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*Original Article*

# Correlation of ACE gene polymorphisms and platelet parameters with morning peak blood pressure in hypertensive patients

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**Abstract:** Objective: To analyze the relationship between platelet parameters, morning peak blood pressure (MPBP) in hypertensive patients, and angiotensin-converting enzyme (ACE) gene polymorphisms. Methods: This study included 245 primary hypertensive patients treated between February 2019 and February 2022, who were divided into two groups based on MPBP status: 144 patients with MPBP and 101 without MPBP. Baseline data and early morning fasting blood samples from the antecubital vein were collected. Multiple linear regression was employed to analyze factors influencing MPBP. Results: Patients with MPBP had significantly higher levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), high-sensitivity C-reactive protein (hs-CRP), and 24-hour systolic (SBP) and diastolic blood pressure (DBP) compared to those without MPBP (all $P < 0.05$). ACE genotypes were classified as I, DD, and ID, showing significant differences between groups. Patients with MPBP had a significantly higher proportion of the DD genotype and D allele frequency than those without MPBP ($P < 0.05$). Platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) were also elevated in MPBP patients all ($P < 0.05$). Multiple linear regression analysis identified TC, LDL-C, hs-CRP, DD genotype, PLT, MPV, PDW and PCT as independent risk factors for MPBP (all $P < 0.05$). Conclusion: In patients with MPBP, platelet parameters and ACE polymorphism, specifically the DD genotype and MPV, are independent risk factors. Monitoring these parameters may help reduce cardiovascular events associated with MPBP.

**Keywords:** Hypertension, angiotensin converting enzyme, blood platelets, blood pressure

## Introduction

Hypertension, affecting approximately 1 billion people worldwide, is characterized by persistently elevated blood pressure levels, often leading to cardiovascular and cerebrovascular complications [1]. Although particularly prevalent among the elderly, hypertension increasingly affects younger populations due to lifestyle changes such as sedentary behavior and poor dietary habits. The early stages of hypertension are marked by subtle symptoms and typically lack distinct clinical manifestations, which can complicate timely diagnosis and management [2]. The etiology and pathogenesis of hypertension remain incompletely understood, although they are closely related to hereditary factors, age, obesity, unhealthy lifestyle habits, and mental stress [2]. Early hypertension, often without specific clinical features, can present vague symptoms such as dizziness, tinnitus, neck discomfort, and inattention. These symptoms may culminate in severe complications like stroke and heart failure, thereby posing significant risks to health and life span [2, 3].

In clinical practice, the understanding of blood pressure fluctuations is paramount, with most dynamic changes following a pattern of elevated daytime levels and reduced nighttime levels [3]. This daily rhythm includes the phenomenon of morning peak blood pressure (MPBP), which typically occurs when individuals awaken and assume upright positions [4]. During this time, blood pressure rapidly rises, creating the first peak in the 24-hour blood pressure cycle, known as the MPBP [4]. For hypertensive

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patients, there is a strong correlation between elevated morning blood pressure and cardiovascular and organ damage severity. High MPBP can exacerbate organ damage and impact hypertension management [5]. Thus, identifying and controlling MPBP is critical for cardiovascular disease prevention and maintaining stable blood pressure levels.

The mechanisms underlying MPBP in hypertension are complex and multifactorial. Many scholars suggest its origins lie in neuroendocrine changes during the transition from sleep to wakefulness [6]. This transition involves heightened sympathetic nervous activity and activation of the renin-angiotensin-aldosterone system, among others, including increased vascular baroreceptor sensitivity and abnormal levels of endothelin and adrenal hormones, all contributing to blood pressure elevation [7]. The angiotensin-converting enzyme (ACE) gene is crucial in this process and is considered a key gene in primary hypertension pathogenesis. Its genetic polymorphism, involving the deletion, insertion, or combined deletion/insertion of a 287 bp fragment sequence in intron 16, has implications for blood pressure regulation. However, research specifically examining the relationship between ACE gene polymorphisms and MPBP in hypertension remains limited [8, 9].

