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Original Article

Promising efficacy of alisartan isoproxil combined with probiotics in elderly hypertensive patients and analysis of cardiovascular prognostic factors

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Abstract: Objective: To evaluate the clinical efficacy of alisartan isoproxil tablets combined with probiotics in elderly hypertensive patients and analyze factors influencing cardiovascular prognosis. Methods: A retrospective analysis was conducted on 147 hypertensive patients treated at the East New Town Branch of Yinzhou People's Hospital Community from September 2021 to September 2023. Patients were divided into two groups based on treatment regimen: the control group (n=75, treated with alisartan isoproxil tablets) and the observation group (n=72, treated with alisartan isoproxil tablets combined with probiotics). The total effective rate, blood pressure, inflammatory markers, blood lipids, and vascular endothelial function were assessed before treatment, at 3 months, and at 6 months. The incidence of major adverse cardiovascular events (MACE) was compared between the two groups 6 months after treatment. Univariate and multivariate logistic regression analyses were used to identify risk factors for MACE. Results: The total effective rate in the observation group was significantly higher than that in the control group ($P < 0.05$). Compared to the control group, the observation group showed lower levels of systolic/diastolic blood pressure, inflammatory markers, blood lipids, endothelin-1, and vascular endothelial growth factor, with a higher level of nitric oxide (all $P < 0.05$). The incidence of MACE was lower in the observation group than in the control group ($P < 0.05$). Univariate and multivariate logistic regression analyses indicated that age, BMI, SBP, and DBP were risk factors for MACE. Conclusion: Alisartan isoproxil combined with probiotics effectively improves blood pressure, inflammatory markers, blood lipids, and vascular endothelial function in elderly hypertensive patients. Age, BMI, SBP, and DBP are identified as risk factors for MACE and should be addressed early with preventive interventions.

Keywords: Hypertension, allisartan isoproxil tablets, probiotics, clinical parameters, cardiovascular outcomes

Introduction

Hypertension is a chronic systemic disease characterized by persistently elevated arterial blood pressure (BP), involving multiple factors such as neuroendocrine dysregulation, vascular endothelial dysfunction, and target organ damage [1]. Epidemiological data from the 2012-2015 China Hypertension Survey show a significant rise in hypertension prevalence among the general population, with a notably higher prevalence of 5% in individuals aged 65 and older, substantially exceeding that of younger populations [2]. Hypertension is also a major risk factor for cardiovascular disease (CVD) [3]. Prolonged uncontrolled hypertension may lead to left ventricular concentric hypertrophy and eccentric dilation, which not only constitutes a critical pathological basis for heart failure (HF) [4], but also accelerates atherosclerosis progression through hemodynamic disturbances [5]. Studies have also shown that time in target range and BP variability of systolic BP (SBP) are independent risk factors for major adverse cardiovascular events (MACE) and all-cause mortality in hypertensive patients [6]. These findings emphasize the importance of maintaining stable, sustained BP while minimizing BP fluctuations to prevent MACE in hypertensive patients.

Current clinical strategies for hypertension management primarily focus on pharmacological interventions and lifestyle modifications [7].

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Angiotensin II type 1 receptor blockers (ARBs), as first-line antihypertensive agents, significantly reduce BP while offering target organ protection during hypertension progression [8]. Alisartan isoproxil, a novel selective non-peptide ARB developed in China, has demonstrated favorable antihypertensive effects in patients with mild-to-moderate essential hypertension, along with cardioprotective, renoprotective, and endothelial protective properties in clinical studies [9]. However, several unresolved challenges remain in this treatment paradigm [10]. A large-scale cross-sectional study revealed that only 30-35% of hypertensive patients receiving pharmacotherapy achieved the predefined BP control targets (office BP < 140/90 mmHg or 24-hour ambulatory BP < 130/80 mmHg) [11]. Additionally, most hypertensive patients have multiple chronic comorbidities, complicating polypharmacy management and increasing the risks of adverse drug reactions, economic burden, and treatment non-adherence [12, 13]. Thus, exploring non-pharmacological interventions and innovative therapeutic strategies has become a critical research priority. Personalized treatment regimens and multimodal combination therapies may offer new avenues for improving BP control rates.

