Independent Influence of Overweight and Obesity on the Regression of Left Ventricular Hypertrophy in Hypertensive Patients

A Meta-analysis

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Abstract: Overweight and obesity are associated with adverse cardiovascular outcomes. However, the role of overweight and obesity in left ventricular hypertrophy (LVH) of hypertensive patients is controversial. The aim of the current meta-analysis was to evaluate the influence of overweight and obesity on LVH regression in the hypertensive population.

Twenty-eight randomized controlled trials comprising 2403 hypertensive patients (mean age range: 43.8–66.7 years) were identified. Three groups were divided according to body mass index: normal weight, overweight, and obesity groups.

Compared with the normal-weight group, LVH regression in the overweight and obesity groups was more obvious with less reduction of systolic blood pressure after antihypertensive therapies (P < 0.001). The renin–angiotensin system inhibitor was the most effective in regressing LVH in overweight and obese hypertensive patients (19.27 g/m², 95% confidence interval [15.25, 23.29], P < 0.001), followed by β-blockers, calcium channel blockers, and diuretics. In the stratified analysis based on blood pressure measurement methods and age, more significant LVH regression was found in 24-h ambulatory blood pressure monitoring (ABPM) group and in relatively young patients (40–60 years’ old) group (P < 0.01).

Overweight and obesity are independent risk factors for LVH in hypertensive patients. Intervention at an early age and monitoring by ABPM may facilitate therapy-induced LVH regression in overweight and obese hypertensive patients.

(Medicine 93(25):e130)

INTRODUCTION

Overweight and obesity are a major health problem worldwide and lead to a large number of deaths annually.1 Overweight and obesity are associated with left ventricular hypertrophy (LVH), which is a strong predictor of cardiovascular morbidity and mortality.2 It is known that overweight and obesity not only are definitive risk factors for hypertension, but also play a key role in the process of LVH.3 Previous studies have shown that body mass index (BMI), the most commonly used index of adiposity, independently predicts left ventricular mass (LVM).4 Undergoing substantial weight loss through bariatric surgery and diet restriction reduced LVH in overweight and obese subjects independent of changes in blood pressure (BP).5,6 However, there are different viewpoints. Hsuan et al7 considered that BP reduction was the major determinant for the regression of LVH in the early stage of surgical weight reduction. In ob/ob mice, although caloric restriction induced weight loss, no decrease in wall thickness and a lesser change in myocyte size were found.8 Thus, the role

Abbreviations: ABPM = ambulatory blood pressure monitoring, ACEI = angiotensin-converting enzyme inhibitors, ARB = angiotensin receptor blockers, β-blockers = beta-receptor blockers, BMI = body mass index, BP = blood pressure, CCB = calcium channel blockers, CI = confidence interval, DBP = diastolic blood pressure, LVM = left ventricular mass, LVH = left ventricular hypertrophy, LVMi = left ventricular mass index, RAS = renin–angiotensin system, RASI = renin–angiotensin system inhibitor, RCT = randomized control trial, SBP = systolic blood pressure, WHO = World Health Organization, WMD = weighted mean difference.
of overweight and obesity in LVH is still under debate and is not known in hypertensive patients.

The aim of the present meta-analysis was mainly to evaluate the influence of overweight and obesity on LVH regression in hypertensive patients. Furthermore, previous studies have shown that different antihypertensive drugs have different antihypertrophic effect. Variant methods used for BP measurement are of different help to demonstrate the BP variability, which is pivotal for LVH. BP measurement methods such as office or clinic BP measurement and 24-h ambulatory BP monitoring were also found to have a close association with clinical cardiovascular outcomes in hypertensive patients. In addition, the ETODH study showed age is related with the prevalence of severe LVH in essential hypertension. However, the influence of antihypertensive drugs, BP measurement methods, and age on LVH regression in overweight and obese hypertensive patients was not completely clear. So in the present study, we also explored the influence of these factors on LVH regression in overweight and obese patients with hypertension.

METHODS

Selection of Studies

We performed an electronic literature search of PubMed database since 1992 to January, 2013, using the terms “cardiac hypertrophy,” “left ventricular hypertrophy,” “LVH,” “hypertension,” “essential hypertension,” “arterial hypertension,” and “regression.” We also searched the reference lists of articles for relevant titles. Selection criteria for inclusion in the meta-analysis were as follows: randomized controlled trials (RCTs) with parallel design; full-text articles published in peer-reviewed journals; English-language publications; follow-up time ≥3 months; the age of the patients of all races were older than 19 years; LVM was measured by echocardiography. And left ventricular mass index (LVMI) that was calculated as LVM in grams divided by body surface area in square meters (the studies that normalized LVMI for height were excluded); reporting BMI at baseline; reporting LVMI at baseline and at the end of follow-up time; and all patients evaluated had treated or never-treated essential, nonmalignant hypertension.

Data Extraction and Quality Assessment

Two investigators independently reviewed all potentially eligible studies and the following data were collected: study design, name of the authors, name of the journal, year of the publication, sample size, age, sex ratio, follow-up time, type of drugs, systolic blood pressure (SBP), diastolic blood pressure (DBP), BP measurement methods, BMI, and LVMI at baseline and at the end of follow-up time. Discrepancies were resolved by reviewing the articles again to achieve consensus. Methodological quality was evaluated using the modified Jadad scale. Eight-point scale was designed to assess the included RCTs. Scores of 4 to 8 denoted high quality, and scores of 0 to 3 represented low quality.

