Effectiveness of Valsartan/Amlodipine Single-pill Combination in Hypertensive Patients With Excess Body Weight: Subanalysis of China Status II

Beihai Ge, MD,* Wenzhong Peng, PhD,† Yi Zhang, PhD,* Yuxiang Wen, MD,* Cong Liu, MD,* and Xiaomei Guo, PhD*

**Abstract:** Obesity is a major global health concern and is associated with hypertension. However, there is a lack of studies evaluating the effectiveness of valsartan/amlodipine single-pill combination in Chinese hypertensive patients with excess body weight uncontrolled by monotherapy. To evaluate this effectiveness and its association with obese categories, we performed a prespecified subanalysis and a post hoc analysis of patients from China status II study. In this subanalysis, 11,289 and 11,182 patients stratified by body mass index (BMI) and waist circumference (WC), respectively, were included. Significant mean sitting systolic and diastolic blood pressure (BP) reductions from baseline were observed at week 8 across all BMI and WC subgroups (P < 0.001). The percentages of patients achieving BP control were 65.2%, 62.8%, and 64.5% (men 64.5% and women 64.4%) in the overweight, obesity, and abdominal obesity subgroups, respectively. The positive association between BP control and obese categories could only be found in subgroups stratified by BMI other than WC. Our study demonstrated the effectiveness of valsartan/amlodipine single-pill combination in Chinese hypertensive patients with excess body weight uncontrolled by monotherapy, and its effectiveness was better associated with BMI than WC.

**Key Words:** amlodipine, body mass index, hypertension, single-pill combination, valsartan, waist circumference

(*J Cardiovasc Pharmacol™ 2015;66:497–503*)

**INTRODUCTION**

The prevalence of obesity is increasing rapidly in recent years worldwide. Although overweight and obesity are more common in developed countries, a large increase in the number of obese and overweight adults is expected in developing countries during the period 2005–2030. Based on data from the China Health and Nutrition Survey, which included 52,621 Chinese adults, prevalence of overweight and abdominal obesity increased greatly from the year 1993 to 2009.

Obesity is a major risk factor for the development of hypertension, and it has been estimated that at least 75% of the incidence of hypertension is related to obesity. Association between obesity and high BP is well known, with an estimated 6.5 mm Hg increase in systolic BP for every 10% increase in body weight. Overweight/obesity and abdominal obesity are highly prevalent in Chinese hypertensive adults, and several studies have shown that obesity is significantly associated with resistant hypertension. Furthermore, the severity of obesity was significantly correlated with the failure to achieve target BP. Therefore, it is essential to develop therapeutic strategies to effectively manage BP in the overweight and obese population.

Previously conducted randomized controlled trials have shown that valsartan/amlodipine (Val/Aml) (80/5 mg) single-pill combination (SPC) was superior to Val or Aml monotherapy in lowering BP and achieving BP control in Chinese mild to moderate hypertensive patients inadequately controlled by either monotherapy. To date, hypertension guidelines do not consider obese hypertensive patients as a special classification, and there are currently no specific recommendations for patients with coexisting hypertension and obesity.

China status II, a phase IV study, has shown the effectiveness and safety of Val/Aml SPC in Chinese hypertensive patients uncontrolled by monotherapy. The present study is a prespecified subanalysis and a post hoc analysis of China status II, which evaluated the effectiveness of Val/Aml SPC in hypertensive patients with excess body weight (stratified based on body mass index (BMI) and waist circumference (WC)).

**METHODS**

**Study Design**

This was a prespecified subgroup analysis and post hoc analysis of the China status II study based on BMI and WC. China status II was a multicenter, postmarketing, prospective observational study conducted in patients with essential hypertension whose BP was not adequately controlled by monotherapy. The study design and overall results have been described in detail elsewhere. Briefly, the study consisted of...
an 8-week open-label treatment period with two 4-week follow-ups. An additional antihypertensive agent was added to those patients whose BP was not controlled at follow-up after 4 weeks. The study was conducted in accordance with the International Conference on Harmonization Good Clinical Practice, applicable local regulations, and routine clinical outpatient practice in China. All procedures followed conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