Recent studies have shown significant gut microbiota dysbiosis and functional impairment in hypertensive patients compared to normotensive individuals [14]. This microbial imbalance plays a crucial role in the pathogenesis and progression of hypertension [15]. Bifidobacterium, a probiotic genus involved in immune regulation, demonstrates protective effects on gastrointestinal mucosa [16]. Comparative analyses reveal distinct gut microbial profiles in hypertensive patients versus healthy controls, with Bifidobacterium abundance serving as a potential biomarker for disease progression. Metabolomic studies suggest that Bifidobacterium and other probiotics may modulate clinical parameters, such as triglycerides (TG) and uric acid, by altering intermediate metabolites [17]. Emerging evidence indicates Bifidobacterium influences BP through both indirect metabolic regulation and direct mechanisms including antioxidant activity and immunomodulation [18]. These findings elucidate potential mechanistic links between Bifidobacterium and hypertension pathophysiology.

Building upon this foundation, this study aims to analyze the therapeutic effect of alisartan isoproxil tablets combined with probiotics in elderly hypertensive patients. The clinical efficacy, BP control, and improvement of physiological and biochemical indexes, as well as cardiovascular outcomes during different treatment cycles, will be systematically evaluated to provide a reference for the clinical treatment of elderly hypertension.

Materials and methods

Case selection

A total of 147 hypertensive patients treated at the East New Town Branch of Yinzhou People's Hospital Medical Community from September 2021 to September 2023 were retrospectively selected. Patients were screened via electronic health records and divided into two groups based on treatment approach: the control group (n=75) and the observation group (n=72). The control group received alisartan isoproxil tablets, while the observation group received alisartan isoproxil tablets combined with Bifidobacterium triple viable capsules (see **Figure 1** for the case enrollment process). The study was approved by the Ethics Committee of Ningbo University Affiliated People's Hospital in compliance with the Helsinki Declaration for secondary data analysis (Ethics approval number: KXXSC2025076).

Inclusion criteria

(1) Patients meeting the hypertension management guidelines issued by the European Society of Cardiology (ESC) in 2024 (office BP ≥ 140 mmHg systolic and/or ≥ 90 mmHg diastolic) [19]; (2) No use of allisartan isoproxil tablets in the past six months; (3) No use of Bifidobacterium Triple Viable Capsules or other probiotic products in the past six months.

Exclusion criteria

(1) Hypertensive patients with malignant tumors; (2) Patients with severe cardiopulmonary dysfunction; (3) Patients who withdrew from the study prematurely or failed to adhere to the medication protocols; (4) Patients who experienced fatal MACE or had incomplete clinical data due to other reasons; (5) Patients taking other antihypertensive medications or probiotic

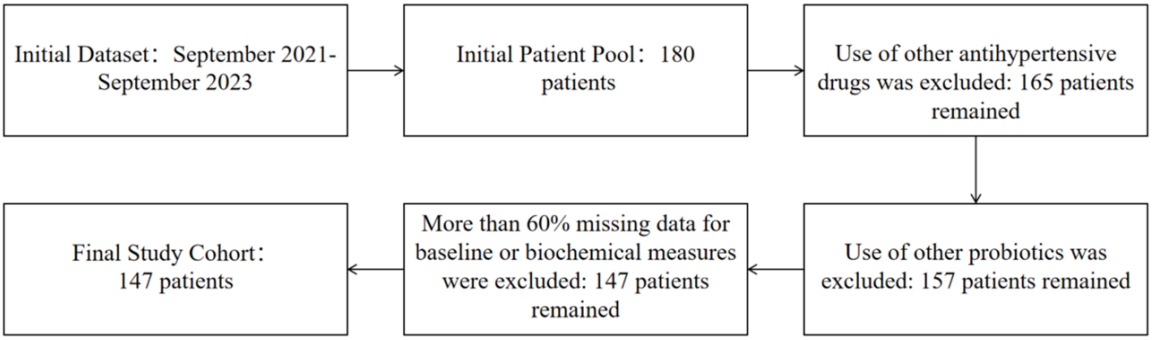

Figure 1. Flow chart of study participants.

products; (6) Patients with incomplete records (> 20% missing data).

Major adverse cardiovascular event (MACE) definition

MACE is defined as the occurrence of one or more of the following cardiovascular outcomes: unstable angina (UA), myocardial infarction (MI), heart failure (HF), or sudden death.

