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Blood pressure lowering efficacy of sacubitril/allisartan versus olmesartan in elderly Chinese hypertensive patients

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ABSTRACT

BACKGROUND Sacubitril/Allisartan, a novel angiotensin receptor-neprilysin inhibitor, has demonstrated antihypertensive efficacy in patients with hypertension. Its effects in the elderly patients, who often present with increased arterial stiffness and comorbidities, remain less understood.

METHODS We performed analysis of data from a randomized clinical trial that compared the blood pressure-lowering effect at 12 weeks of treatment with sacubitril/allisartan (240 mg/d or 480 mg/d) and olmesartan (20 mg/d). Eligible patients with mild-to-moderate hypertension and aged 65–75 years were included in the analysis. The primary outcome was change in clinic and 24-hour ambulatory blood pressure from baseline to week 12.

RESULTS Of the 1197 randomized patients, 338 elderly patients (41.5%) (mean age: 67.9 ± 2.3 years, 49.9% male) were included in this analysis. Baseline characteristics were comparable among treatment groups. At 12 weeks, least square mean (± standard error) changes from baseline in clinic systolic/diastolic blood pressure in the sacubitril/allisartan (240 mg/d or 480 mg/d) group and the olmesartan (20 mg/d) group were −24.0 ± 1.6/−5.7 ± 0.9 mmHg, −26.2 ± 1.6/−6.5 ± 0.9 mmHg, and −21.5 ± 1.6/−6.3 ± 0.9 mmHg, respectively. Greater reductions were also observed with sacubitril/allisartan (480 mg) compared with olmesartan (20 mg) in 24-hour, daytime and nighttime systolic blood pressure (all *P*-values < 0.05). The reductions in ambulatory blood pressure were dose-dependent ($P = 0.007$), and significantly greater with sacubitril/allisartan (480 mg) compared with olmesartan (20 mg) for nighttime blood pressure [−17.5 ± 1.8/−8.1 ± 1.0 mmHg, with a difference of −10.9 mmHg (−16.1 to −5.8, $P < 0.0001$) for systolic blood pressure and −4.5 mmHg (−7.3 to −1.8, $P = 0.002$) for diastolic blood pressure].

CONCLUSIONS In elderly patients with hypertension, sacubitril/allisartan provided dose-dependent greater blood pressure reductions compared with olmesartan.

Prevalence of hypertension increases significantly with age, and more than two-thirds of adults aged ≥ 65 years have hypertension.[1] According to a nationwide hypertension survey conducted in 31 provinces of China between 2012 and 2015, the prevalence of hypertension among individuals aged 65–74 years and ≥ 75 years was 55.7% and 60.2%, respectively. However, the control rates were only 18.4% and 17.0%, respectively.[2] Elevated systolic blood pressure (SBP) and widened pulse pressure (PP) are the most prominent clinical features of elderly hypertension,[3] and they are strongly associated with adverse cardiovascular outcomes such as stroke,[4] coronary artery disease,[5] and heart failure.[6] Abnormal circadian rhythms of blood pressure are also common in older patients, manifesting as nocturnal hypertension or hypotension, exaggerated morning surge, or morning hypertension. These abnormalities are related to impaired neuroendocrine regulation at night, increased salt sensitivity, and altered volume regulation mechanisms.[7,8] The coexistence of comorbidities, such as metabolic disorders and chronic kidney disease, or geriatric syndromes, such as frailty

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and cognitive impairment, substantially increases the complexity of hypertension management in the elderly.[9]

Sacubitril/Allisartan is a newly developed angiotensin receptor-neprilysin inhibitor that simultaneously blocks the renin-angiotensin system while enhancing the activity of endogenous natriuretic peptides.[10] Through this dual mechanism, the drug may produce more sustained vasodilatory and natriuretic effects than conventional angiotensin receptor blockers. Sacubitril/Allisartan has established efficacy in general hypertensive patients,[11,12] yet evidence specific to elderly patients remains scarce given their substantial disease burden and altered drug response. We therefore conducted a *post-hoc* analysis to compare clinic and 24-hour ambulatory blood pressure reductions with sacubitril/allisartan versus olmesartan in elderly Chinese hypertensive patients.

METHODS

Study Design

This study was a *post-hoc* analysis of data obtained from a multicenter, randomized, double-blind, active-controlled clinical trial conducted at 71 hospitals in China (https://www.chictr.org.cn/, trial registration number: ChiCTR2100051183). The trial compared the antihypertensive efficacy and safety of sacubitril/allisartan with that of olmesartan in patients with primary hypertension.[12] The original study was not stratified by age at randomization and was not specifically powered for efficacy analyses in the elderly subgroup. The study protocol was approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China as well as the Institutional Review Boards of all participating centers. All participants provided written informed consent before enrollment.

Participants

Participants aged 18–75 years with mild-to-moderate essential hypertension were enrolled in the original randomized trial. Eligibility required a mean sitting SBP between 150 mmHg and 179 mmHg during both the screening and post-run-in visits. Individuals with severe hypertension, secondary hypertension, or other major medical conditions were excluded.

For the present analysis, we included only participants aged 65 years or older at baseline to evaluate treatment effects specifically in the elderly patients.

Study Procedures and Treatments

After screening, eligible participants underwent a one-week wash-out period to remove the effects of any previously used antihypertensive medications. During this phase, patients who had not been receiving treatment remained untreated, whereas those previously receiving antihypertensive therapy discontinued their medications. Subsequently, participants entered a four-week single-blind placebo run-in phase. Patients who continued to meet the eligibility criteria at the end of this period were randomly assigned in a 1:1:1 ratio to receive sacubitril/allisartan 240 mg/d (sacubitril 116 mg plus allisartan 124 mg), sacubitril/allisartan 480 mg/d (sacubitril 232 mg plus allisartan 248 mg), or olmesartan 20 mg/d.