Statistical Analysis

Descriptive data of all participants are given the mean and range or median (minimum, maximum). Each RCT was composed of ≥2 treatment arms, and each type of treatment was taken as a separate observation, which made possible multivariate adjustments for differences in parameters (such as age, sex, BP, and LVMI at baseline) among BMI classification. Continuous data were analyzed using weighted mean differences (WMDs) and 95% confidence intervals (CIs). We used fixed or random effects model to estimate the differences among groups according to the absence or presence of heterogeneity among studies. Statistical heterogeneity across studies was assessed using I² statistic with significance being set at I² > 50%. Multivariable weighted metaregression was used to analyze the possible sources of heterogeneity. Unpaired t test and nonparametric test were used for comparisons between or among groups, respectively. Publication bias was evaluated by using funnel plots, Begg test, and Egger test. A 2-tailed P < 0.05 was considered significant. Statistical analyses were performed using Stata version 12.0 (Stata Corp, College Station, TX).

RESULTS

Study Selection

A total of 28 RCTs with 2403 hypertensive patients were identified for inclusion from 6042 relevant publications. The flow of selecting studies for the meta-analysis was shown in Figure 1.

Baseline Characteristics and Study Quality

Table 1 summarized the baseline characteristics and study quality of the included trials. Sample size of the studies ranged from 24 to 411 participants, totaling 2403 participants. The average age ranged from 43.8 to 66.7 years, and men accounted for 23.7% to 100% in each study. The range of mean SBP at baseline was 144 to 189 mmHg, whereas the range of mean DBP was 86 to 106 mmHg. At baseline, the average BMI ranged from 19.5 to 30.5 g/m², whereas the echocardiographic hypertrophic indicator, LVMI, ranged from 98.2 to 163.5 g/m². Mean follow-up time was 10.4 months (range: 3–48 months), and the study quality score ranged from 3 to 7. Five types of antihypertensive drugs were used in studies: angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), beta-receptor blockers (β-blockers), and diuretics. We grouped the studies
according to BMI classification of the World Health Organization (WHO) guideline\(^4\): normal weight (18.5–24.9 kg/m\(^2\)) group, overweight (25–29.9 kg/m\(^2\)) group, and obesity (≥30 kg/m\(^2\)) group. No significant difference in age, SBP, DBP, and LVMI at baseline was found among these 3 groups (Table 2).

**LVH Regression in Different BMI Subgroups**

Although the LVMI at baseline was consistent among the 3 BMI groups (Table 2), LVMI significantly decreased during the follow-up period: normal-weight group (WMD 13.78 g/m\(^2\), 95% CI [9.06, 18.50], \(P < 0.001\)), overweight group (WMD 14.27 g/m\(^2\), 95% CI [11.00, 17.54], \(P < 0.001\)), and obesity

| Author (year) | n | Mean Age, y | Mean Follow-up, month | Mean SBP, mmHg | Mean DBP, mmHg | Mean BMI, g/m\(^2\) | Mean LVMI, g/m\(^2\) | Type of Drugs | Modified Jadad Score |
|---------------|---|-------------|-----------------------|----------------|----------------|-----------------|-----------------|-----------------|------------------|
| Dahlof and Hansson (1992)\(^{13}\) | 28 | 100 | 46 | 16 | 155 | 102 | 27 | 125 | ACEI, diuretics | 4 |
| Jula and Karanko (1994)\(^{14}\) | 76 | 60.5 | 43.8 | 12 | 147 | 97 | 27.4 | 119 | None | 4 |
| Diez and Laviades (1994)\(^{15}\) | 87 | 57.5 | 47 | 6 | 156 | 106 | 24.8 | 140.5 | ACEI, CCB | 4 |
| Grandi et al (1995)\(^{16}\) | 36 | 50 | 44 | 12 | 146 | 94 | 27.8 | 145 | \(\beta\)-blockers, other | 4 |
| Schoebel et al (1996)\(^{17}\) | 43 | 67.4 | 52 | 6 | 173 | 103 | 25.2 | 118.7 | ACEI, CCB, other | 4.5 |
| Ueno et al (1997)\(^{18}\) | 36 | 44.4 | 52 | 12 | 150 | 95 | 27.8 | 98.2 | ACEI, diuretics | 4 |
| Roman et al (1998)\(^{19}\) | 50 | 74 | 51.2 | 6 | 157 | 101 | 27.8 | 141.8 | CCB, diuretics | 5 |
| Agabiti-Rosei et al (1998)\(^{20}\) | 32 | 56.3 | 50.4 | 6 | 150 | 101 | 30.5 | 149.5 | ARB, CCB | 4 |
| Martina and Lau (1999)\(^{21}\) | 25 | 64 | 51 | 4 | 150 | 101 | 25.3 | 140.4 | ACEI, \(\beta\)-blockers, diuretics | 3 |
| Cheung et al (1999)\(^{22}\) | 46 | 58.7 | 54 | 10 | 172 | 103 | 27.8 | 144.7 | ACEI, ARB | 4 |
| Schobel et al (1996)\(^{17}\) | 43 | 67.4 | 52 | 6 | 173 | 103 | 25.2 | 118.7 | ACEI, CCB, other | 4.5 |
| Ueno et al (1997)\(^{18}\) | 36 | 44.4 | 52 | 12 | 150 | 95 | 27.8 | 98.2 | ACEI, diuretics | 4 |
| Roman et al (1998)\(^{19}\) | 50 | 74 | 51.2 | 6 | 157 | 101 | 27.8 | 141.8 | CCB, diuretics | 5 |
| Skudicky et al (2002)\(^{26}\) | 173 | 23.7 | 51 | 4 | 151 | 97 | 30.3 | 118 | ACEI, CCB | 4 |
| Cuspidi et al (2002)\(^{27}\) | 196 | 62.2 | 53 | 12 | 163 | 101.3 | 26.2 | 142.2 | ARB, ACEI | 7 |
| Takami and Shigematsu (2003)\(^{28}\) | 45 | 100 | 61.1 | 6 | 174 | 97 | 23.1 | 129.8 | CCB | 4 |
| Sakata et al (2003)\(^{29}\) | 60 | 50 | 62 | 12 | 154 | 90 | 22.5 | 124.5 | ACEI, CCB | 3 |
| Yasunari et al (2004)\(^{30}\) | 104 | 59.6 | 63 | 8 | 152 | 93 | 30.2 | 118.2 | diuretics | 4 |
| Rinder et al (2004)\(^{31}\) | 28 | 82.1 | 65.9 | 6 | 154 | 91 | 27.8 | 144.7 | ACEI, ARB | 4 |
| de Luca et al (2004)\(^{32}\) | 214 | 64.5 | 53.5 | 12 | 162 | 99 | 26.8 | 127.4 | ACEI, \(\beta\)-blockers, diuretics | 5 |
| Bilge et al (2005)\(^{33}\) | 27 | 63 | 48 | 6 | 144 | 96 | 26.4 | 120 | ACEI, CCB | 3 |
| Anan et al (2005)\(^{34}\) | 31 | 54.8 | 59 | 10 | 157 | 97 | 25.6 | 151.3 | ACEI, ARB | 3 |
| Agabiti-Rosei et al (2005)\(^{35}\) | 174 | 60.3 | 53.3 | 48 | 160 | 100 | 27.3 | 104.9 | CCB, \(\beta\)-blockers | 5 |
| Grandi et al (2008)\(^{36}\) | 24 | 79.2 | 49 | 6 | 154 | 94 | 28.6 | 150.5 | ACEI, ARB, CCB | 3 |
| Takami and Saito (2011)\(^{37}\) | 50 | 70 | 66.7 | 6 | 152 | 86 | 25.8 | 122.8 | ARB, CCB | 4 |
| Pan et al (2011)\(^{38}\) | 41 | 61 | 64 | 12 | 189 | 101 | 24.8 | 129.5 | ARB, other | 4 |
| Caglar and Dincer (2011)\(^{39}\) | 106 | 48.1 | 50.8 | 10 | 160 | 99 | 29.5 | 147.4 | ACEI, \(\beta\)-blockers | 5 |
| Fogari et al (2012)\(^{40}\) | 181 | 51.4 | 64 | 12 | 147 | 92 | 27.2 | 132.7 | ARB, CCB | 5 |