Treatment methods

The control group received alisartan isoproxil tablets (Shenzhen Salubris Pharmaceuticals, 240 mg qd), while the observation group received alisartan isoproxil tablets combined with Bifidobacterium triple viable capsules (Shanghai Sine Pharmaceutical, 210 mg bid). Both groups underwent 6 months of treatment with assessments at months 3 and 6.

Data collection

Primary endpoints: (1) Therapeutic Efficacy Evaluation: Significant effect: Both SBP and diastolic BP (DBP) reduced to normal ranges, or SBP decreased by ≥ 20 mmHg and DBP by ≥ 10 mmHg.

Effective: SBP decreased by 10-19 mmHg, and DBP decreased by < 10 mmHg. Ineffective: Does not meet the above criteria.

The total effective rate was calculated as: (Number of significantly effective cases + Number of effective cases)/Total number of cases × 100%.

(2) BP: Serial BP measurements were obtained before treatment, 3 and 6 months after treatment using validated portable sphygmomanometers (Shenzhen Yuyue Medical Equipment Co., Ltd., model: ABPM 6100). Triplicate readings were averaged for analysis.

(3) MACE Incidence Analysis: The composite MACE was recorded throughout the 6-month intervention period. The incidence rate was calculated as: (MACE cases/Total participants) × 100%.

Secondary endpoints: (1) Baseline characteristics: Demographic data, including BMI, duration of hypertension, SBP/DBP, smoking, drinking, diabetes, and CVD, were collected.

(2) Inflammatory factors: The levels of inflammatory markers, including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), were measured before treatment, 3 and 6 months after treatment via enzyme-linked immunosorbent assay (United Biotech Co., Ltd.). C-reactive protein (CRP) levels were determined by immunonephelometry (Oukai Biotechnology Co., Ltd.).

(3) Blood lipids: Serum total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) concentrations were measured before treatment, 3 and 6 months after treatment using an automated biochemistry analyzer (Beckman Coulter, Inc., model: AU5800), following manufacturer-recommended protocols and daily quality control verification.

(4) Vascular endothelial function indicators: Endothelial-derived mediators nitric oxide (NO), endothelin-1 (ET-1), and vascular endothelial growth factor (VEGF) were measured before treatment, 3 and 6 months after treatment via radioimmunoassay using commercially avail-

Table 1. Comparison of baseline characteristics

Indicators		Control group (n=75)	Observation group (n=72)	t/χ^2	*P*
Gender (n, %)	Man	38 (50.67)	37 (51.39)	0.008	0.930
	Woman	37 (49.33)	35 (48.61)		
Age (year)		66.1±7.4	68.3±9.5	-1.615	0.108
BMI (kg/m^2)		21.56±3.45	22.47±2.91	-1.714	0.089
Course of hypertension (year)		6.43±1.10	6.34±1.12	0.488	0.626
SBP (mmHg)		173.58±9.61	172.49±10.29	0.706	0.482
DBP (mmHg)		103.26±10.21	102.47±9.28	0.489	0.626
Smoking (n, %)	Yes	33 (44.00)	34 (47.22)	1.154	0.695
	No	42 (56.00)	38 (52.78)		
Drinking (n, %)	Yes	40 (53.33)	38 (52.78)	0.005	0.946
	No	35 (46.67)	34 (47.22)		
Diabetes (n, %)	Yes	32 (42.67)	33 (45.83)	0.149	0.699
	No	43 (57.33)	39 (54.17)		
CVD (n, %)	Yes	36 (48.00)	31 (43.06)	0.362	0.547
	No	39 (52.00)	41 (56.94)		

Note: BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; CVD: Cardiovascular Disease.

able kits (Beijing Northern Institute of Biotechnology).

Univariate and multivariate logistic regression analysis

In the observation group, patients were categorized into the MACE group (27 cases) and the non-MACE group (45 cases) based on the occurrence of MACE 6 months after treatment. A univariate analysis was performed to compare baseline characteristics between the two groups. Statistically significant variables were included in the logistic regression model to identify factors influencing MACE events in elderly hypertensive patients treated with the combination of alisartan isoproxil tablets and probiotics.

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics 19.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as percentages (%) and analyzed using the χ^2 test. Continuous variables conforming to a normal distribution (evaluated by the Shapiro-Wilk test) and homogeneity of variance (evaluated by Levene's test) were expressed as mean ± standard deviation (Mean ± SD). Independent sample t-tests were used for pairwise comparisons between groups, and paired sample t-tests were used for comparisons within groups. GraphPad Prism 10.1.2 was used to analyze the data and create line graphs. Multivariate logistic regression was employed to analyze risk factors for MACE occurrence. A two-tailed $P < 0.05$ was considered statistically significant. All statistical analyses were performed in strict accordance with the pre-specified study protocol to ensure methodological rigor.