The randomized double-blind treatment period lasted for 12 weeks (Period 1), during which participants received only the assigned study medication. After completion of the double-blind phase, all patients entered a forty-week open-label extension period consisting of two stages. During the first stage (weeks 13–24), all participants were switched to sacubitril/allisartan 240 mg/d, with the possibility of dose escalation to 480 mg/d and/or the addition of amlodipine (5–10 mg/d) if necessary to achieve target blood pressure (< 140/90 mmHg). During the second stage (weeks 24–52), treatment could be further adjusted based on blood pressure control, including up-titration of sacubitril/allisartan, continuation or addition of amlodipine, and the subsequent addition of hydrochlorothiazide (12.5–25 mg/d) when needed.

Follow-up Visits and Assessments

During the 12-week randomized treatment phase, patients attended clinic visits at weeks 4, 8, and 12 for evaluation of blood pressure and safety outcomes. During the extension phase, assessments of blood pressure control and safety were performed every four weeks in the extended treatment stage and every 4 to 12 weeks during the prolonged treatment stage.

Clinic blood pressure and pulse rate were measured using an automated electronic blood pressure monitor (A&D UA-651A, Tokyo, Japan). Measurements were obtained after the patient had rested in a seated position for at least 5 min and prior to the intake of study medication. At the screening visit, blood pressure was measured in both arms. If the difference in SBP between arms exceeded 10 mmHg, the arm with the higher reading was used for all subsequent measurements; otherwise, the non-dominant arm was used. At each clinic visit, three consecutive readings were recorded at one-minute intervals, and the mean value was used for analysis.

The 24-hour ambulatory blood pressure monitoring was performed in a subset of participants at baseline and at week 12. Ambulatory blood pressure monitoring recordings were obtained using a validated monitor (A&D TM-2430, Tokyo, Jap-

an) placed on the same arm used for clinic measurements. The device was programmed to measure blood pressure every 20 min during daytime (06:00–22:00) and every 30 min during nighttime (22:00–06:00). Participants were instructed to maintain their usual daily activities but to avoid vigorous exercise on the monitoring day and to keep the arm still during measurements. Daytime and nighttime periods were determined based on patient diaries documenting the time of going to bed and awakening. Ambulatory blood pressure monitoring recordings were considered valid if they included at least 20 daytime readings and 7 nighttime readings, with at least 70% of scheduled measurements successfully obtained. For efficacy analyses, only valid ambulatory blood pressure monitoring recordings were included.

Renal function was assessed by the estimated glomerular filtration rate (eGFR) from serum creatinine levels using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, which incorporates age and sex.

Clinical End Points

The primary outcome of the present analysis was the change from baseline to week 12 in clinic SBP as well as 24-hour, daytime, and nighttime ambulatory SBP in elderly patients. Secondary outcomes included changes from baseline in clinic and ambulatory diastolic blood pressure (DBP) at weeks 12 and 24. Safety evaluations included the occurrence of adverse events and serious adverse events, as well as clinically relevant abnormalities identified through physical examination, laboratory testing, or 12-lead electrocardiography. All adverse events were recorded with details regarding symptoms, severity, causal relationship to study medication, management, and outcome.

Statistical Analysis

All statistical analyses were performed using the SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Continuous variables are presented as mean ± SD, and categorical variables are presented as counts (percentages). Baseline characteristics were compared across treatment groups using analysis of variance (ANOVA) for continuous variables and Fisher's exact test for categorical variables.

Changes in blood pressure over time were analyzed using a mixed-effects model for repeated measures (MMRM). In this model, the dependent variable was the change from baseline in blood pressure at each follow-up visit. Fixed effects included treatment group, study visit, and the interaction between treatment group and visit, with baseline blood pressure and study center included as covariates. Least-squares mean changes from baseline, along with their standard errors and 95% CIs, were estimated from the model.

Between-group differences were calculated by subtracting the change observed in the olmesartan group from that in the sacubitril/allisartan groups, with negative values indicating a greater reduction in blood pressure with sacubitril/allisartan. All available post-baseline measurements were included in the MMRM analyses under the assumption that missing data were missing at random, and no explicit imputation procedures were applied. Comparisons between the two sacubitril/allisartan dose groups within the elderly subgroup were exploratory and were not adjusted for multiplicity.

RESULTS

Study Population

Of the 1197 trial participants, 338 patients (28.2%) aged ≥ 65 years were included in this analysis [26.3%, 30.6%, and 27.8% in the sacubitril/allisartan (240 mg or 480 mg) group and the olmesartan (20 mg) group, respectively] (supplemental material, Figure 1S). Overall, 50% were male. The mean age was 67.8 ± 2.3 years. Clinic SBP/DBP at baseline was 161.6 ± 7.2 mmHg/88.1 ± 8.8 mmHg. 57.7% of patients had isolated systolic hypertension. Clinic and 24-hour ambulatory PP at baseline were 73.5 ± 10.4 mmHg and 62.9 ± 12.2 mmHg, respectively. 91.7% of patients had received prior treatment for hypertension. There were no remarkable differences among the randomized groups (all *P*-values > 0.05) (Table 1).

Blood Pressure Lowering Effects of Sacubitril/Allisartan in the Elderly

Blood pressure lowering was maintained throughout the 24-week follow-up (Figure 1). Significantly greater reductions in clinic SBP and PP from baseline to 12 weeks of follow-up were observed during treatment with sacubitril/allisartan 480 mg versus olmesartan 20 mg in the elderly, with between-group differences of -4.7 mmHg for SBP and -5.1 mmHg for PP (Figure 2). A complete-case sensitivity analysis yielded results consistent with the primary MMRM analysis (supplemental material, Figure 2S).

