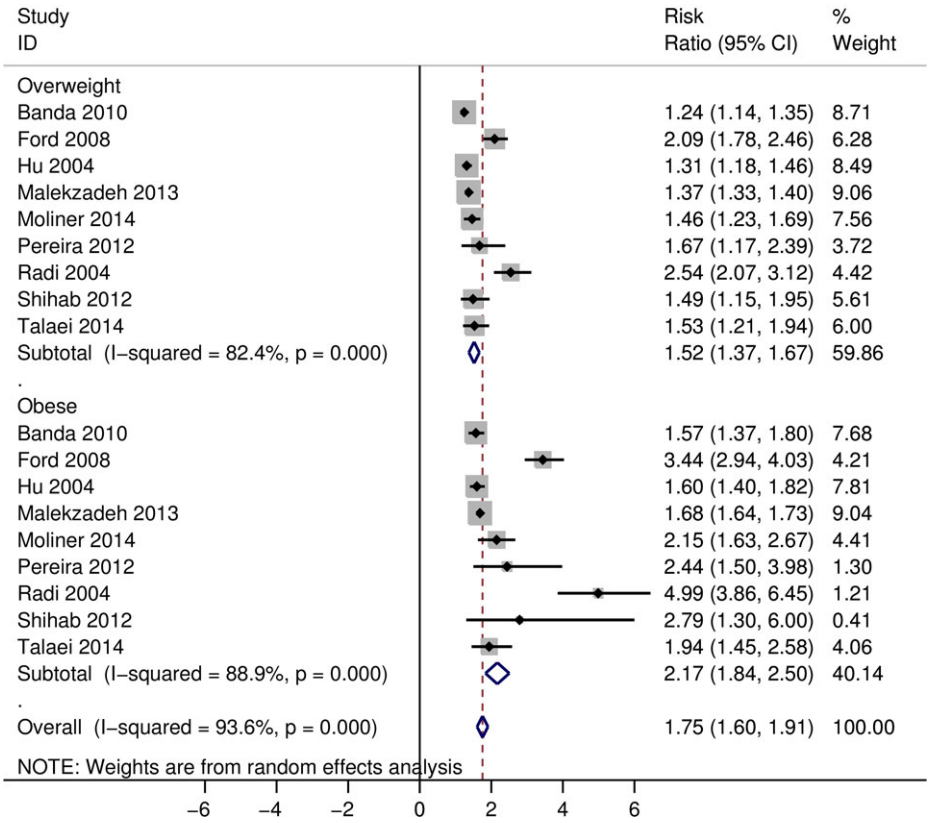

Fig. 2 Forest plot of the strength of association (RR) between overweight/obesity and hypertension.

effective preventive measures such as relative reduction in the harmful use of alcohol, tobacco use, intake of salt and insufficient physical activity should be taken into consideration.

There was evidence of moderate to high heterogeneity among the results of the included studies. There are several reasons that may explain the observed heterogeneity. Some studies reported the effect of overweight and obesity on hypertension by age groups and/or gender. Therefore, in order to include the results of these studies in the meta-analysis, we primarily need to pool these estimates by statistical methods and obtain a summary measure and then include the pooled estimate in the meta-analysis. This process reduced the within-study variance and hence the CIs narrowed. In addition, some studies had a very large sample size and therefore a narrow CI, as was the case for the study conducted by Tsujimoto *et al.*[27] We know that I^2 statistic is a measure of inconsistency across the findings of the studies and reflects the extent of overlap of CIs.[29] Therefore, one reason that may explain this heterogeneity may be the small within-study variance and the narrower CIs. Other reasons that may explain part of the observed heterogeneity across studies is that studies come from different settings with different populations, sample sizes and follow-up periods.

What is already known on this topic

Raised blood pressure is a major risk factor for cardiovascular diseases and stroke.[4,30] Evidence has shown that raised blood pressure happens in individuals of all body sizes, ranging from lean to obese.[31] However, people who are overweight or obese are at greater risk of developing high blood pressure.[32,33] It is estimated that an increase of ~10.3 kg/m^2 in BMI or an increase of ~0.5 in waist-to-hip ratio can increase the risk of hypertension by 2-fold.[6] However, hypertension is a multifactorial diseases that is associated with a number risk factors. Salt intake has a potential impact on the development of hypertension. A systematic review, based on 34 trials (3230 participants) indicated that a modest reduction in salt intake (4.4 g salt/day) for a duration of at least 4 weeks will lead to significant falls in blood pressure by 4.18 mm Hg (95% CI: 3.18–5.18) for systolic blood pressure and 2.06 mm Hg (95% CI: 1.45–2.67) for diastolic blood pressure.[34]

The effects of smoking cessation on changes in blood pressure are unclear. A study reported that the adjusted RRs of hypertension in those who had quit smoking for less than 1 year, 1–3 years and more than 3 years were 0.6 (95% CI: 0.2–1.9), 1.5 (95% CI: 0.8–2.8) and 3.5 (95% CI 1.7–7.4), respectively, compared with current smokers. These results