Results

Study population

Figure 1 shows the enrollment process of the study. A total of 180 hypertensive patients were included, with 15 patients excluded for taking other antihypertensive drugs, 8 for taking other probiotics, and 10 for missing > 60% of baseline or biochemical indicator data. Finally, 147 patients were included in the analysis, with 75 in the control group and 72 in the observation group.

Comparison of baseline characteristics

There were no statistically significant differences in baseline characteristics including age, BMI, SBP, and DBP, between the groups (all $P > 0.05$) (**Table 1**).

Comparison of clinical efficacy

The results demonstrated that both groups exhibited a significant improvement in total effi-

Table 2. Comparison of clinical efficacy (n, %)

Treatment	Control group (n=75)		Observation group (n=72)	
	3 months	6 months	3 months	6 months
Significantly effective	15 (20.00)	34 (45.33)	47 (65.28)	65 (90.28)
Effective	16 (21.33)	11 (14.67)	5 (6.94)	4 (5.56)
Ineffective	44 (58.67)	30 (40.00)	20 (27.78)	3 (4.17)
Total Effective	31 (41.33)	45 (60.00)	52 (72.22)[a]	69 (95.83)[b]
χ^2	5.228		14.954	
P	0.022		< 0.001	

Note: a indicates *P* < 0.05 in the observation group compared with the control group at 3 months of treatment; b indicates *P* < 0.05 in the observation group compared with the control group at 6 months of treatment.

Table 3. Comparison of BP levels (Mean ± SD)

Indicators		Control group (n=75)	Observation group (n=72)	*t*	*P*
SBP (mmHg)	Pre-treatment	173.58±9.61	172.49±10.29	0.706	0.482
	3 months	154.35±9.62[a]	143.69±10.59[a]	6.392	< 0.001
	6 months	142.36±7.36[a,b]	128.44±8.42[a,b]	10.684	< 0.001
DBP (mmHg)	Pre-treatment	103.26±10.21	102.47±9.28	0.489	0.626
	3 months	94.58±7.64[a]	87.63±8.95[a]	5.070	< 0.001
	6 months	86.32±9.62[a,b]	75.48±7.63[a,b]	7.549	< 0.001

Note: a indicates *P* < 0.05 compared with before treatment in the same group; b indicates *P* < 0.05 compared with 3 months of treatment in the same group.

cacy at 6 months compared to 3 months of treatment (P < 0.05). Notably, the observation group showed significantly higher total efficacy rates compared to the control group at both the 3-month and 6-month follow-up assessments (P > 0.05) (**Table 2**).

Comparison of BP levels

There was no significant difference in BP levels between the two groups at baseline (both P > 0.05). Compared to pre-treatment values, both groups showed significant reductions in SBP and DBP 3 and 6 months after treatment (both P < 0.05). Notably, the observation group exhibited significantly lower SBP and DBP than the control group at both the 3-month and 6-month follow-ups (both P < 0.05) (**Table 3**).

Comparison of inflammatory factor levels

As shown in **Figure 2**, before treatment, there was no statistically significant difference in inflammatory factor levels between the two groups (all P > 0.05). Compared to pre-treatment levels, both the control and observation groups showed decreased inflammatory factors 3 and 6 months after treatment (all P < 0.05). Three and 6 months after treatment, the levels of TNF-α, IL-6, and CRP in the observation group were significantly lower than in the control group (all P < 0.05).

Comparison of blood lipid levels

As shown in **Figure 3**, before treatment, there were no significant differences in TC, TG, and LDL-C levels between the two groups (all P > 0.05). Compared to pre-treatment values, blood lipid levels in both the control and observation groups were significantly reduced 3 and 6 months after treatment, with differences being statistically significant (all P < 0.05). Three and 6 months after treatment, the levels of TC, TG, and LDL-C in the observation group were significantly lower than those in the control group (all P < 0.05).