**Study Population**

Briefly, the study population included adult Chinese patients (both male and female patients aged ≥18 years) with essential hypertension [mean sitting systolic BP (MSSBP) ≥140 mm Hg (≥130 mm Hg for those with diabetes or chronic kidney disease) and/or mean sitting diastolic BP (MSDBP) ≥90 mm Hg (=80 mm Hg for those with diabetes or chronic kidney disease)], whose BP was not adequately controlled by monotherapy as mentioned in the Val/Aml package insert approved by the State Food and Drug Administration. Signed informed consent was obtained from all patients before study enrollment. Patients were excluded if they had any conditions that precluded administration of the drug based on the investigator’s discretion. Women were also excluded if they were pregnant, lactating, or of child-bearing potential and not using adequate contraception measures. Details of inclusion/exclusion criteria, treatment assignment, and outcome measures had been previously described. Subjects from full analysis set who participated in China status II trial were included in this study.

According to the guidelines for prevention and control of overweight and obesity in Chinese adults (2003), overweight was defined as BMI ≥24 to <28 kg/m² and obesity was defined as BMI ≥28 kg/m². According to the Chinese guidelines for the management of hypertension (2010), abdominal obesity was defined as WC ≥90 cm for males or WC ≥85 cm for females.

**Effectiveness Assessments**

The primary effectiveness variable of the subanalysis included changes in MSSBP and MSDBP from baseline to endpoint (week 8). The secondary effectiveness variable was BP control [defined as the patients achieving MSSBP/MSDBP <140/90 mm Hg (<130/80 mm Hg for diabetes)] at endpoint. As the prevalence of diabetes increases with increasing weight, the above results might be affected by the difference in the numbers of diabetic patients in different subgroups. Hence, we redefined the patients achieving MSSBP/MSDBP <140/90 mm Hg as BP control at endpoint irrespective of the diabetic status and performed a post hoc analysis in both BMI and WC subgroups.

**Statistical Analyses**

Subanalysis included patients with at least 2 post-baseline effectiveness evaluations. All statistical analyses were performed using SPSS Software version 21 (IBM Institute Inc, NY) at 2-sided significance level (P) of <0.05. Demographic and baseline variables were summarized using descriptive statistics, including the mean, SD for numeric variables, and the count number and percentage for categorical variables. Paired t test and 2-way analysis of variance were used to analyze effectiveness endpoints, as appropriate. The adjusted odds ratio (OR) and 95% confidence interval (CI) of BP control (including redefined) associated with obese categories relative to a reference category of normal body weight or normal weight were determined from multivariable logistic regression models that adjusted for gender (male, female), age (year), baseline MSSBP (mm Hg), baseline MSDBP (mm Hg), diabetes (absent, present), and previous antihypertensive history [β-blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), diuretics, angiotensin II receptor blockers (ARBs), others, unknown].

**RESULTS**

**Demographic and Baseline Characteristics**

A total of 11,312 patients with hypertension were enrolled in the study, of which 23 and 130 patients were excluded because of nonavailability of effectiveness assessments based on BMI and WC, respectively. Hence, 11,289 patients in the BMI subgroup and 11,182 patients in the WC subgroup were included in this analysis (Fig. 1). Detailed demographic and baseline characteristics of the BMI and WC subgroups are presented in Tables 1 and 2, respectively. Of 11,289 patients in the BMI subgroup, 4715 (41.8%) were classified as normal body weight, 5126 (45.4%) as overweight, and 1448 (12.8%) as obese. Patients with overweight and obesity were predominantly in the age range 50 to <65 years (23.1%, n = 2606). Among 6574 overweight and obese patients, males were more prevalent (61.8%, n = 4065) than females (38.2%, n = 2509). Baseline MSDBP increased with increasing BMI indices (overall P < 0.0001). Similar to the BMI subgroup, abdominal obesity was more prevalent in the age range 50 to <65 years and were predominantly males. In

---

**FIGURE 1.** Patient disposition.
both BMI and WC subgroups, the most common comorbidities were dyslipidemia and type 2 diabetes mellitus and the most used agents were CCBs in previous antihypertensive history.

**Primary Effectiveness in Different Subgroups**

At endpoint, Val/Aml SPC resulted in significant MSSBP/MSDBP reductions (27.5/15.0, 27.1/15.3, and 26.2/15.5 mm Hg) from baseline in normal, overweight, and obese patients (all \( P, 0.001 \) vs. baseline), respectively (Fig. 2). Furthermore, patients in the normal body weight and overweight subgroups achieved greater MSSBP reductions than in the obesity subgroup (\( P, 0.05 \)). Similarly, significant MSSBP and MSDBP reductions from baseline were observed across all WC subgroups among males and females at endpoint (all \( P, 0.001 \) vs. baseline) (Fig. 3).