The average number of 24-hour ambulatory blood pressure readings was 59.2 and 56.7 at baseline and 12 weeks of follow-up, respectively. At week 12, mean ambulatory blood pressure was reduced from baseline throughout the whole 24-hour period. The least square mean (± standard error) changes fr-

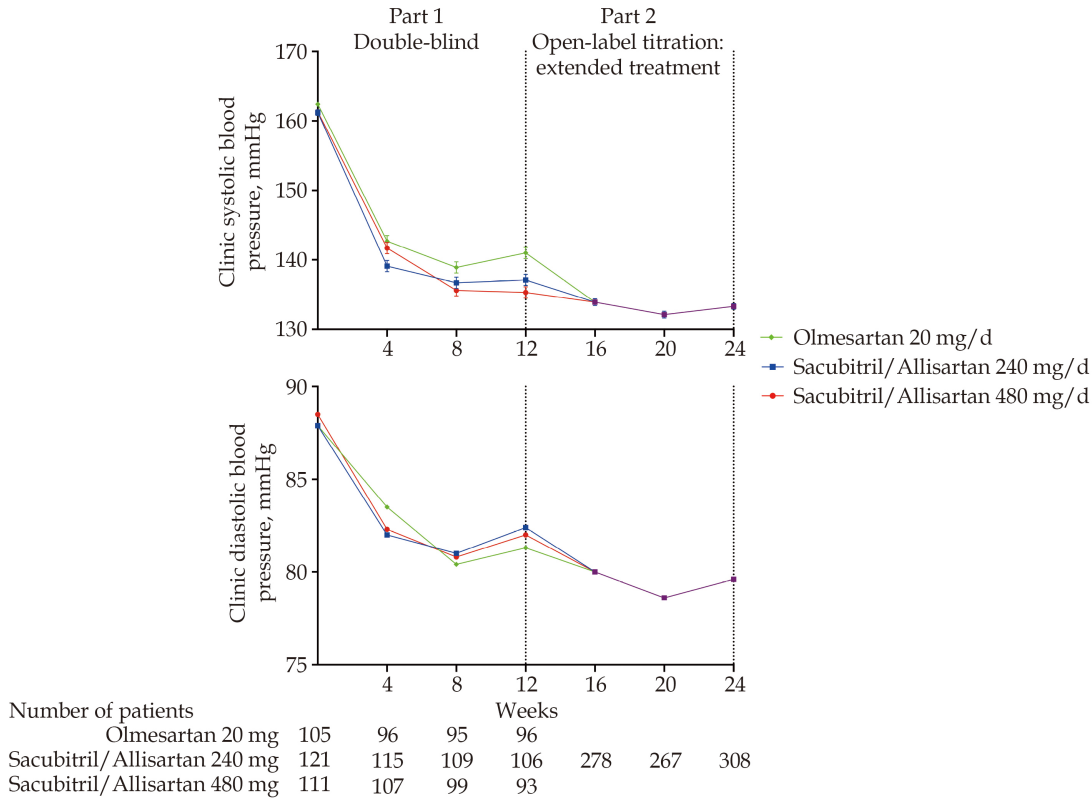


Figure 1 Time course of clinic systolic/diastolic blood pressure in elderly patients during 24 weeks of treatment. Symbols denote mean clinic systolic/diastolic blood pressure. Vertical lines denote standard error.

Table 1 Baseline characteristics of elderly patients (≥ 65 years) by treatment group (*n* = 338).

Characteristic	Sacubitril/Allisartan		Olmesartan 20 mg (*n* = 111)	*P*-value
	240 mg (*n* = 105)	480 mg (*n* = 122)		
Male	56 (53.3%)	63 (51.6%)	50 (45.0%)	0.43
Age, yrs	67.9 ± 2.3	67.9 ± 2.3	67.8 ± 2.3	0.72
Body mass index, kg/m^2	25.6 ± 2.4	24.9 ± 2.6	25.1 ± 2.4	0.16
Blood pressure, mmHg				
Clinic systolic blood pressure	161.2 ± 7.0	161.3 ± 6.9	162.4 ± 7.5	0.36
Clinic diastolic blood pressure	87.9 ± 9.1	87.9 ± 9.4	88.5 ± 7.7	0.83
Clinic pulse pressure	73.3 ± 10.4	73.4 ± 10.1	73.9 ± 10.8	0.90
24-hour systolic blood pressure	146.0 ± 28.8	147.7 ± 23.5	149.6 ± 14.6	0.52
24-hour diastolic blood pressure	83.9 ± 16.7	84.7 ± 13.7	86.0 ± 8.0	0.49
24-hour pulse pressure	62.1 ± 14.3	62.9 ± 12.2	63.6 ± 10.0	0.68
Previous antihypertensive treatment	98 (93.3%)	111 (91.0%)	101 (91.0%)	0.77
Current smoking	24 (22.9%)	26 (21.3%)	23 (20.7%)	0.93
Alcohol intake	19 (18.1%)	22 (18.0%)	25 (22.5%)	0.62
Blood biochemistry				
Serum low-density lipoprotein cholesterol, mmol/L	3.0 ± 0.8	3.1 ± 0.9	3.0 ± 0.9	0.35
Serum total cholesterol, mmol/L	4.9 ± 0.9	5.1 ± 1.0	5.0 ± 1.0	0.38
Serum potassium, mmol/L	4.2 ± 0.3	4.2 ± 0.3	4.2 ± 0.4	0.80
Plasma glycated hemoglobin A1c, %	5.9 ± 0.8	5.8 ± 0.6	5.9 ± 0.8	0.75

Data are presented as *n* (%) or means ± SD.