ACEI = angiotensin-converting enzyme inhibitors, ARB = angiotensin receptor blockers, \(\beta\)-blockers = beta-receptor blockers, BMI = body mass index, CCB = calcium channel blockers, DBP = diastolic blood pressure, LVH = left ventricular hypertrophy, LVMI = left ventricular mass index, SBP = systolic blood pressure.

# TABLE 2. The Baseline Characteristics Among the 3 Body Mass Index Groups

| Baseline | Normal Weight | Overweight | Obesity |
|----------|--------------|------------|---------|
| Age, y   | 60.9 (44–64) | 53 (43.5–67.5) | 51.5 (47–66.4) |
| SBP, mmHg| 155.6 (152–174) | 155.4 (143–174) | 152 (145–154) |
| DBP, mmHg| 96.8 (90–106) | 97 (85.8–106) | 98.5 (90–102) |
| LVMI, g/m\(^2\)| 129.9 (120.8–166) | 128.2 (92.7–155) | 128.2 (118–163) |

Values are expressed as median (minimum, maximum). \(P\) value showed the comparison of baseline characteristics among 3 body mass index groups. DBP = diastolic blood pressure, LVMI = left ventricular mass index, SBP = systolic blood pressure.
group (WMD 22.05 g/m², 95% CI [13.67, 30.44], P < 0.001) (Figure 2). The comparison among the 3 groups showed that the regression of LVH was the most obvious in obesity group, followed by overweight group and normal-weight group (P < 0.001).

SBP Reduction in Different BMI Subgroups

To explore whether LVMI regression is associated with the degree of SBP reduction, we analyzed SBP reduction in different BMI subgroups. Interestingly, although SBP at baseline showed no difference among the 3 groups (Table 2), SBP significantly reduced in normal-weight group (WMD 24.92 mmHg, 95% CI [16.46, 33.39], P < 0.001), followed by overweight group (WMD 20.34 mmHg, 95% CI [17.05, 23.6], P < 0.001), and obesity group (WMD 16.68 mmHg, 95% CI [10.79, 22.56], P < 0.001) (Figure 3). The comparison of SBP reduction among the 3 BMI subgroups was significant (P < 0.001).

DBP Reduction in Different BMI Subgroups

We also analyzed DBP reduction in different BMI subgroups. The results showed that all subgroups had a significant DBP reduction (P < 0.001, Figure 4). Both overweight group and obesity group had a larger DBP reduction than normal group (t = 2.14, P = 0.033; t = 2.15, P = 0.032, respectively). However, no significant difference was found between overweight group and obesity group (t = 0.82, P = 0.41).

Different Antihypertensive Drugs and the Regression of LVH in Overweight and Obese Hypertensive Patients

Different antihypertensive drugs exhibited different anti-LVH effect in overweight and obese hypertensive patients. As shown in Figure 5, the regression of LVH was 19.27 g/m² (WMD) (95% CI [12.35, 26.19], P < 0.001) in the renin-angiotensin system inhibitor (RASI) (ACEI/ARB) group, 18.72 g/m² (WMD) (95% CI [10.79, 26.66], P < 0.001) in β-blockers subgroup, 14.93 g/m² (WMD) (95% CI [10.98, 18.87], P < 0.001) in CCB subgroup, 13.26 g/m² (WMD) (95% CI [10.46, 16.06], P < 0.001) in diuretics subgroup, and 9.58 g/m² (WMD) (95% CI [6.83, 12.33], P < 0.001) in other treatment subgroup. We found that RASI was the most effective drug for LVH regression in overweight and obese patients with hypertension (P < 0.01).

Different BP Measurement Methods and the Regression of LVH in Overweight and Obese Hypertensive Patients

According to the BP measurement methods, we grouped the overweight and obese hypertensive patients into 2 groups: 24-h ambulatory BP monitoring (ABPM) group and office/clinic BP measurement group. More LVH regression was found in 24-h ABPM group compared with office/clinic BP measurement group (18.56 vs 12.14 g/m², P < 0.001) (Figure 6). This finding indicated that the degree of BP reduction measured by 24-h ABPM had a closer association with the level of LVH regression.