**Secondary Effectiveness in Different Subgroups**

At endpoint, the percentages of patients achieving BP control were 65.2\%, 62.8\%, and 64.5\% (men 64.5\% and women 64.4\%) in the overweight, obesity, and abdominal obesity subgroups, respectively (Table 3). Compared with patients in the normal body weight subgroup, the multivariable adjusted OR (95% CI) was 1.16 (1.05–1.28) (\( P = 0.004 \)) and 1.22 (1.06–1.41) (\( P = 0.007 \)) in the overweight and obese subgroups at endpoint (Table 3). Compared with patients in normal weight subgroup, the corresponding multivariable adjusted OR (95% CI) was 1.09 (0.99–1.19) (\( P = 0.070 \)) in the abdominal obesity subgroup (Table 3).

**Post Hoc Analysis**

Independent of diabetic status, the multivariable adjusted ORs (95% CI) in overweight and obesity subgroups were 1.21 (1.10–1.33) (\( P < 0.001 \)) and 1.30 (1.13–1.51) (\( P < 0.001 \)) compared with normal body weight subgroup at endpoint (Table 4). Among WC subgroups, the corresponding multivariable adjusted OR (95% CI) was 1.10 (1.00–1.20) (\( P = 0.050 \)) in the abdominal obesity subgroup (Table 4). Upon analysis of the positive association between BP control and obese categories, only among subgroups based on BMI did the association at endpoint show a positive result, independent of a stringent BP target assigned to patients with diabetes (Tables 3 and 4).

**DISCUSSION**

China status II, a multicentric, observational real-world study, reported the effectiveness and safety of Val/Aml SPC in
a very large population of Chinese hypertensive patients.12 The present prespecified and post hoc analysis of patients from the China status II study stratified based on BMI and WC confirmed the BP-lowering effectiveness of Val/Aml SPC in Chinese hypertensive patients with excess body weight uncontrolled by monotherapy. The association between BP control and obese categories was positive at endpoint in patients based on BMI, rather than those based on WC. This association was independent of gender, age, baseline MSDBP, baseline MSSBP, diabetes, and previous antihypertensive history. This suggests that BMI has a better association than WC with the BP-lowering effectiveness of Val/Aml SPC.

Presence of both obesity and hypertension is associated with poor BP control and may have additive effects in increasing cardiovascular risk.4 Several clinical studies confirm that combination therapy might be more effective in controlling BP and reducing cardiovascular risk in hypertensive patients with risk factors.16,17 The European Society of
Hypertension (ESH) and European Society of Cardiology (ESC) 2013 guidelines recommend initiation of combination therapy containing agents with complementary mechanisms of action in patients with markedly high baseline BP or at high cardiovascular risk.18 Furthermore, patients with obesity have abnormal metabolism of glucose and lipids, and both ARBs and CCBs can reduce serum cholesterol, which contributes to favorable metabolic effects.19

Previous randomized clinical trials have reported significant BP-lowering effects of the Val/Aml combination in patients with hypertension,20–22 including Chinese hypertensive patients.1,12–15 It has been shown that patients using valsartan-based SPCs are significantly more likely to achieve BP goal than those treated with ARB-based free combinations in real-world clinical practice.27 In our study, Val/Aml SPC resulted in significant reductions in MSSBP and MSDBP from baseline across all subgroups, regardless of the BMI and WC status. Moreover, in our study, the percentage of all obese patients achieving BP control was more than 60%, which was similar to a previous study.28 Similarly, the Val/Aml combination has shown significant BP-lowering efficacy in obese (BMI ≥30 kg/m²) hypertensive patients in previous clinical trials20,22,29 and real-world observational studies.30,31 Hence, Val/Aml SPC might be a better treatment option for hypertensive patients with excess body weight.32