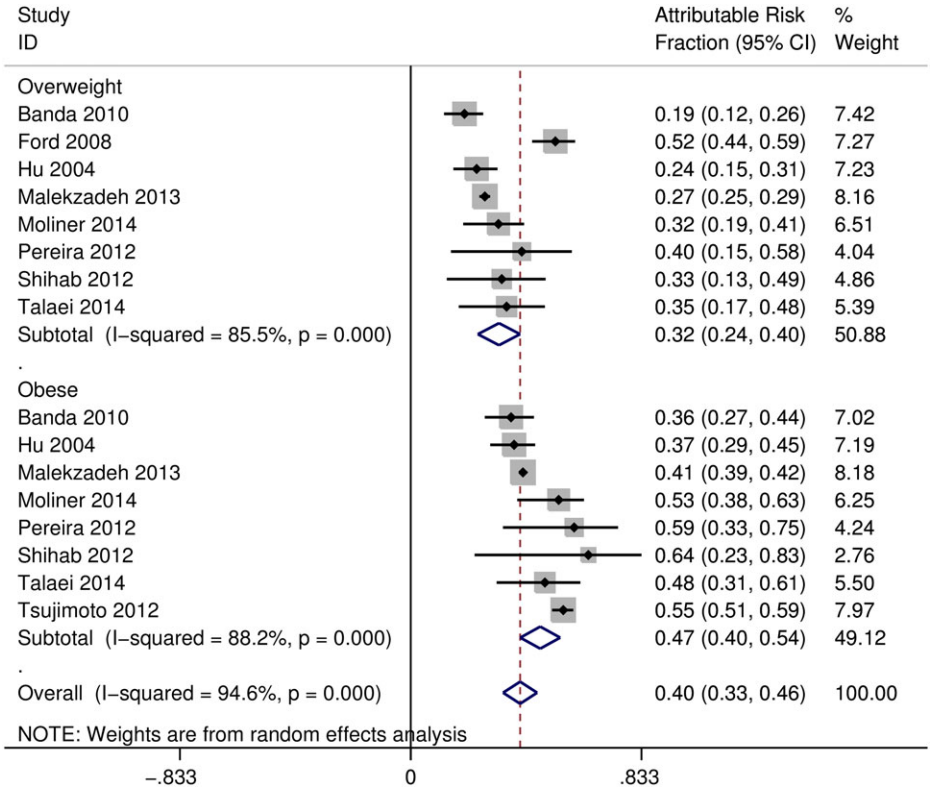

Fig. 3 Forest plot of the excess risk (ARF) of hypertension attributable to overweight and obesity.

imply that the cessation of smoking may increases the risk of hypertension.[35] These results are confirmed by similar studies.[36] On the other hand, other evidence indicated that smoking cessation reduced blood pressure, when patients typically smoke.[37,38] However, there is inconsistency among the literatures regarding the effect of smoking cessation on blood pressure. Weight gain is common after smoking cessation and may contribute to raise blood pressure.[36,39]

The effect of weight reduction upon obesity-associated hypertension is noticeable.[40] Even modest, but continued, weight loss may be sufficient for lowering blood pressure.[41] However, long-term weight maintenance is difficult and a sufficient weight management program is required to achieve a significant weight loss.[42] The evidence has shown that a family-focused intervention, based on high-protein and low-glycemic diets, can achieve an 11 kg weight loss and maintain nearly all of it for 6 months.[43] In addition, a combination of caloric restriction and exercise is recommended to control blood pressure levels in obese hypertensive patients.[44]

What this study adds?

In this meta-analysis, we could estimate the incidence rate of hypertension attributed to overweight and obesity based on prospective cohort studies. We also estimated how much the incidence rate of hypertension will decrease if body weight is controlled within the normal range. However, the limited number of studies reported the burden of hypertension attributable to the excess body weight. Therefore, further evidence based on large prospective cohort studies may contribute to better estimation of the incidence rate of hypertension attributed to overweight and obesity.

Limitations of this study

The main limitation of this meta-analysis was the possibility of the confounding effect in our results. In order to control the effect of potential confounding variables, we used the adjusted forms of RR wherever reported. However, the results were adjusted for a wide variety of variables in some studies or even were not adjusted at all in others. Furthermore, a majority of the studies did not report ARF, which was the main objective of this review. Therefore, we had to use the raw data extracted from the included studies to calculate the ARF and include the crude forms of ARF in the meta-analysis. This issue may raise the possibility of confounding effect.

Conclusion

The results of this meta-analysis showed the effect of overweight and obesity on the raised blood pressure and the effect of excess weight loss on the relative reduction in the incidence rate of hypertension. According to our results, weight loss can effectively reduce the incidence rate of hypertension, therefore, excess weight loss is a vital strategy for controlling hypertension and is sufficient for achieving the global target of 25% relative reduction in the incidence of raised blood pressure. However, other well-known risk factors of hypertension should be taken into consideration when planning for prevention and control of cardiovascular diseases.

Acknowledgements

We would like to thank the Vice Chancellor of Research and Technology, Hamadan University of Medical Sciences, for financial support of this study.

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