Recently, there has been an increasing focus on the role of platelet activity in the pathophysiology of cardiovascular diseases, particularly hypertension [10]. Platelet parameters such as mean platelet volume (MPV) and platelet distribution width (PDW) serve as potential indicators of platelet activation [10, 11]. Increased platelet reactivity contributes to thrombosis, which, in conjunction with hypertension, exacerbates organ damage and increases the risk of cardiovascular events [10].

Empirical studies have elucidated correlations between platelet metrics and clinical outcomes among hypertensive patients, proposing these parameters as possible biomarkers for the early identification and management of cardiovascular complications [10, 11]. Barrett et al. further explored the link between platelet activity and cardiovascular events, observing changes in the fibrinolytic-coagulation system upon morning arousal [10]. However, studies specifically examining the relationship between platelet parameters and MPBP in hypertensive patients remain limited [11].

Given the complex interplay between platelet activity and hypertension, further investigation into the connections among platelet parameters, ACE gene polymorphisms, and blood pressure fluctuations is needed, with particular attention given to MPBP. Clarifying these relationships is essential for developing innovative and effective hypertension management strategies. In response to these challenges, this study analyzed 245 patients with essential hypertension, assessing their 24-hour blood pressure profiles, ACE genotype, and platelet parameters, comparing those in patients with and without MPBP. The aim is to provide a theoretical foundation for the prevention and treatment of hypertension and associated cardiovascular events, ultimately improving patient outcomes through evidence-based interventions.

## Materials and methods

### *Materials*

This retrospective study included 245 primary hypertension patients treated at Wujin Hospital, affiliated with Jiangsu University, between February 2019 and February 2022. Demographic information, including age, gender, body mass index (BMI), hypertension duration, smoking history, alcohol use, diabetes, and hyperlipidemia, was collected from medical records. Patients were classified into two groups based on the difference between 24-hour morning systolic blood pressure (SBP) and nighttime SBP, using a 35 mmHg threshold. Among them, 144 patients had MPBP, and 101 did not. Ethical approval was obtained from the Ethics Committee of Wujin Hospital affiliated with Jiangsu University, and all participants provided informed consent. The study design flowchart is presented in **Figure 1**.

The sample size for this study was calculated using the following formula: $n = \left( \frac{z_{\alpha/2} + z_{\beta}}{\Delta} \right)^2 \times (p_1(1 - P_1) + p_2(1 - p_2))$: where: $Z_{\alpha/2}$ is the critical value of the standard normal distribution corresponding to the significance level ($\alpha = 0.05$); $Z_{\beta}$ is the critical value corresponding to the study power ($\beta = 0.20$); $\Delta$ represents the minimum detectable difference in the outcome measure; $p_1$ and $p_2$ are the esti-