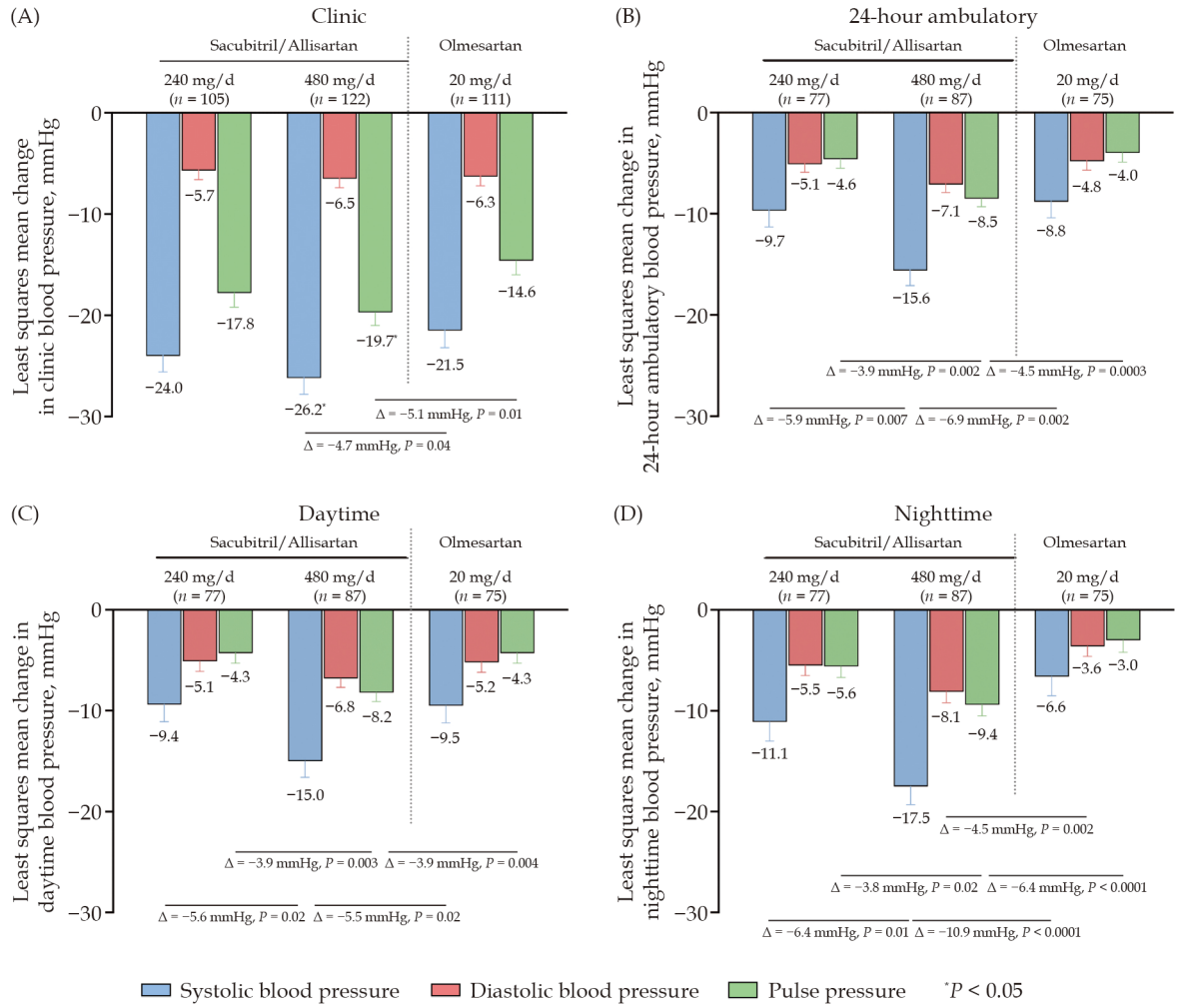


Figure 2 Least square mean changes in clinic (A) and 24-hour (B), daytime (C) and nighttime (D) ambulatory blood pressure from baseline to week 12. Data are shown for clinic, 24-hour, daytime, and nighttime systolic/diastolic blood pressure. Least square means were estimated using an analysis of covariance model adjusted for baseline values. Error bars indicate standard errors.

om baseline in 24-hour mean ambulatory SBP/DBP in the sacubitril/allisartan (240 mg/d or 480 mg/d) group were -9.7 ± 1.6/-5.1 ± 0.9 mmHg and -15.6 ± 1.5/-7.1 ± 0.8 mmHg, respectively (Figure 2). The olmesartan-corrected reduction from baseline (95% CI) reached statistical significance only in the sacubitril/allisartan (480 mg/d) group for SBP [mean ambulatory SBP: -6.9 (-11.2 to -2.5) mmHg, P = 0.002]. All three treatment regimens decreased the daytime and nighttime mean ambulatory SBP/DBP from baseline to week 12 (Figure 3). Moreover, we observed significant dose-response relationships between sacubitril/allisartan (240 mg or 480 mg) for 24-hour, daytime and nighttime SBP, with greater reductions in the sacubitril/allisartan (480 mg) group [5.9 (1.6 to 10.2) mmHg, P = 0.007 for 24-hour; 5.6 (1.0 to 10.2) mmHg, P = 0.02 for daytime; and 6.4 (1.3 to 11.5) mmHg, P = 0.01 for nighttime SBP].