LVH Regression in Different Age Subgroups of Overweight and Obese Hypertensive Patients

Three age subgroups were divided according to the mean age in overweight and obese hypertensive patients: G1, 40 to 49 years’ old; G2, 50 to 59 years’ old; and G3, age ≥60 years’ old. As shown in Figure 7, all 3 groups had a significant LVH regression: G1 (WMD 13.09 g/m², 95% CI [6.96, 19.23], P < 0.001), G2 (WMD 14.93 g/m², 95% CI [10.83, 19.04], P < 0.001), and G3 (WMD 12.36 g/m², 95% CI [5.98, 18.72], P < 0.001). G3 (age ≥60 years’ old) group showed a less LVMI regression comparing with the other 2 groups (P < 0.01). Furthermore, we explored the changes of SBP and DBP in different age subgroups. It was found that BP decreased most in G3 group, followed by G1 and G2 groups (Table 3). The above results indicated that obesity influenced LVH regression independent of BP reduction in the aged population (age ≥60 years’ old).

Determinants for the Heterogeneity Among the Studies

Table 4 gave the results of the multivariate meta-regression analysis to identify the potential determinants for statistical heterogeneity among studies. Both BP measurement methods and LVMI at baseline contributed to the statistical heterogeneity (BP measurement methods, P = 0.017; LVMI at baseline, P = 0.023, Table 4). However, factors like age, follow-up time, sample size, study quality, BP, and type of drugs showed no contributions (P > 0.05, Table 4).

Publication Bias

When we explored for potential publication bias, the funnel plot did not appear asymmetrically (Figure 8), and no significant difference was found in the Begg and Egger test (Begg test, P = 0.38; Egger test, P = 0.10).

DISCUSSION

The main findings of this current meta-analysis were that the regression of LVH during the follow-up time was the most obvious in overweight and obese hypertensive patients. The degree of LVH regression was not in the same ranking order of the BP reduction. RASI was the most effective antihypertensive drug for LVH regression in overweight and obese hypertensive patients. The 24-h ABPM method was more useful to guide BP controlling to reflect LVH regression in overweight and obese hypertensive patients. Furthermore, in overweight and obese hypertensive patients, older age (age ≥60 years) was also an influencing factor for the reduction of LVH.

LVH is a definite cardiac damage in hypertensive patients and associates with a series of cardiovascular events. Overweight and obesity are also important risk factors for cardiovascular diseases such as heart failure and hypertension. Thus, if a person simultaneously had overweight/obesity and LVH, the incidence of cardiovascular events will be significantly increased. It was found that overweight and obese hypertensive patients had an absolute LVM 15% to 41% higher than that in a reference normal group of normal-weight normotensive subjects, independent of sex and SBP. In the present study, no difference of LVMI at baseline between overweight/obese patients and normal-weight patients may because there are many factors determinate the LVM such as race, the duration of hypertension, etc. Our results showed that after adjustment of the BP and LVMI at baseline, the regression of LVH was the most obvious in overweight and obese hypertensive patients and was not accompanied with the degree of SBP reduction. It suggested that overweight and obesity might be the independent risk factors for LVH. And during the treatment for
FIGURE 2. LVH regression in different BMI subgroups. BMI = body mass index, CI = confidence interval, LVH = left ventricular hypertrophy, WMD = weighted mean difference.
regression of LVH, we should pay more attention to the body weight control. However, to what extent an increase in LVM directly resulting from overweight and obesity is unclear. We observed that SBP reduction was less in overweight and obese hypertensive patients, whereas the reduction of DBP was higher in overweight and obese hypertensive patients. This discrepancy may indicate that DBP reduction contributes more to the regression of LVH.\textsuperscript{12} Overweight and obesity are conditions of increased adipose tissue mass. An excess of body fat requires a high cardiac output to meet the metabolic demand. When this hemodynamic burden is sustained, LVH will form.\textsuperscript{47} Insulin resistance is considered to be another important

![FIGURE 3. SBP reduction in different BMI subgroups. BMI = body mass index, CI = confidence interval, SBP = systolic blood pressure, WMD = weighted mean difference.](image)