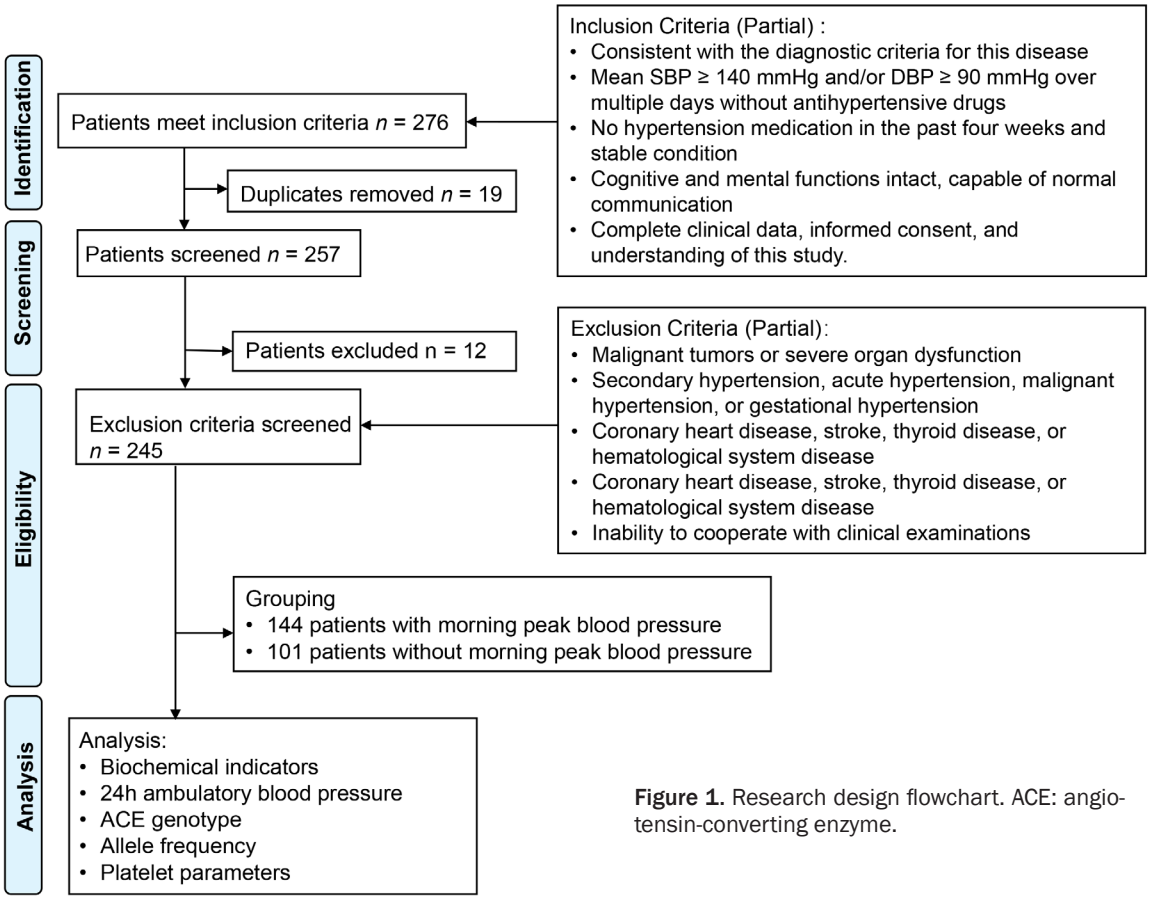


**Figure 1.** Research design flowchart. ACE: angiotensin-converting enzyme.

mated proportions of the outcome in the two groups. Based on the above formula and the expected prevalence of MPBP, the minimum sample size was determined to be 210 patients.

*Inclusion and exclusion criteria*

Inclusion criteria: (1) Conforming to the diagnostic criteria outlined in the Chinese Guidelines for the Prevention and Treatment of Hypertension (2018) [12]; (2) Mean SBP measured over consecutive days without antihypertensive medication, showing SBP ≥ 140 mmHg and/or Diastolic Blood Pressure (DBP) ≥ 90 mmHg; (3) No hypertension treatment in the past four weeks, with stable condition; (4) Normal cognitive function and mental status, enabling effective communication; (5) Complete clinical data; (6) Understanding of the study content.

Exclusion criteria: (1) Presence of malignant tumors or severe impairment of tissue and organ function; (2) Secondary, acute, malignant, or gestational hypertension; (3) Coronary heart disease, stroke, thyroid disease, hematological disorders, etc; (4) Diabetes or severe infections; (5) Non-cooperation in clinical examinations.

*Determination of biochemical indicators*

Three mL fasting venous blood was collected from patients in the two groups in the morning and placed in an anticoagulant test tube. A 3.8% sodium citrate solution was added for anticoagulation, and the sample was diluted. After centrifugation and thorough mixing, the supernatant was collected for analysis. Serum biochemical indicators were measured using the COBAS 8000 automated biochemical analyzer (Roche, Germany), assessing parameters such as high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), and fasting blood glucose (FBG). High-sensitivity C-reactive protein was measured using an automatic chemiluminescence immunoassay analyzer.