Comparison of vascular endothelial function

As shown in **Figure 4**, before treatment, there were no significant differences in NO, ET-1, and VEGF levels between the two groups (all P > 0.05). Compared to pre-treatment levels, NO levels in both groups significantly increased, while ET-1 and VEGF levels significantly decreased 3 and 6 months after treatment (all P < 0.05). Notably, 3 and 6 months after treat-

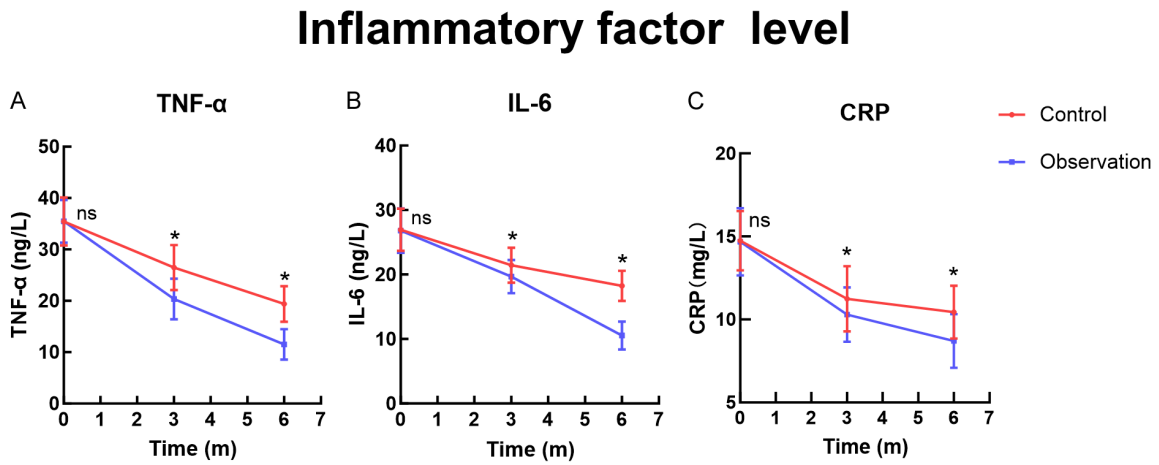

Figure 2. Comparison of inflammatory factor levels between the two groups. A: TNF-α (Tumor Necrosis Factor-α); B: IL-6 (Interleukin-6); C: CRP (C-Reactive Protein). Compared with the observation group: ns, not significant; *$P < 0.05$.

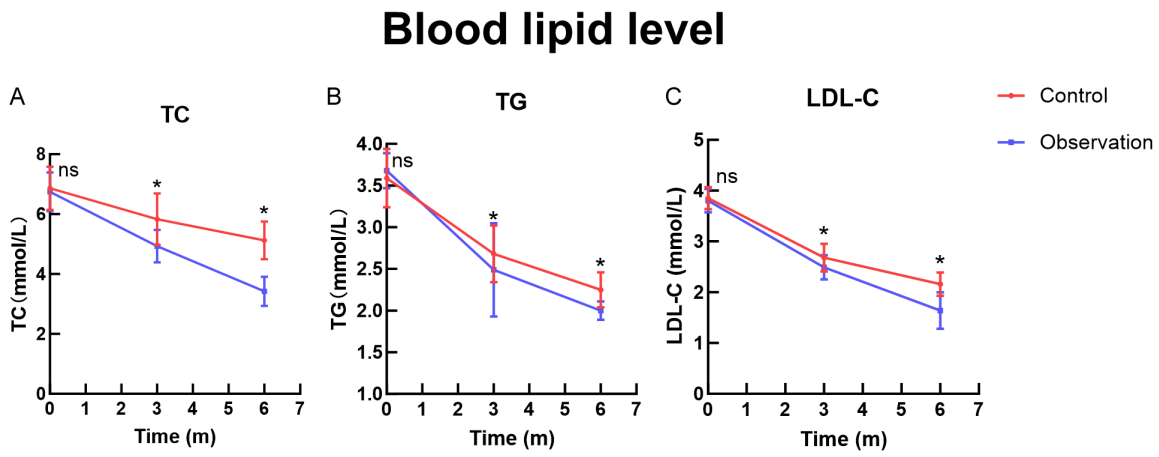

Figure 3. Comparison of lipid levels between the two groups. A: TC (Total Cholesterol); B: TG (Triglyceride); C: LDL-C (Low-Density Lipoprotein Cholesterol). Compared with the observation group: ns, not significant; *$P < 0.05$.