In this subgroup analysis, baseline MSDBP increased with increasing BMI. Therefore, BMI is closely associated with the degree of hypertension. In our study, the prevalence of overweight/obesity was higher in males than in females across both BMI and WC subgroups, and a similar trend has been published previously.3 Val/Aml SPC treatment resulted in significant reductions in MSSBP and MSDBP from baseline to endpoint, independent of BMI and WC in this study. Both normal weight and overweight subgroups achieved greater MSSBP reductions than the obesity subgroup. This might be because of a higher incidence of resistant hypertension in obese individuals with 35 kg/m² or with morbid obesity.7

At endpoint, the association between BP control and obese categories was positive in patients based on BMI rather than WC. Eckert et al31 also showed that patients with a higher BMI had lower overall BP control rates. It seems that BMI has a stronger association than WC with BP because an increase in BMI increases body volume, peripheral resistance (eg, cell membrane alteration, hyperinsulinemia, and hyperactivity of the rennin-angiotensin system lead to structural hypertrophy and functional constriction), and cardiac output; however, WC is only a proxy indicator for increasing metabolic risk.33

### TABLE 3. Association Between BP Control and Obese Categories

| Categories            | Patients* | BP Control n* (%) | OR (95% CI) | P     | OR (95% CI) | P     |
|-----------------------|-----------|-------------------|-------------|-------|-------------|-------|
|                       |           |                   | Model 1†    |       | Model 2‡    |       |
| BMI subgroups         |           |                   |             |       |             |       |
| Normal body weight    | 4715      | 3307 (70.1)       | 1.00 (1.00–1.01) | 0.988 | 1.00 (1.00–1.01) | 0.988 |
| Overweight            | 5126      | 3340 (65.2)       | 1.08 (1.05–1.11) | <0.001 | 1.16 (1.05–1.28) | 0.004 |
| Obesity               | 1448      | 909 (62.8)        | 1.12 (1.07–1.17) | <0.001 | 1.22 (1.06–1.41) | 0.007 |
| WC subgroups          |           |                   |             |       |             |       |
| Normal weight         | 6084      | 4189 (68.9)       | 1.07 (1.04–1.10) | <0.001 | 1.09 (0.99–1.19) | 0.070 |
| Abdominal obesity     | 5098      | 3287 (64.5)       | 1.07 (1.04–1.10) | <0.001 | 1.09 (0.99–1.19) | 0.070 |

BP control was defined as the patients achieving MSSBP/MSDBP <140/90 mm Hg (<130/80 mm Hg for diabetes) at endpoint.

*Unweighted sample size.
†Unadjusted OR (95% CI) and P value.
‡Multivariable adjusted OR (95% CI) and P value as described in statistical analysis section.

### TABLE 4. Association Between BP Control (Redefined) and Obese Categories

| Categories            | Patients* | BP Control (Redefined) n* (%) | OR (95% CI) | P     | OR (95% CI) | P     |
|-----------------------|-----------|-------------------------------|-------------|-------|-------------|-------|
|                       |           |                               | Model 1†    |       | Model 2‡    |       |
| BMI subgroups         |           |                               |             |       |             |       |
| Normal body weight    | 4715      | 3687 (78.2)                  | 1.00 (1.00–1.01) | 0.988 | 1.00 (1.00–1.01) | 0.988 |
| Overweight            | 5126      | 3892 (75.9)                  | 1.03 (1.01–1.05) | 0.007 | 1.21 (1.10–1.33) | <0.001 |
| Obesity               | 1448      | 1091 (75.4)                  | 1.04 (1.00–1.07) | 0.023 | 1.30 (1.13–1.51) | <0.001 |
| WC subgroups          |           |                               |             |       |             |       |
| Normal weight         | 6084      | 4714 (77.5)                  | 1.02 (1.04–1.10) | 0.063 | 1.10 (1.00–1.20) | 0.050 |
| Abdominal obesity     | 5098      | 3874 (76.0)                  | 1.02 (1.04–1.10) | 0.063 | 1.10 (1.00–1.20) | 0.050 |

BP control was redefined as the patients achieving MSSBP/MSDBP <140/90 mm Hg at endpoint.

*Unweighted sample size.
†Unadjusted OR (95% CI) and P value.
‡Multivariable adjusted OR (95% CI) and P value as described in statistical analysis section.
a previous report, BMI had a strong association with hypertension, whereas WC had a strong association with type 2 diabetes and dyslipidemia. The key risk factors of cardiovascular disease included diabetes mellitus and dyslipidemia, which were both strongly linked to WC; so, it seems that WC has a strong association with cardiovascular disease. Our study results are in agreement with previous studies and confirm that BMI is better associated with hypertension and can better predict blood pressure levels.