*Blood pressure measurements*

Blood pressure was measured following standard clinical procedures [13]. Participants rested quietly for 15 minutes before assessment. A

calibrated sphygmomanometer was used to record blood pressure, minimizing errors in consecutive readings. Ambulatory blood pressure monitoring was conducted with an automated device (Oxford Instruments), positioning cuffs correctly on the upper arm. Measurements were taken every 30 minutes during the day (6:00-22:00) and hourly at night, with a compliance rate exceeding 80% for recorded data. MPBP was defined as the mean SBP within 2 hours after waking minus the lowest mean SBP during nighttime sleep [14].

MPBP specifically reflects the physiological occurrence typically observed within the first two hours post-awakening. Studies show this phenomenon occurs during when SBP rises sharply from its nighttime low to a peak value [13, 14]. This increase is clinically relevant due to its potential impact on cardiovascular risk factors. Importantly, MPBP uniquely targets the sleep-to-wake transition, a critical period for evaluating hypertension-related risks, rather than a general 24-hour blood pressure profile [13].

The time frame of MPBP was chosen based on the understanding that waking triggers various hormonal and neural mechanisms, leading to a blood pressure surge. This spike results from increased sympathetic nervous system activity and the release of circulating hormones like cortisol, which are vital for transitioning to an active daytime state [14]. Accurate delineation of MPBP is essential to assess its role in hypertensive patients and its association with adverse cardiovascular events.

*ACE genotype and allele frequency [15]*

Three milliliters of Fasting venous blood (3 ml) were collected in the morning, with 2 ml treated with 2% EDTA as an anticoagulant. Leukocytes were isolated using the hypotonic hemolysis-salting out method, and genomic DNA was extracted using a phenol/chloroform method with a genomic DNA extraction kit, then stored at -20°C. For ACE genotyping, polymerase chain reaction (PCR) was used. The reaction conditions included pre-denaturation at 95°C for 10 minutes, followed by 35 cycles of denaturation at 94°C for 30 seconds, annealing at 58°C for 30 seconds, and extension at 72°C for 40 seconds, with a final extension at 72°C for 10 minutes and storage at 4°C. The forward primer sequence was 5'-CTGGAGACCACTCCCATCCTTTCT-3' and the reverse primer was 5'-GATGTGGCCATCACArrCGTCAGAT-3'. PCR products were electrophoresed on a 1.5% agarose gel containing ethidium bromide (EB) for 20 minutes, stained with EB, and detected under a UV lamp. Digestion reactions were performed for samples with significant hybridization absence, using CutSmart buffer at 37°C with heat inactivation at 80°C for 20 minutes. ACE gene I/D polymorphisms were identified as follows: a 490 bp band for insertion homozygous II, a 190 bp band for deletion homozygous DD, and both 490 bp and 190 bp bands for insertion/deletion heterozygous ID.

*Platelet levels*

Platelet parameters were measured using the Sysmex XE-5000 automated blood analyzer, which assesses platelet distribution width (PDW), platelet count (PLT), and other related indicators. The testing kit was supplied by Beijing Telikang Xin Technology Co., Ltd., and all procedures followed the manufacturer's instructions. Mean values were calculated, and if the PLT error was exceeded 10% after three attempts, re-sampling was performed. Reference ranges for normal values were as follows: PLT 100-300 × 10^9/L, PDW 9-11%, mean platelet volume (MPV) 6.8-13.5 fL, and plateletcrit (PCT) 0.11-0.23% [16].

*Statistical analysis*

Data analysis was conducted using SPSS version 29.0. The Shapiro-Wilk test was applied to assess the normality of continuous variables. Normally distributed continuous variables were presented as mean (X ± standard deviation [s]) and analyzed using the t-test with corrected variance. Categorical data were expressed as frequencies (%) and case numbers (n). Chi-square tests were applied with the standard formula when the sample size was $\geq 40$ and the theoretical frequency (T) was $\geq 5$. For cases where the sample size was $\geq 40$ and $1 \leq T < 5$, Yates' correction was used. Fisher's test was applied when the sample size was $< 40$ or $T < 1$. A two-sided $P < 0.05$ was considered statistically significant. Pearson correlation analysis was used to examine the relationship between continuous variables and MPBP, while Spearman rank correlation analysis was applied for categorical variables. Variables with significant differences in both differential and correlation analyses were included as covariates in a logistic regression analysis.