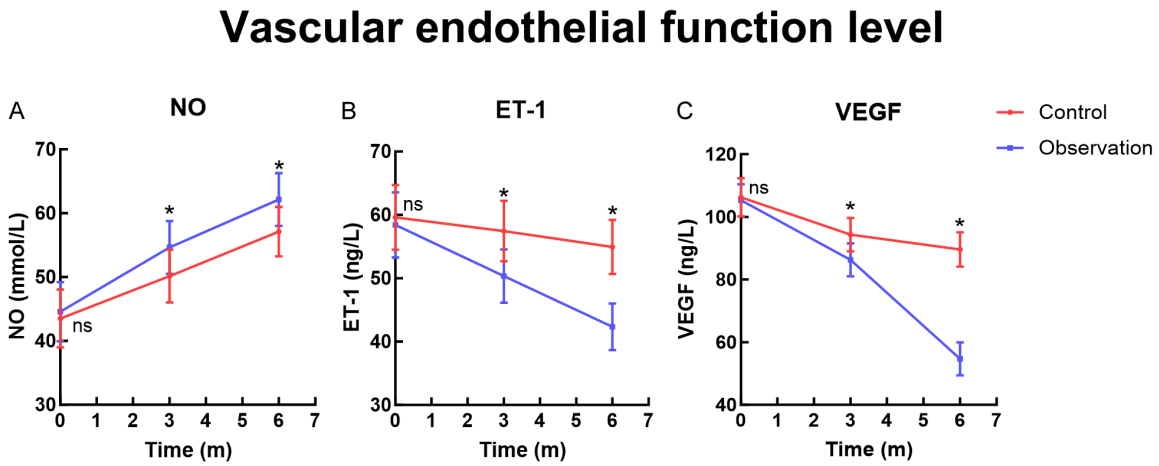

Figure 4. Comparison of the level of vascular endothelial function between the two groups. A: NO (Nitric Oxide); B: ET-1 (Endothelin-1); C: VEGF (Vascular Endothelial Growth Factor). Compared with the observation group: ns, not significant; *$P < 0.05$.

Table 4. Comparison of the incidence of MACE (n, %)

MACE events	Control group (n=75)	Observation group (n=72)
UA	11 (14.67)	5 (6.94)
MI	9 (12.00)	3 (4.17)
HF	13 (17.33)	7 (9.72)
Sudden death	23 (30.67)	12 (16.67)
ALL-MACE	56 (74.67)	27 (37.50)
χ^2	20.642	
P (ALL-MACE)	< 0.001	

Note: UA: Unstable Angina; MI: Myocardial Infarction; HF: Heart Failure.

ment, NO levels in the observation group were higher than in the control group, while ET-1 and VEGF levels were lower in the observation group, with differences being statistically significant (all P < 0.05).

Comparison of the incidence of MACE events

Six months after treatment, the incidence of UA, MI, HF, and sudden death was significantly reduced in the observation group compared to the control group. The incidence of MACE events in the observation group was 37.5%, significantly lower than in the control group, which had an incidence rate of 74.67% (P < 0.05) (**Table 4**).

Univariate analysis of MACE events in the observation group 6 months after treatment

Univariate analysis showed that, compared to the MACE group, the non-MACE group had significantly lower mean age, BMI, SBP, and DBP levels (P < 0.05). No significant differences were observed in other baseline characteristics between the two groups (P > 0.05) (**Table 5**).

Logistic regression analysis of MACE events in the observation group

The logistic regression results indicated that age, BMI, SBP, and DBP were significant risk factors for MACE events in elderly hypertensive patients in the observation group (all P < 0.05) (**Table 6**).

Discussion

Hypertension is the leading risk factor for death and disability worldwide, with its pathogenesis involving complex interactions between genetic and environmental factors [20]. Studies have shown that approximately 40% of BP variation can be attributed to genetic factors [21], while environmental factors also play a crucial role [22]. Recently, the importance of the intestinal microbiota in disease treatment has gained increasing attention, with the microbiota maintaining a complex interaction with the gut environment [23, 24]. Intestinal flora imbalance has been closely linked to various CVDs [25, 26]. Probiotics such as Bifidobacterium and Lactobacillus play vital roles in maintaining gut microbiota homeostasis, suppressing inflammation, and enhancing intestinal epithelial barrier function [27, 28]. Recent evidence suggests that probiotic interventions not only directly improve BP but may also influence offspring cardiovascular health through cross-generational epigenetic mechanisms [29-31]. These findings highlight the potential value of probiotics in the prevention and treatment of hypertension, offering a new perspective based on the “gut-heart axis”. However, there is still a lack of systematic studies on the synergistic effects of probiotics and traditional antihypertensive drugs, such as alisartan isoproxil, particularly in elderly patients. This study aims to explore the combined effects of this intervention strategy on BP control, metabolic improvement, and long-term prognosis in elderly hypertensive patients, providing new insights for integrated hypertension treatment.