| Study ID | WMD (95% CI) | % Weight |
|----------|--------------|----------|
| Normal weight |
| Grandi AM (1995) | 20.00 (15.38, 24.62) | 9.13 |
| Grandi AM (1995) | 20.00 (15.43, 24.57) | 9.13 |
| Cheung BM (1999) | 8.50 (4.72, 12.28) | 9.21 |
| Takami T (2003) | 40.00 (37.85, 42.15) | 9.33 |
| Takami T (2003) | 39.00 (36.85, 41.15) | 9.33 |
| Takami T (2003) | 39.00 (36.47, 41.53) | 9.30 |
| Sakata K (2003) | 17.00 (11.04, 22.96) | 8.07 |
| Sakata K (2003) | 21.00 (15.23, 26.77) | 8.99 |
| Yasunari K (2004) | 12.00 (9.11, 14.89) | 9.28 |
| Yasunari K (2004) | 12.00 (9.69, 14.31) | 9.32 |
| Pan XD (2011) | 47.95 (36.56, 59.34) | 9.02 |
| Subtotal (I-squared = 98.7%, P = 0.000) | 24.92 (18.46, 33.39) | 100.00 |
| Overweight |
| Dahlof B (1992) | 19.50 (–22.89, 61.89) | 0.51 |
| Dahlof B (1992) | 17.30 (–6.33, 40.93) | 1.25 |
| Jula AM (1994) | 15.50 (9.39, 21.61) | 3.11 |
| Jula AM (1994) | 8.80 (3.95, 13.65) | 3.24 |
| Schobel HP (1996) | 11.00 (4.35, 17.65) | 3.05 |
| Schobel HP (1996) | 14.00 (4.35, 23.65) | 2.68 |
| Ueno H (1997) | 33.00 (24.16, 41.84) | 2.79 |
| Ueno H (1997) | 33.00 (22.43, 43.57) | 2.56 |
| Ueno H (1997) | 31.00 (21.12, 40.88) | 2.65 |
| Agabiti-Rosei E (1998) | 16.00 (10.27, 21.73) | 3.15 |
| Agabiti-Rosei E (1998) | 10.50 (3.48, 17.52) | 3.01 |
| Cheung BM (1999) | –5.30 (–7.97, –2.63) | 3.14 |
| Novo S (2001) | 30.00 (20.32, 39.68) | 2.88 |
| Novo S (2001) | 18.00 (6.32, 27.68) | 2.68 |
| Novo S (2001) | 27.00 (18.15, 35.86) | 2.78 |
| Novo S (2001) | 19.00 (10.51, 27.49) | 2.83 |
| Skudicky D (2002) | 23.00 (17.97, 28.03) | 3.22 |
| Flander MR (2004) | 26.60 (20.50, 32.70) | 3.11 |
| de Luca N (2004) | 21.30 (17.48, 25.12) | 3.33 |
| de Luca N (2004) | 15.30 (10.00, 20.60) | 3.20 |
| Bilge AK (2005) | 19.00 (14.06, 23.94) | 3.23 |
| Bilge AK (2005) | 16.00 (10.12, 21.88) | 3.14 |
| Anan F (2005) | 23.00 (16.86, 29.14) | 3.11 |
| Anan F (2005) | 23.00 (16.61, 29.39) | 3.08 |
| Anan F (2005) | 24.00 (16.77, 31.23) | 2.98 |
| Agabiti-Rosei E (2005) | 20.60 (17.13, 24.07) | 3.36 |
| Agabiti-Rosei E (2005) | 22.50 (19.26, 25.74) | 3.37 |
| Grandi AM (2008) | 20.00 (12.75, 27.25) | 2.98 |
| Grandi AM (2008) | 19.00 (13.34, 24.66) | 3.16 |
| Takami T (2011) | 15.10 (12.59, 17.61) | 3.42 |
| Takami T (2011) | 14.50 (12.41, 16.59) | 3.44 |
| Pan XD (2011) | 62.96 (53.41, 72.51) | 2.69 |
| Fogari R (2012) | 19.70 (16.67, 22.73) | 3.39 |
| Fogari R (2012) | 20.50 (17.63, 23.37) | 3.40 |
| Subtotal (I-squared = 93.1%, P = 0.000) | 20.34 (17.05, 23.63) | 100.00 |
| Obesity |
| Martina B (1999) | 22.00 (9.53, 34.47) | 14.84 |
| Martina B (1999) | 11.00 (1.99, 20.01) | 21.76 |
| Skudicky D (2002) | 21.00 (17.15, 24.85) | 37.33 |
| Flander MR (2002) | 12.20 (4.79, 19.61) | 26.07 |
| Subtotal (I-squared = 59.2%, P = 0.062) | 16.68 (10.79, 22.56) | 100.00 |

NOTE: Weights are from random effects analysis
determinant for LVH in overweight and obese patients. It can lead to LVH through its growth-stimulating effect, increased sodium reabsorption in kidney, etc. Both obesity and insulin resistance are the characteristics of metabolic syndrome (MetS). A previous study showed that BMI, but not the age and SBP, is the driving factor behind MetS-related LVM increase. Furthermore, other risk factors such as neurohormonal activation and increased inflammatory cytokines are all reported to be involved in the process of LVH in obesity. However, the dominant mechanism is still unknown.

| Study ID | WMD (95% CI) | % Weight |
|----------|--------------|----------|

### Normal weight
- Grandi AM (1995) 14.00 (9.74, 18.26) 8.35
- Grandi AM (1995) 14.00 (10.39, 17.61) 8.91
- Cheung BM (1999) 5.10 (3.30, 6.90) 10.22
- Takami T (2003) 15.00 (13.40, 16.60) 10.32
- Takami T (2003) 14.00 (12.40, 15.60) 10.32
- Takami T (2003) 14.00 (11.74, 16.26) 9.94
- Sakata K (2003) 11.00 (7.00, 15.00) 8.58
- Sakata K (2003) 13.00 (8.03, 17.97) 7.73
- Yasunari K (2004) 7.00 (5.08, 8.92) 10.15
- Yasunari K (2004) 8.00 (5.88, 10.12) 10.03
- Pan XD (2011) 20.77 (12.91, 28.63) 5.44