**Table 1.** Comparison of basic data

| | Without morning peak blood pressure (n = 101) | With morning peak blood pressure (n = 144) | t | P |
|---|---|---|---|---|
| Gender (cases) | | | 0.476 | 0.490 |
| Male | 55 (54.46%) | 86 (59.72%) | | |
| Female | 46 (45.54%) | 58 (40.28%) | | |
| Age (years) | 61.41 ± 3.5 | 61.35 ± 3.49 | 0.128 | 0.898 |
| Disease courses of hypertension (years) | 10.55 ± 2.76 | 10.53 ± 2.74 | 0.063 | 0.949 |
| Alcoholic history (cases) | 39 (38.61%) | 56 (38.89%) | 0.000 | 1.000 |
| Smoking history (cases) | 49 (48.51%) | 78 (54.17%) | 0.550 | 0.458 |
| BMI (kg/m$^2$) | 23.16 ± 2.97 | 23.11 ± 2.98 | 0.125 | 0.900 |
| Diabetes | 13 (12.87%) | 22 (15.28%) | 0.119 | 0.731 |
| Hyperlipidemia | 15 (14.85%) | 26 (18.06%) | 0.238 | 0.626 |
| Employment status (%) | | | 0.206 | 0.650 |
| Employed | 73 (72.28%) | 109 (75.69%) | | |
| Unemployed | 28 (27.72%) | 35 (24.31%) | | |
| Marital status (%) | | | 1.714 | 0.424 |
| Married | 69 (68.32%) | 108 (75%) | | |
| Single | 21 (20.79%) | 21 (14.58%) | | |
| Divorced | 11 (10.89%) | 15 (10.42%) | | |

**Table 2.** Comparison of biochemical indicators

| | Without morning peak blood pressure (n = 101) | With morning peak blood pressure (n = 144) | t | P |
|---|---|---|---|---|
| FBG (mmol/L) | 4.95 ± 0.88 | 5.07 ± 1.16 | 0.974 | 0.331 |
| HDL-C (mmol/L) | 1.2 ± 0.21 | 1.35 ± 0.27 | 4.895 | < 0.001 |
| LDL-C (mmol/L) | 2.64 ± 0.67 | 2.88 ± 0.71 | 2.708 | 0.007 |
| TG (mmol/L) | 2.01 ± 1.08 | 2.12 ± 1.23 | 0.762 | 0.447 |
| TC (mmol/L) | 5.02 ± 1.74 | 7.69 ± 2.36 | 10.155 | < 0.001 |
| Blood uric acid (μmol/L) | 359.89 ± 95.36 | 395.16 ± 98.69 | 2.809 | 0.005 |
| hs-CRP (mg/L) | 0.63 ± 0.14 | 0.71 ± 0.16 | 4.661 | < 0.001 |
| Serum creatinine (μmol/L) | 86.26 ± 19.37 | 90.32 ± 26.85 | 1.374 | 0.171 |

Note: FBG: fasting blood glucose; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides; hs-CRP: high-sensitivity C-reactive protein.

## Results

*Comparison of basic data between the two groups*

**Table 1** shows that there were no significant differences between the two groups in terms of baseline characteristics such as uric acid blood levels, alcohol consumption history, or hypertension duration (all P > 0.05).

*Comparison of biochemical indicators between the two groups*

Patients with MPBP had significantly higher levels of serum TC, HDL-C, and other indicators compared to those without MPBP (both P < 0.05), indicating a significant difference between groups. Detailed results are provided in **Table 2**.