Through a 6-month follow-up, it was found that the total effective rate in the observation group both 3 and 6 months after treatment was significantly higher than that in the single drug group. This suggests that combining probiotics with conventional antihypertensive treatment can enhance the overall efficacy of hypertensive treatment through synergistic effects, consistent with previous findings in drug microbiology [32]. Multiple clinical studies have confirmed that specific probiotic strains positively affect BP regulation. For instance, a randomized double-blind placebo-controlled trial demonstrated that lactobacillus-fermented dairy products significantly improved SBP and DBP in patients with borderline and prehypertension [33]. An intervention study on middle-aged smokers showed that continuous supplementation with *Lactobacillus plantarum*-fermented foods could effectively reduce SBP levels [34].

Table 5. Univariate analysis of MACE events in the observation group 6 months after treatment

Indicators		MACE group (n=27)	Non-MACE group (n=45)	t/χ^2	*P*
Gender (n, %)	Man	15 (55.56)	22 (48.89)	0.300	0.584
	Woman	12 (44.44)	23 (51.11)		
Age (year)		75.8±9.1	63.9±6.5	6.335	< 0.001
BMI (kg/m^2)		24.63±2.41	21.17±2.41	5.894	< 0.001
Course of hypertension (year)		6.50±1.21	6.24±1.08	0.936	0.353
SBP (mmHg)		180.34±9.13	167.78±7.96	6.133	< 0.001
DBP (mmHg)		109.15±7.76	98.46±7.85	5.617	< 0.001
Smoking (n, %)	Yes	15 (55.56)	19 (42.22)	1.204	0.273
	No	12 (44.46)	26 (57.78)		
Drinking (n, %)	Yes	17 (62.96)	21 (46.67)	1.798	0.180
	No	10 (37.04)	24 (53.33)		
Diabetes (n, %)	Yes	12 (44.44)	21 (46.67)	0.034	0.855
	No	15 (55.56)	24 (53.33)		
CVD (n, %)	Yes	13 (48.15)	18 (40.00)	0.457	0.499
	No	14 (51.85)	27 (60.00)		

Note: BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; CVD: Cardiovascular Disease.

Table 6. Logistic regression analysis of MACE events in the observation group

	B	*S.E.*	*Wald*	*OR* (95% *CI*)	*P*
Age	0.247	0.124	3.931	1.280 (1.003-1.633)	0.047
BMI	0.885	0.364	5.896	2.422 (1.186-4.946)	0.015
SBP	0.395	0.170	5.388	1.485 (1.063-2.072)	0.020
DBP	0.178	0.087	4.205	1.194 (1.008-1.415)	0.040

Note: BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.

Additionally, the interaction between gut microbiota and antihypertensive drugs may be a key mechanism enhancing the efficacy of combination therapy. First-line antihypertensive drugs, such as amlodipine and losartan, significantly interact with gut microbes, affecting drug bioavailability. These drugs also reshape the structure and function of intestinal flora, further regulating the microbial metabolic environment [35]. In conclusion, adjunctive therapy with probiotics may offer a new strategy for hypertension management by modulating microbial-drug interactions.

Probiotics such as *Bifidobacterium* have been widely recognized for their immunomodulatory functions. A randomized trial found that metabolic syndrome patients experienced significant reductions in inflammatory factors TNF-α and IL-6 after *Bifidobacterium* supplementation, leading to a reduced cardiovascular risk [36]. This is consistent with our study, where TNF-α, IL-6, and CRP levels were significantly decreased in the observation group. These anti-inflammatory effects are thought to result from specific molecules secreted by *Bifidobacterium*, such as immunomodulatory proteins and exopolysaccharides, which interact with gut microbiota or host cells to drive specific immunoregulatory processes [37]. Several studies also support the beneficial effects of probiotics on metabolic indicators. A meta-analysis of 13 studies showed that probiotics significantly improved blood glucose, blood lipids, and BP, particularly reducing TG [38]. In our study, the levels of TC, TG and LDL-C in the observation group were lower than those in the control group, aligning with the aforementioned conclusion. Another retrospective analysis also reported that BP and TG levels were lower in those who consumed probiotics [39]. Regarding vascular endothelial function, our study showed that the level of NO in the observation group was higher than in the control group, while ET-1 and VEGF levels were lower. Animal models have shown that probiotics can prevent both