After 12-week treatment, the least square mean reductions in clinic, 24-hour, daytime, and nighttime PP were superior with sacubitril/allisartan (480 mg) versus olmesartan (20 mg), with between-treatment differences of -5.1 mmHg (P = 0.01) for clinic, -4.5 mmHg (P = 0.0003) for 24-hour ambulatory, -3.9 mmHg (P = 0.004) for daytime, and -6.4 mmHg (P < 0.0001) for nighttime. Also, significant dose-response relationships were observed between sacubitril/allisartan (240 mg or 480 mg) for 24-hour, daytime and nighttime PP, with greater reductions in the sacubitril/allisartan (480 mg) group [3.9 (1.4 to 6.3) mmHg, P = 0.002 for 24-hour; 3.9 (1.3 to 6.5) mmHg, P = 0.003 for daytime; and 3.8 (0.7 to 6.9) mmHg, P = 0.02 for nighttime PP].

Up-titration or Add-on Therapy from Week 12 to 24

Between weeks 12 and 24, requirement of up-titration or additional antihypertensive therapy did not differ signific-

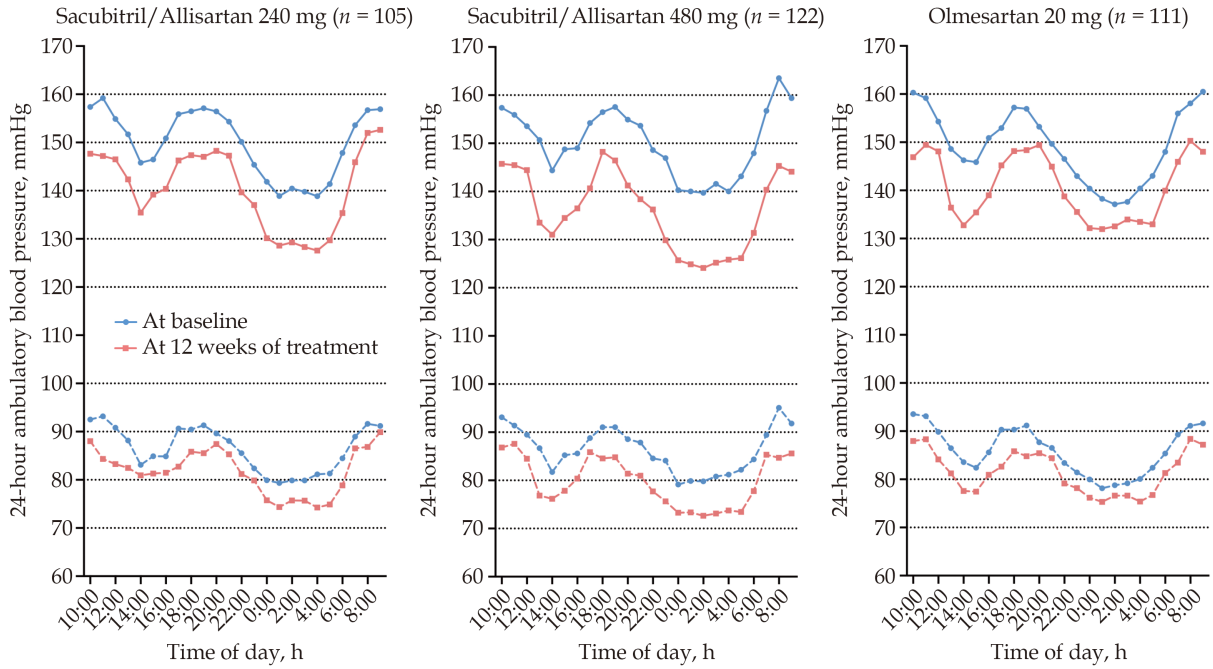


Figure 3 24-hour ambulatory blood pressure profile at baseline and 12 weeks of treatment in elderly hypertensive patients (*n* = 338). Symbols denote hourly mean. Vertical lines denote standard error. *P*-values are all < 0.05 for the comparison between blood pressure at baseline and 12 weeks of follow-up in all three treatment groups.

antly between patients initially treated with sacubitril/allisartan and those treated with olmesartan ($P = 0.73$). Within the sacubitril/allisartan group, 53.7% of patients remained on the 240 mg/d dose, compared with 51.4% in the olmesartan group. Add-on amlodipine (5–10 mg) was required in 43 patients (18.9%) in the sacubitril/allisartan group and in 24 patients (21.6%) in the olmesartan group.

Renal Function

Changes in serum creatinine and eGFR from baseline to weeks 12 and 24 did not differ significantly among three treatment groups (Figure 4), except for serum creatinine at week 24. The change in serum creatinine from baseline to week 24 was -1.6 ± 0.9 μmol/L and 0.8 ± 0.8 μmol/L in the sacubitril/allisartan (240 mg) group and in the olmesartan (20 mg) group, respectively; with a difference of -2.5 (-4.9 to -0.1, $P = 0.04$) μmol/L. No cases of hyperkalemia or acute kidney injury were reported during the study period in any treatment group among elderly participants.

DISCUSSION

This study demonstrated that sacubitril/allisartan provided superior, sustained blood pressure reduction versus olmesartan in elderly Chinese hypertensive patients, with consistent efficacy across daytime and nighttime periods. These findings extend prior evidence to an older population with increased arterial stiffness, impaired vascular compliance, and high isolated systolic hypertension prevalence.

The greater blood pressure-lowering effect of sacubitril/allisartan than olmesartan in the elderly may be attributed to its dual mechanism of combining angiotensin II receptor blockade with neprilysin inhibition. This results in simultaneous suppression of the renin-angiotensin-aldosterone system and augmentation of endogenous natriuretic peptides.[13] In elderly patients, the limited effect of renin-angiotensin system inhibition on age-related aortic stiffness partly explains the difficulty in achieving adequate blood pressure control.[14] The added vasodilating and diuretic effects from neprilysin inhibition may provide extra benefits. The present findings are consistent with prior clinical studies demonstrating that angiotensin receptor neprilysin inhibitors provide greater reductions in central and ambulatory SBP compared with angiotensin receptor blockers alone in various patient populations.[15,16] Although greater blood pressure reductions were observed with sacubitril/allisartan 480 mg than with 240 mg, these comparisons were exploratory and should be interpreted with caution because no formal multiplicity adjustment was performed.