This study has some inherent limitations. It did not contain a washout period. The information regarding the numbers and types of added treatments at week 4 might have influenced effectiveness of Val/Aml SPC in reducing BP in Chinese hypertensive patients with excess body weight uncontrolled by monotherapy. A short treatment duration (8 weeks) might have influenced the accuracy of the results of this subanalysis.

In conclusion, the present findings from subanalysis of the China status II study confirmed the effectiveness of Val/Aml (80/5 mg) SPC in reducing BP in Chinese hypertensive patients with excess body weight uncontrolled by monotherapy. Furthermore, BMI had a better association with the blood pressure lowering effectiveness of Val/Aml SPC than WC. Future studies should seek to compare the efficacy and safety of Val/Aml SPC with that of other ARB-based SPCs in hypertensive patients with overweight and obesity. This would aid in identifying a preferred ARB-based SPC to treat hypertension in this high-risk patient population.

ACKNOWLEDGMENTS

The authors acknowledge China Status II study group (Dayu Hu, Lisheng Liu, and Weimin Li, et al.), National Nature Science Foundation of China (30971244, 81270353), and Yong Xie and her colleagues of Novartis Pharma Co Ltd (India) for the support in accomplishing this article. The sources of Val/Aml (80/5 mg) SPC are not available commercially. The authors also thank Krishnaveni Chevoor and Parvathy Ramakrishnan, Novartis Healthcare Pvt Ltd (India), for editorial support.