dysbiosis and vascular oxidative stress in hypertensive rats with chronic NO blockade [40]. Clinical studies have also found that endothelial markers such as ET-1, NO, and VEGF are closely related to changes in intestinal flora structure in hypertensive patients [41].

In summary, our study confirms that the combined treatment of probiotics and alisartan isoproxil exhibits synergistic effects in improving inflammatory status, lipid metabolism, and vascular endothelial function in hypertensive patients. These effects may be mediated through probiotic modulation of the gut microbiota-immune-vascular axis.

Our study showed that 6 months after treatment, the incidence of UA, MI, HF, and sudden death was significantly lower in hypertensive patients treated with probiotics combined with alisartan isoproxil tablets compared to those treated with alisartan isoproxil tablets alone. Current research suggests that probiotic intervention may serve as a potential strategy for preventing and treating CVD and their associated major adverse MACE, a viewpoint that is increasingly gaining academic consensus [42]. Functional dietary interventions using probiotics to maintain or restore beneficial gut microbiota and preserve intestinal microbial homeostasis may reduce CVD risk [43]. Metagenomic analysis has revealed a decreased abundance of *Bifidobacterium* in patients with UA, and supplementation with *Bifidobacterium* can remodel the imbalanced gut microbiota in these patients, reduce trimethylamine N-oxide (TMAO) levels, and exert cardiovascular protective effects via the gut-liver-heart axis [44]. A single-center randomized double-blind clinical study indicated that probiotic supplementation might beneficially influence the cardiac remodeling process in myocardial infarction patients [45]. In conclusion, probiotic adjuvant therapy may have a synergistic protective effect on reducing the risk of MACE and improving cardiac outcomes in hypertensive patients by regulating intestinal flora homeostasis, affecting metabolites (such as TMAO), and influencing multi-organ axis signaling.

Our findings also indicate that, among elderly hypertensive patients who experienced MACE, advanced age, elevated BMI, and higher SBP and DBP were prominent characteristics. Logistic regression analysis further confirmed that these factors were independent risk factors for MACE in this patient population. This observation is consistent with previous studies showing that elderly hypertensive patients have a significantly higher cardiovascular event risk compared to younger individuals [46]. Cluster analysis revealed that high-risk hypertensive patients, as opposed to low-risk patients, generally had a greater obesity burden and a significantly increased risk of MACE [47]. These results highlight the importance of heightened vigilance for MACE events in elderly hypertensive patients with these risk factors.

Several limitations in this research should be noted. The relatively small sample size and short follow-up period may limit the comprehensive evaluation of long-term efficacy and safety, especially regarding the precise assessment of preventive effects against major MACE events. Additionally, the study did not thoroughly investigate the strain-specific mechanisms of action for different probiotic strains, nor did it systematically monitor dynamic changes in gut microbiota and inter-individual variations in microbial composition. These factors may restrict a deeper understanding of the mechanisms of probiotic action. Future research should involve large-scale, long-term, age-stratified randomized controlled trials, integrating multi-omics technologies such as metagenomics, metabolomics, and proteomics. This approach will help elucidate the biological mechanisms of the aging-gut-heart axis, identify differential responses to probiotic interventions across various hypertension phenotypes, and explore pharmacokinetic interactions between probiotics and conventional antihypertensive drugs. Ultimately, this research will provide a stronger theoretical foundation for precision hypertension treatment strategies based on gut microbiota profiles, helping to optimize hypertension prevention and management through modulation of the gut-heart axis.

In conclusion, alisartan combined with probiotics has a significant effect on BP control in hypertensive patients, improving inflammatory factor levels, blood lipid profiles, and vascular endothelial function. It also effectively reduces the incidence of MACE. Age, BMI, SBP, and DBP are identified as risk factors for MACE in these patients. Clinical practice can benefit from early identification of at-risk patients and timely intervention based on these factors.

Disclosure of conflict of interest

None.

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