Systolic hypertension is the predominant form of hypertension in elderly individuals and is strongly associated with widened PP, reflecting increased arterial stiffness and reduced

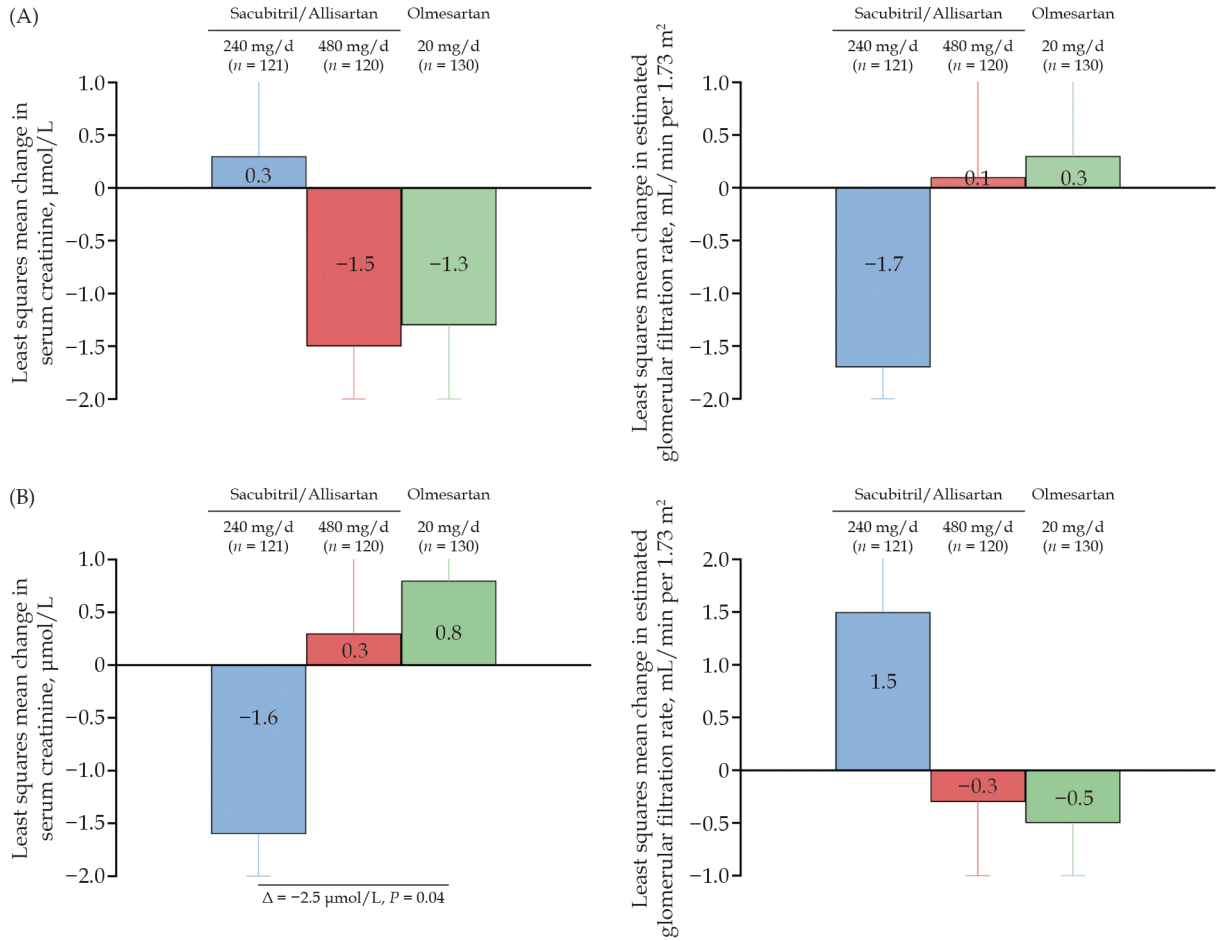


Figure 4 Least square mean changes in serum creatinine and estimated glomerular filtration rate from baseline to week 12 (A) and week 24 (B). Least square means were estimated using an analysis of covariance model adjusted for baseline values. Error bars indicate standard errors.

vascular compliance.[17] Both SBP and PP are major predictors of cardiovascular morbidity.[18,19] In this study, sacubitril/allisartan achieved greater reductions in SBP and PP compared with olmesartan, suggesting improved arterial elasticity and reduced vascular stiffness. Although greater reductions in PP were observed with sacubitril/allisartan, PP represents an indirect hemodynamic marker and may be influenced by multiple physiological factors. The PARAMETER (Prospective Comparison of Angiotensin Receptor Neprilysin Inhibitor With Angiotensin Receptor Blocker Measuring Arterial Stiffness in the Elderly) study[20] and other randomized trials[21] in older adults with systolic hypertension demonstrated that treatment with angiotensin receptor neprilysin inhibitors produced significantly greater reductions in central aortic systolic pressure and central PP compared with olmesartan, indicating a stronger impact on arterial stiffness and wave reflection. These findings are supported by animal studies and systematic reviews indicating that enhanced natriuretic peptide activity contributes to improved arterial compliance and central blood pressure reduction.[22,23] Consistent evidence from pooled randomized trials further shows that sacubitril/valsartan achieves larger decreases in both clinic and ambulatory systolic and PPs than olmesartan or valsartan,[24] with the benefits particularly evident among elderly patients with widened PP. Through its dual mechanism, angiotensin receptor neprilysin inhibitors may therefore be especially effective for patients with isolated systolic hypertension.