**Subtotal (I-squared = 91.7%, P = 0.000)**
- 11.92 (8.90, 14.53) 100.00

### Overweight
- Dahlof B (1992) 15.10 (0.17, 30.03) 1.34
- Dahlof B (1992) 11.00 (–7.14, 29.14) 1.04
- Jula AM (1994) 8.80 (6.15, 11.45) 3.29
- Jula AM (1994) 5.00 (2.79, 7.21) 3.34
- Schoel HP (1996) 9.00 (4.79, 13.21) 3.07
- Schoel HP (1996) 12.00 (1.34, 16.66) 2.99
- Ueno H (1997) 17.00 (10.99, 23.01) 2.75
- Ueno H (1997) 17.00 (11.34, 22.66) 2.82
- Ueno H (1997) 19.00 (13.40, 24.60) 2.83
- Agabiti-Rosei E (1998) 14.00 (10.42, 17.58) 3.17
- Agabiti-Rosei E (1998) 8.00 (5.23, 10.77) 2.38
- Cheung BM (1999) –1.10 (–2.81, 0.61) 3.38
- Novo S (2001) 21.00 (14.41, 27.59) 2.54
- Novo S (2001) 16.00 (8.99, 23.01) 2.56
- Novo S (2001) 20.00 (14.87, 25.13) 2.91
- Novo S (2001) 14.00 (9.75, 18.25) 3.06
- Skudicky D (2002) 4.00 (–0.73, 8.73) 2.98
- Rinder MR (2002) 11.60 (6.40, 16.80) 2.90
- de Luca N (2004) 12.10 (9.97, 14.23) 3.35
- de Luca N (2004) 11.30 (8.76, 13.84) 3.30
- Bilge AK (2005) 13.00 (10.66, 15.34) 3.32
- Bilge AK (2005) 15.00 (10.86, 19.14) 3.08
- Anan F (2005) 12.00 (5.86, 18.14) 2.73
- Anan F (2005) 12.00 (1.38, 16.62) 3.00
- Anan F (2005) 13.00 (6.41, 19.59) 2.64
- Agabiti-Rosei E (2005) 16.90 (15.14, 18.66) 3.38
- Agabiti-Rosei E (2005) 17.10 (15.82, 18.38) 3.41
- Grandi AM (2008) 16.00 (9.99, 22.01) 2.75
- Grandi AM (2008) 14.00 (8.78, 19.22) 2.90
- Takami T (2011) 3.20 (0.83, 5.57) 3.32
- Takami T (2011) 2.50 (0.23, 4.77) 3.33
- Pan XD (2011) 22.30 (14.16, 30.44) 2.36
- Fogari R (2012) 15.10 (13.36, 16.84) 3.38
- Fogari R (2012) 15.90 (14.18, 17.62) 3.38
- **Subtotal (I-squared = 94.2%, P = 0.000)**
  - 12.46 (10.25, 14.67) 100.00

### Obesity
- Martina B (1999) 14.00 (1.64, 20.36) 7.67
- Martina B (1999) 14.00 (9.49, 18.51) 15.31
- Skudicky D (2002) 12.00 (9.86, 14.14) 67.84
- Rinder MR (2002) 8.90 (3.08, 14.72) 9.17
- **Subtotal (I-squared = 0.0%, P = 0.534)**
  - 12.18 (10.41, 13.94) 100.00

NOTE: Weights are from random effects analysis

**FIGURE 4.** DBP reduction in different BMI subgroups. BMI = body mass index, CI = confidence interval, DBP = diastolic blood pressure, WMD = weighted mean difference.
### FIGURE 5.

Different antihypertensive drugs and the regression of LVH in overweight and obese hypertensive patients. **β-blockers** = beta-receptor blockers, **CCB** = calcium channel blockers, **CI** = confidence interval, **LVH** = left ventricular hypertrophy, **RASI** = renin-angiotensin system inhibitor, **WMD** = weighted mean difference.

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| Study ID | WMD (95% CI) | % Weight |
|----------|--------------|----------|
| **Others**<br>Jula AM (1994) | 6.00 (–4.83, 16.83) | 6.63 |
| Jula AM (1994) | –1.00 (–11.12, 9.12) | 7.18 |
| Schobel HP (1996) | 14.00 (–3.25, 31.25) | 3.45 |
| Ujeno H (1997) | –28.00 (–50.84, –5.16) | 2.16 |
| Cheung BM (1999) | –3.10 (–8.99, 2.79) | 11.50 |
| Skudicky D (2002) | 14.00 (4.15, 23.85) | 7.40 |
| Skudicky D (2002) | 19.00 (10.95, 27.05) | 9.08 |
| Rinder MR (2004) | 16.80 (–5.62, 39.22) | 2.23 |
| Rinder MR (2004) | 16.70 (–4.41, 39.81) | 2.11 |
| de Luca N (2004) | 6.61 (–0.05, 13.28) | 10.58 |
| Grandi AM (2008) | 19.00 (3.78, 34.22) | 4.18 |
| Takami T (2011) | 6.60 (4.85, 8.35) | 16.00 |
| Takami T (2011) | 3.00 (1.30, 4.70) | 16.03 |
| Pan XD (2011) | 36.25 (7.96, 64.54) | 1.47 |
| Subtotal (I-squared = 74.7%, P = 0.000) | 6.90 (3.30, 10.50) | 100.00 |

| **RASI**<br>Dahlof B (1992) | 21.60 (0.47, 42.73) | 2.37 |
| Diez J (1994) | 13.00 (–1.13, 27.13) | 3.72 |
| Diez J (1994) | 15.00 (0.87, 29.13) | 3.72 |
| Diez J (1994) | 11.00 (–4.30, 26.30) | 3.45 |
| Ujeno H (1997) | 29.00 (4.20, 53.80) | 1.90 |
| Roman MJ (1998) | 8.70 (–3.18, 20.58) | 4.30 |
| Martina B (1999) | 30.00 (–5.01, 65.01) | 1.11 |
| Grosse P (2000) | 1.90 (–5.23, 9.03) | 5.68 |
| Avanza AC (2000) | 18.00 (15.31, 20.69) | 6.68 |
| Avanza AC (2000) | 14.00 (11.61, 16.39) | 6.73 |
| Avanza AC (2000) | 30.00 (27.55, 32.45) | 6.72 |
| Novo S (2001) | 22.00 (12.35, 31.64) | 4.93 |
| Novo S (2001) | 18.00 (10.31, 25.69) | 5.50 |
| Cuspidi C (2002) | 15.00 (6.70, 23.30) | 5.33 |
| Cuspidi C (2002) | 13.30 (5.61, 20.99) | 5.50 |
| Bilge AK (2005) | 17.00 (2.36, 31.64) | 3.60 |
| Anan F (2005) | 27.00 (14.22, 39.78) | 4.06 |
| Anan F (2005) | 24.00 (12.53, 35.47) | 4.41 |
| Anan F (2005) | 35.00 (26.57, 43.43) | 5.29 |
| Grandi AM (2008) | 33.00 (18.58, 47.42) | 3.65 |
| Caglar N (2011) | 14.80 (5.98, 23.62) | 5.17 |
| Fogari R (2012) | 26.10 (20.91, 31.29) | 6.16 |
| Subtotal (I-squared = 86.1%, P = 0.000) | 19.27 (15.25, 23.29) | 100.00 |