REFERENCES

1. Kelly T, Yang W, Chen CS, et al. Global burden of obesity in 2005 and projections to 2030. Int J Obes (Lond). 2008;32:1431–1437.
2. Xi B, Liao Y, He T, et al. Secular trends in the prevalence of general and abdominal obesity among Chinese adults, 1993–2009. Obes Rev. 2012;13:287–296.
3. Sowers JR. Obesity as a cardiovascular risk factor. Am J Med. 2003;115 (suppl 8A):376–415.
4. Landsberg L, Aronne LJ, Belin LJ, et al. Obesity-related hypertension: pathogenesis, cardiovascular risk, and treatment—a position paper of the Obesity Society and the American Society of Hypertension. Obesity (Silver Spring). 2013;21:8–24.
5. Singer GM, Setaro JF. Secondary hypertension: obesity and the metabolic syndrome. J Clin Hypertens (Greenwich). 2008;10:567–574.
6. Qin X, Zhang Y, Cai Y, et al. Prevalence of obesity, abdominal obesity and associated factors in hypertensive adults aged 45–75 years. Clin Nutr. 2013;32:361–367.
7. Holecki M, Dulaeva J, Chudek J. Resistant hypertension in visceral obesity. Eur J Intern Med. 2012;23:643–648.
8. Kumara WA, Perera T, Dissanayake M, et al. Prevalence and risk factors for resistant hypertension among hypertensive patients from a developing country. BMC Res Notes. 2013;6:373.
9. Sim JJ, Bhanderi SK, Shi J, et al. Characteristics of resistant hypertension in a large, ethnically diverse hypertension population of an integrated health system. Mayo Clin Proc. 2013;88:1099–1107.
10. Ozturk S, Baltaci D, Turker Y, et al. Effects of the degree of obesity on achieving target blood pressure and metabolic deterioration in obese individuals: a population-based study. Kidney Blood Press Res. 2013;37:531–539.
11. Ke YN, Huang J, Zhu JR. Efficacy and safety of the single pill combination of valsartan 80 mg plus amlodipine 5 mg in mild to moderate essential hypertensive patients without adequate blood pressure control by monotherapy [in Chinese]. Zhonghua Xin Xue Guan Bing Za Zhi. 2009;37:794–799.
12. Hu D, Liu L, Li W. Efficacy and safety of valsartan/amldopine single-pill combination in 11,422 Chinese patients with hypertension: an observational study. Adv Ther. 2014;31:762–775.
13. Chen C, Lu FC. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci. 2004;17 (suppl):1–36.
14. Liu LS. 2010 Chinese guidelines for the management of hypertension [in Chinese]. Zhonghua Xin Xue Guan Bing Za Zhi. 2011;39:579–615.
15. Mandal A. Study of prevalence of type 2 diabetes mellitus and hypertension among overweight and obese people. J Fam Med Prim Care. 2010;64:1367–1374.
16. Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. N Engl J Med. 2008;359:2417–2428.
17. Mallat SG, Itani HS, Tanios BY. Current perspectives on combination therapy in the management of hypertension. Int J Blood Press Control. 2013;6:69–78.
18. Maelfeyt M, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC practice guidelines for the management of arterial hypertension. Blood Press. 2014;23:3–16.
19. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: the Anti-hypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). JAMA. 2002;288:2998–3007.
20. Destro M, Luckow A, Samson M, et al. Efficacy and safety of amloidipine/valsartan compared with amlodipine monotherapy in patients with stage 2 hypertension: a randomized, double-blind, multicenter study: the EX-Effects Study. J Am Soc Hypertens. 2008;2:294–302.
21. Smith TR, Glazer RD, Koren MJ, et al. Combination therapy with amloidipine/valsartan in essential hypertension: a 52-week, randomised, open-label, extension study. Int J Clin Pract. 2010;64:1367–1374.
22. Flack JM, Calhouan DA, Satlin L, et al. Efficacy and safety of initial combination therapy with amloidipine/valsartan compared with amloidipine monotherapy in black patients with stage 2 hypertension: the EX-STAND study. J Hum Hypertens. 2009;23:479–489.
23. Ke Y, Zhu D, Hong H, et al. Efficacy and safety of a single-pill combination of amlodipine/valsartan in Asian hypertensive patients inadequately controlled with amlodipine monotherapy. Curr Med Res Opin. 2010;26:1705–1713.
24. Zhu D, Yang K, Sun N, et al. Amlodipine/valsartan 5/160 mg versus valsartan 160 mg in Chinese hypertensives. Int J Cardiol. 2013;167:2024–2030.
25. Huang J, Sun NL, Hao YM, et al. Efficacy and tolerability of a single-pill combination of amlodipine/valsartan in Asian hypertensive patients not adequately controlled with valsartan monotherapy. Clin Exp Hypertens. 2011;33:179–186.
26. Wang JG, Zeng WF, He YS, et al. Valsartan/amlodipine compared to nifedipine GITS in patients with hypertension inadequately controlled by monotherapy. Adv Ther. 2013;30:771–783.
27. Chang J, Yang W, Fellers T, et al. Chart review of patients on valsartan-based single-pill combinations vs ARB-based free combinations for BP goal achievement. Curr Med Res Opin. 2010;26:2203–2212.
28. Cheng J, Engel S, Boyce SW, et al. Direct renin inhibition with aliskiren in obese patients with arterial hypertension. Hypertension. 2007;49:1047–1055.
29. Allemann Y, Fraile B, Lambert M, et al. Efficacy of the combination of amloidipine and valsartan in patients with hypertension uncontrolled with previous monotherapy: the Exforge in Failure after Single Therapy (EX-FAST) study. J Clin Hypertens (Greenwich). 2008;10:185–194.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.
30. Assaad-Khalil SH, Najem R, Sison J, et al. Real-world effectiveness of amlodipine/valsartan and amlodipine/valsartan/hydrochlorothiazide in high-risk patients and other subgroups. Vasc Health Risk Manag. 2015;11:71–78.

31. Eckert S, Freytag SB, Muller A, et al. Meta-analysis of three observational studies of amlodipine/valsartan in hypertensive patients with additional risk factors. Blood Press. 2013;22(suppl 1):11–21.

32. Parati G. Optimization of hypertension management: the role of angiotensin receptor blocker-calcium channel blocker combinations. J Cardiovasc Pharmacol. 2009;53:352–358.

33. Tuan NT, Adair LS, Stevens J, et al. Prediction of hypertension by different anthropometric indices in adults: the change in estimate approach. Public Health Nutr. 2010;13:639–646.

34. Feng RN, Zhao C, Wang C, et al. BMI is strongly associated with hypertension, and waist circumference is strongly associated with type 2 diabetes and dyslipidemia, in northern Chinese adults. J Epidemiol. 2012;22:317–323.

35. Balkau B, Deanfield JE, Despres JP, et al. International Day for the Evaluation of Abdominal Obesity (IDEA): a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. Circulation. 2007;116:1942–1951.