Beyond its greater antihypertensive efficacy, sacubitril/allisartan showed a favorable renal safety profile in elderly patients. Serum potassium levels remained stable, and no significant deterioration in renal function was observed during the treatment period. These findings suggest that sacubitril/allisartan maintains renal perfusion while lowering SBP. The renal protective effects of sacubitril/allisartan are likely related to its dual action-reducing intraglomerular pressure through angiotensin II receptor blockade while enhancing natriuretic pe-

ptide activity, which promotes sodium excretion, afferent arteriolar dilation, and inhibition of renal fibrosis.[25,26] Previous studies with sacubitril/valsartan have shown slower declines in eGFR and lower incidence of renal adverse events compared with angiotensin receptor blocker monotherapy,[27,28] particularly in hypertensive or heart failure patients. Although renal biomarkers were not extensively evaluated in this analysis, the absence of hyperkalemia or renal impairment and the reduction in serum uric acid further support a favorable renal safety and metabolic profile of sacubitril/allisartan in elderly hypertensive patients. Longer-term studies are warranted to confirm whether these short-term renal benefits translate into improved renal outcomes in this population.

Sacubitril/Allisartan is a new agent in the class of angiotensin-receptor neprilysin inhibitors with allisartan as a replacement of valsartan in a single compound.[29] Allisartan is developed as a new angiotensin-receptor blocker from EXP3174, an active metabolite of losartan, and has been widely used in the treatment of hypertension in China in a dose range from 80 mg/d to 240 mg/d. A recent meta-analysis including six randomized controlled trials with 767 hypertensive patients demonstrated that allisartan isoproxil significantly reduced SBP compared with placebo (weighted mean difference of -8.08 mmHg) and achieved blood pressure control comparable to established angiotensin receptor blockers.[30] The greater blood pressure reductions observed with sacubitril/allisartan in the present study are consistent with the results reported with sacubitril/valsartan. Nevertheless, potential differences in pharmacokinetic characteristics, higher dose of sacubitril,[31] or prolonged AT1 receptor blockade mediated by allisartan may contribute to variation in clinical responses. In the absence of direct head-to-head comparisons between sacubitril/allisartan and sacubitril/valsartan, conclusions regarding compound-specific advantages cannot be drawn. Future comparative studies evaluating different angiotensin-receptor neprilysin inhibitors in patients with hypertension will be important to clarify potential differences in efficacy, tolerability, and cardiovascular protection between these agents in the same class of drugs.

LIMITATIONS

Our study should be interpreted within the context of its limitations. Firstly, this study was a *post-hoc* exploratory analysis of elderly participants enrolled in a randomized clinical trial. Consequently, the balance achieved through randomization in the original study may not have been fully preserved within the elderly subgroup and the possibility of type I error cannot be excluded. Secondly, the inclusion criteria of our study included clinic blood pressure but not ambulatory blood pressure. Thirdly, direct assessments of arterial stiffness, such as carotid-femoral pulse wave velocity, central blood pressure, or augmentation index, were not performed, the present findings should not be interpreted as definitive evidence of improved arterial stiffness. Fourthly, the impact of sacubitril/allisartan on target organ damage, such as left ventricular mass or urinary albumin excretion, and long-term outcomes such as cardiovascular events was not assessed in the present study. Last but not least, the study population consisted exclusively of Chinese patients aged 65–75 years. Therefore, the findings may not be directly generalizable to very old individuals (≥ 80 years), frail elderly patients, or populations with different ethnic and geographic backgrounds.

CONCLUSIONS

In this *post-hoc* analysis of elderly Chinese patients with hypertension, sacubitril/allisartan provided greater reductions in clinic and ambulatory SBP and DBP compared with olmesartan, accompanied by a significant decrease in PP and stable renal profiles. These results indicate that sacubitril/allisartan offers superior and sustained blood pressure control in the elderly, particularly those with systolic hypertension. The findings support its potential as an effective and well-tolerated therapeutic option for hypertension management in older adults. These findings provide preliminary evidence supporting the design of a prospective, adequately powered clinical trial specifically enrolling elderly patients.