| **CCB**<br>Ujeno H (1997) | 14.00 (–20.99, 48.99) | 1.49 |
| Agabiti-Rosei E (1998) | 27.15 (5.48, 48.82) | 3.89 |
| Martina B (1999) | 10.00 (–8.15, 28.15) | 5.55 |
| Bilge AK (2005) | 17.00 (–0.51, 34.51) | 5.97 |
| Agabiti-Rosei E (2005) | 13.30 (6.21, 20.39) | 36.35 |
| Fogari R (2012) | 13.40 (7.15, 19.66) | 46.75 |
| Subtotal (I-squared = 0.0%, P = 0.878) | 13.93 (9.66, 18.21) | 100.00 |

| **β-blockers**<br>Schobel HP (1996) | 15.00 (–1.11, 31.11) | 15.79 |
| Novo S (2001) | 27.00 (19.31, 34.69) | 21.03 |
| de Luca N (2004) | 2.04 (–4.51, 8.59) | 21.61 |
| Agabiti-Rosei E (2005) | 13.70 (7.19, 20.21) | 21.63 |
| Caglar N (2011) | 31.90 (22.29, 41.51) | 19.94 |
| Subtotal (I-squared = 89.0%, P = 0.000) | 17.81 (6.53, 29.09) | 100.00 |

| **Diuretics**<br>Dahlof B (1992) | 13.30 (–10.32, 36.92) | 4.82 |
| Roman MJ (1998) | 0.80 (–10.55, 12.15) | 20.88 |
| Agabiti-Rosei E (1998) | 18.00 (–1.29, 37.29) | 7.23 |
| Grosse P (2000) | 8.30 (1.07, 15.53) | 51.50 |
| Novo S (2001) | 10.00 (–3.15, 23.15) | 15.56 |
| Subtotal (I-squared = 0.0%, P = 0.580) | 7.94 (2.75, 13.13) | 100.00 |

NOTE: Weights are from random effects analysis.
The benefit effect of antihypertensive drugs for LVH regression has been studied extensively. It was found that different antihypertensive drugs had different antihypertrophic effect.\(^9,52\) As for overweight and obese hypertensive patients, there is still a lack of guideline for treating LVH. In the present study, we found that RASI was the most effective antihypertensive drug for regressing LVH in overweight and obese hypertensive patients, which is consistent with recent viewpoints that RASI is considered to be the most appropriate drugs for antihypertensive treatment of obese patients for their possible benefit that they unlikely worsen glucose or lipid metabolism.\(^53\) Activation of the renin–angiotensin system
(RAS) is commonly observed in patients with obesity and the levels of angiotensin II (Ang II) and aldosterone are increased in obese patients, so RASI may partly reverse LVH through decreasing the improper activation of RAS. Furthermore, RASI may improve LVH by inhibiting the obesity-induced insulin resistance, because RASI can improve the insulin sensitivity in obese patients. As for other antihypertensive drugs, although we found they also had an effect on LVH regression, there is still a lack of sufficient evidence to suggest that they have an affirmative effect for LVH regression in overweight and obese hypertensive patients. More studies are needed to explore this issue.

In addition, we found in this study that in overweight and obese hypertensive patients, the 24-h ABPM group had a greater

| Study ID | Weight | % Weight |
|----------|--------|----------|
| G1: 40 to 49 years old | | |
| Dahlof B (1992) | 21.60 (0.47, 42.73) | 4.87 |
| Dahlof B (1992) | 13.30 (–10.32, 36.92) | 4.76 |
| Jula AM (1994) | 6.00 (–4.83, 16.83) | 8.50 |
| Jula AM (1994) | –1.00 (–11.12, 9.12) | 8.79 |
| Diez J (1992) | 13.00 (–1.13, 27.13) | 7.16 |
| Diez J (1992) | 15.00 (0.87, 29.13) | 7.17 |
| Diez J (1992) | 11.00 (–4.30, 26.30) | 6.73 |
| Schobel HP (1996) | 14.00 (–3.25, 31.25) | 6.04 |
| Agabiti-Rosei E (1998) | 27.15 (5.48, 48.82) | 4.73 |
| Martina B (1999) | 30.00 (–5.01, 65.01) | 2.43 |
| Cheung BM (1999) | –3.10 (–9.99, 2.79) | 10.44 |
| Skudicky D (2002) | 14.00 (4.15, 23.85) | 8.90 |
| Bilge AK (2005) | 17.00 (–0.51, 34.51) | 5.95 |
| Bilge AK (2005) | 17.00 (2.36, 31.64) | 6.97 |
| Grandi AM (2008) | 33.00 (18.58, 47.42) | 7.05 |
| Subtotal (I-squared = 65.5%, P = 0.000) | 13.09 (6.96, 19.23) | 100.00 |