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REFERENCES

[1] Wang JG, Zhang W, Li Y, *et al*. Hypertension in China: epidemiology and treatment initiatives. *Nat Rev Cardiol* 2023; 20: 531–545.
[2] Wang Z, Chen Z, Zhang L, *et al*. Status of hypertension in China: results from the China Hypertension Survey, 2012-2015. *Circulation* 2018; 137: 2344–2356.
[3] Flint AC, Conell C, Ren X, *et al*. Effect of systolic and diastolic blood pressure on cardiovascular outcomes. *N Engl J Med* 2019; 381: 243–251.
[4] Rapsomaniki E, Timmis A, George J, *et al*. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet* 2014; 383: 1899–1911.
[5] Bangalore S, Messerli FH, Franklin SS, *et al*. Pulse pressure and risk of cardiovascular outcomes in patients with hypertension and coronary artery disease: an INternational VErapamil SR-trandolapril STudy (INVEST) analysis. *Eur Heart J* 2009; 30: 1395–1401.
[6] Lu H, Kondo T, Claggett BL, *et al*. Systolic blood pressure and pulse pressure in heart failure: pooled participant-level analysis of 4 trials. *J Am Coll Cardiol* 2025; 85: 710–722.
[7] Balafa O, Kalaitzidis RG. Salt sensitivity and hypertension. *J Hum Hypertens* 2021; 35: 184–192.
[8] Kario K, Shin J, Chen CH, *et al*. Expert panel consensus recommendations for ambulatory blood pressure monitoring in Asia: the HOPE Asia Network. *J Clin Hypertens (Greenwich)* 2019; 21: 1250–1283.
[9] Lee JH, Kim KI, Cho MC. Current status and therapeutic considerations of hypertension in the elderly. *Korean J Intern Med* 2019; 34: 687–695.
[10] Hu Y, Zhang H, Li X, *et al*. A randomized, double-blind, placebo-controlled, single, and multiple dose-escalation Phase I clinical trial to investigate the safety, pharmacokinetic, and pharmacodynamic profiles of oral S086, a novel angiotensin receptor-neprilysin inhibitor, in healthy Chinese volunteers. *Expert Opin Investig Drugs* 2022; 31: 977–985.
[11] Zhang J, Zhang W, Yan J, *et al*. Efficacy and safety of sacubitril/allisartan for the treatment of primary hypertension: a phase 2 randomized, double-blind study. *Hypertens Res* 2023; 46: 2024–2032.
[12] Zhang W, Zhang J, Yan J, *et al*. Efficacy and safety of sacubitril/allisartan for the treatment of primary hypertension. *JACC Asia* 2024; 4: 697–707.
[13] Vardeny O, Miller R, Solomon SD. Combined neprilysin and renin-angiotensin system inhibition for the treatment of heart failure. *JACC Heart Fail* 2014; 2: 663–670.
[14] Smulyan H, Mookherjee S, Safar ME. The two faces of hypertension: role of aortic stiffness. *J Am Soc Hypertens* 2016; 10: 175–183.
[15] Huo Y, Li W, Webb R, *et al*. Efficacy and safety of sacubitril/valsartan compared with olmesartan in Asian patients with essential hypertension: a randomized, double-blind, 8-week study. *J Clin Hypertens (Greenwich)* 2019; 21: 67–76.
[16] Wang TD, Tan RS, Lee HY, *et al*. Effects of sacubitril/valsartan (LCZ696) on natriuresis, diuresis, blood pressures, and NT-proBNP in salt-sensitive hypertension. *Hypertension* 2017; 69: 32–41.
[17] Park JB, Kario K, Wang JG. Systolic hypertension: an increasing clinical challenge in Asia. *Hypertens Res* 2015; 38: 227–236.
[18] Yano Y, Stamler J, Garside DB, *et al*. Isolated systolic hypertension in young and middle-aged adults and 31-year risk for cardiovascular mortality: the Chicago Heart Association Detection Project in Industry study. *J Am Coll Cardiol* 2015; 65: 327–335.
[19] Benetos A, Thomas F, Joly L, *et al*. Pulse pressure amplification a mechanical biomarker of cardiovascular risk. *J Am Coll Cardiol* 2010; 55: 1032–1037.
[20] Williams B, Cockcroft JR, Kario K, *et al*. Effects of sacubitril/valsartan versus olmesartan on central hemodynamics in the elderly with systolic hypertension: the PARAMETER study. *Hypertension* 2017; 69: 411–420.
[21] Supasyndh O, Wang J, Hafeez K, *et al*. Efficacy and safety of sacubitril/valsartan (LCZ696) compared with olmesartan in elderly Asian patients (≥65 years) with systolic hypertension. *Am J Hypertens* 2017; 30: 1163–1169.
[22] Schellinger IN, Dannert A, Hoffmann A, *et al*. Angiotensin receptor-neprilysin inhibition (sacubitril/valsartan) reduces structural arterial stiffness in middle-aged mice. *J Am Heart Assoc* 2024; 13: e032641.
[23] Dargad RR, Prajapati MR, Dargad RR, *et al*. Sacubitril/valsartan: a novel angiotensin receptor-neprilysin inhibitor. *Indian Heart J* 2018; 70: S102–S110.
[24] Raja R, Kumari S, Umer Khan M, *et al*. Antihypertensive effects of sacubitril/valsartan versus olmesartan: an updated systemic review and meta-analysis of randomized controlled trials. *Cureus* 2023; 15: e48692.
[25] Pontremoli R, Borghi C, Perrone Filardi P. Renal protection in chronic heart failure: focus on sacubitril/valsartan. *Eur Heart J Cardiovasc Pharmacother* 2021; 7: 445–452.
[26] Jing W, Vaziri ND, Nunes A, *et al*. LCZ696 (sacubitril/valsartan) ameliorates oxidative stress, inflammation, fibrosis and improves renal function beyond angiotensin receptor blockade in CKD. *Am J Transl Res* 2017; 9: 5473–5484.
[27] Spannella F, Giulietti F, Filipponi A, *et al*. Effect of sacubitril/valsartan on renal function: a systematic review and meta-analysis of randomized controlled trials. *ESC Heart Fail* 2020; 7: 3487–3496.
[28] Kang H, Zhang J, Zhang X, *et al*. Effects of sacubitril/valsartan in patients with heart failure and chronic kidney disease: a meta-analysis. *Eur J Pharmacol* 2020; 884: 173444.
[29] Rakugi H, Kario K, Yamaguchi M, *et al*. Efficacy of sacubitril/valsartan versus olmesartan in Japanese patients with essen-

tial hypertension: a randomized, double-blind, multicenter study. *Hypertens Res* 2022; 45: 824–833.
[30] Zhao F, Liu Y, Chen L. Efficacy and safety evaluation of Allisartan Isoproxil in patients with hypertension: a meta-analysis. *Front Cardiovasc Med* 2024; 11: 1355014.
[31] Izzo JL Jr, Zappe DH, Jia Y, *et al*. Efficacy and safety of crystalline valsartan/sacubitril (LCZ696) compared with placebo and combinations of free valsartan and sacubitril in patients with systolic hypertension: the RATIO study. *J Cardiovasc Pharmacol* 2017; 69: 374–381.

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