| G2: 50 to 59 years old | | |
| Schobel HP (1996) | 15.00 (–1.11, 31.11) | 2.92 |
| Ueno H (1997) | 14.00 (–20.99, 48.99) | 1.09 |
| Ueno H (1997) | 29.00 (4.20, 53.80) | 1.81 |
| Ueno H (1997) | –29.00 (–50.84, –5.16) | 2.01 |
| Roman MJ (1998) | 6.70 (–3.18, 20.58) | 3.68 |
| Roman MJ (1998) | 0.80 (–10.55, 12.15) | 3.78 |
| Agabiti-Rosei E (1998) | 18.00 (–1.29, 37.29) | 2.44 |
| Martina B (1999) | 10.00 (–8.15, 28.15) | 2.60 |
| Bosse P (2000) | 8.30 (1.07, 15.53) | 4.56 |
| Bosse P (2000) | 19.00 (–5.23, 9.03) | 4.58 |
| Avanzza AC (2000) | 18.00 (15.31, 20.69) | 5.19 |
| Avanzza AC (2000) | 14.00 (11.61, 16.39) | 5.22 |
| Avanzza AC (2000) | 30.00 (27.55, 32.45) | 5.21 |
| Skudicky D (2002) | 19.00 (10.95, 27.05) | 4.41 |
| Cuspidi C (2002) | 15.00 (6.70, 23.30) | 4.36 |
| Cuspidi C (2002) | 13.30 (5.61, 20.99) | 4.48 |
| de Luca N (2004) | 6.61 (–0.06, 13.28) | 4.66 |
| de Luca N (2004) | 2.04 (–4.51, 8.59) | 4.68 |
| Anan F (2005) | 27.00 (14.22, 39.78) | 3.51 |
| Anan F (2005) | 24.00 (12.53, 35.47) | 3.75 |
| Anan F (2005) | 35.00 (26.57, 43.43) | 4.34 |
| Anan F (2005) | 3.40 (26.57, 35.47) | 3.75 |
| Agabiti-Rosei E (2005) | 13.70 (7.19, 20.21) | 4.69 |
| Agabiti-Rosei E (2005) | 13.30 (6.21, 20.39) | 4.58 |
| Grandi AM (2008) | 19.00 (3.78, 34.22) | 3.07 |
| Caglar N (2011) | 14.80 (5.98, 23.62) | 4.26 |
| Caglar N (2011) | 31.90 (22.29, 41.51) | 4.11 |
| Subtotal (I-squared = 88.9%, P = 0.000) | 14.93 (10.83, 19.04) | 100.00 |

| G3: Age ≥ 60 years old | | |
| Rinder MR (2004) | 16.80 (–5.62, 39.22) | 6.05 |
| Rinder MR (2004) | 16.10 (–6.41, 39.81) | 5.78 |
| Takami T (2011) | 6.60 (4.85, 8.35) | 23.81 |
| Takami T (2011) | 3.00 (1.30, 4.70) | 23.83 |
| Fogari R (2012) | 26.10 (20.91, 31.29) | 20.88 |
| Fogari R (2012) | 13.40 (7.15, 19.65) | 19.65 |
| Subtotal (I-squared = 93.5%, P = 0.000) | 12.35 (5.98, 18.72) | 100.00 |

NOTE: Weights are from random effects analysis

FIGURE 7. LVH regression in different age subgroups of overweight and obese hypertensive patients. CI = confidence interval, LVH = left ventricular hypertrophy, WMD = weighted mean difference.
LVH regression. There are several BP measurement methods such as office or clinic BP measurement and 24-h ABPM. Previous studies have shown that ABPM had a stronger relationship with morbidity or fatal events than office BP measurement and was a more sensitive risk predictor of cardiovascular outcomes than office BP.\(^\text{10,59,60}\) Our study further demonstrated that in overweight and obese hypertensive patients, ABPM was also associated with the target organs’ damage, for example LVH. Because of the limitation of the data on the publications, we only analyzed this at baseline. However, 24-h ABPM may provide a more reliable measurement for actual BP burden in overweight and obese hypertensive patients. Furthermore, we found significant regression of LVH in different age subgroups, implying that even in older overweight and obese hypertensive patients, as long as the strategy is appropriate, LVH can also be regressed. However, at the same time, we found that the older age (≥60 years) influenced the degree of LVH regression in overweight and obese hypertensive patients after adjustment for SBP and DBP reduction. The possible explanation may be because the arterial stiffness is more severe in overweight and obese elderly patients.\(^\text{51}\) However, there are other studies showing that obesity is associated with LVH independent of age.\(^\text{49}\) And when compare the influence of age, the effects of antihypertensive therapies cannot be overlooked. So more studies are needed to clarify this issue.

**TABLE 3.** The Reduction of SBP and DBP in Different Age Subgroups of Overweight and Obese Hypertensive Patients

| Variable                  | SBP, mmHg       | DBP, mmHg       |
|---------------------------|-----------------|-----------------|
| G1                        | 19.97 (14.80–21.14) | 9.54 (4.02–15.06) |
| G2                        | 14.62 (17.35–21.90) | 9.85 (5.87–13.82) |
| G3                        | 22.12 (19.78–24.46) | 13.68 (11.88–15.47) |

G1, 40–49 years’ old; G2, 50–59 years’ old, and G3, age ≥60 years. DBP = diastolic blood pressure, SBP = systolic blood pressure.

**FIGURE 8.** Begg funnel plot for publication bias. WMD = weighted mean difference.

### Study Limitations

Some limitations of our meta-analysis may restrict the interpretation of results. First, the characteristics among included studies are different, such as the ratio of gender, follow-up time, and drugs used. Inconsistency of these factors may influence the results to some degree. To explore the influence of the abovementioned factors, better designed RCTs are required. Second, there are insufficient data on race, dietary salt intake, and pulse wave for a reliable stratified analysis in this study. Third, we only enrolled the studies that evaluated LVH by echocardiography and LVMI was calculated as LVM in grams divided by body surface area in square meters. Whether data from studies evaluating LVH by magnetic resonance imaging and electrocardiogram or by echocardiography but LVMI normalized by height\(^\text{52}\) will show similar findings to our results needs further exploring. Fourth, our study is a ‘post-hoc’ categorization of the studies; other analyzed ways, such as those according to prespecified inclusion criteria, should be used in future studies.

In summary, we found that overweight and obesity were associated with LVH independent of BP. RASI was the most effective antihypertensive drug for regressing LVH in overweight and obese hypertensive patients. Monitoring 24-h ABPM may effectively help to evaluate the LVH in overweight and obese hypertensive patients. Antihypertensive treatment at early age could make the overweight and obese hypertensive patients benefit more for LVH regression.

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