*Comparison of 24-hour ambulatory blood pressure in patients with and without MPBP*

Results indicated no significant differences in 24-hour mean arterial pressure levels of DBP, daytime DBP (DDBP), nighttime DBP (NDBP), nighttime SBP (NSBP), or the 24-hour mean arterial pressure between patients with and without MPBP (all P > 0.05). However, as shown in **Table 3**, patients with MPBP exhibited significantly higher 24-hour SBP and daytime SBP

**Table 3.** Comparison of 24h ambulatory blood pressure

| | Without morning peak blood pressure(n = 101) | With morning peak blood pressure (n = 144) | t | *P* |
|---|---|---|---|---|
| 24 h DBP | 82.6 ± 8.74 | 81.6 ± 7.45 | 0.937 | 0.350 |
| 24 h SBP | 147.65 ± 9.3 | 141.94 ± 8.67 | 4.869 | < 0.001 |
| DDBP | 87.52 ± 8.43 | 85.61 ± 7.52 | 1.815 | 0.0710 |
| DSBP | 154.76 ± 10.86 | 146.3 ± 9.17 | 6.394 | < 0.001 |
| NDBP | 76.33 ± 7.42 | 76.14 ± 6.15 | 0.218 | 0.827 |
| NSBP | 135.04 ± 8.19 | 134.86 ± 8.1 | 0.166 | 0.868 |
| 24 h average ambulatory blood pressure | 104.02 ± 6.57 | 102.86 ± 6.49 | 1.364 | 0.174 |

Note: DBP: diastolic blood pressure; SBP: systolic blood pressure; DDBP: daytime DBP; NDBP: nighttime DBP; DSBP: daytime SBP; NSBP: nighttime SBP.

**Table 4.** Comparison of results in terms of ACE genotype

| | | Without morning peak blood pressure (n = 101) | With morning peak blood pressure (n = 144) | t | *P* |
|---|---|---|---|---|---|
| Genotype | II | 26 (25.74%) | 41 (28.47%) | 11.856 | 0.003 |
| | DD | 11 (10.89%) | 39 (27.08%) | | |
| | ID | 64 (63.37%) | 64 (44.44%) | | |

Note: ACE: angiotensin-converting enzyme.

**Table 5.** Comparison of results in terms of allele frequency

| | | Without morning peak blood pressure(n = 101) | With morning peak blood pressure (n = 144) | t | *P* |
|---|---|---|---|---|---|
| Allele frequency | I | 34 (33.66%) | 81 (56.25%) | 11.269 | < 0.001 |
| | D | 67 (66.34%) | 63 (43.75%) | | |

(DSBP) levels compared to those without MPBP, with a significant difference between the gr oups (both P < 0.05). Detailed results are provided in **Table 3**.

*Comparison of ACE genotype between patients with and without MPBP*

The ACE genotypes among patients with and without MPBP were classified as type II, DD, and ID. Analysis of the genotype distribution revealed significant differences between groups, with patients exhibiting MPBP having a significantly higher proportion of the DD genotype compared to those without MPBP (P < 0.05) (**Table 4**).

*Comparison of ACE genotype and allele frequency between patients with and without MPBP*

In terms of I and D allele frequencies, comparison between the two groups demonstrated statistically significant differences. Patients with MPBP had a significantly higher frequency of the D allele compared to those without MPBP (P < 0.05), as detailed in **Table 5**.

*Comparison of platelet parameters in patients with and without MPBP*

This study demonstrated that patients with MPBP had significantly higher levels of PLT, PDW and other platelet-related indicators compared to those without MPBP (all P < 0.05). Detailed findings are shown in **Figure 2**.

*Correlation analysis between MPBP and various clinical parameters*

Correlation analysis between MPBP and clinical parameters in hypertensive patients identified several significant associations (**Table 6**). High-density lipoprotein cholesterol (HDL-C) showed a positive correlation with MPBP (r = 0.289, P < 0.001), as did LDL-C with a weaker correlation (r = 0.169, P = 0.008). TC demonstrated a strong positive correlation with MPBP (r = 0.526,

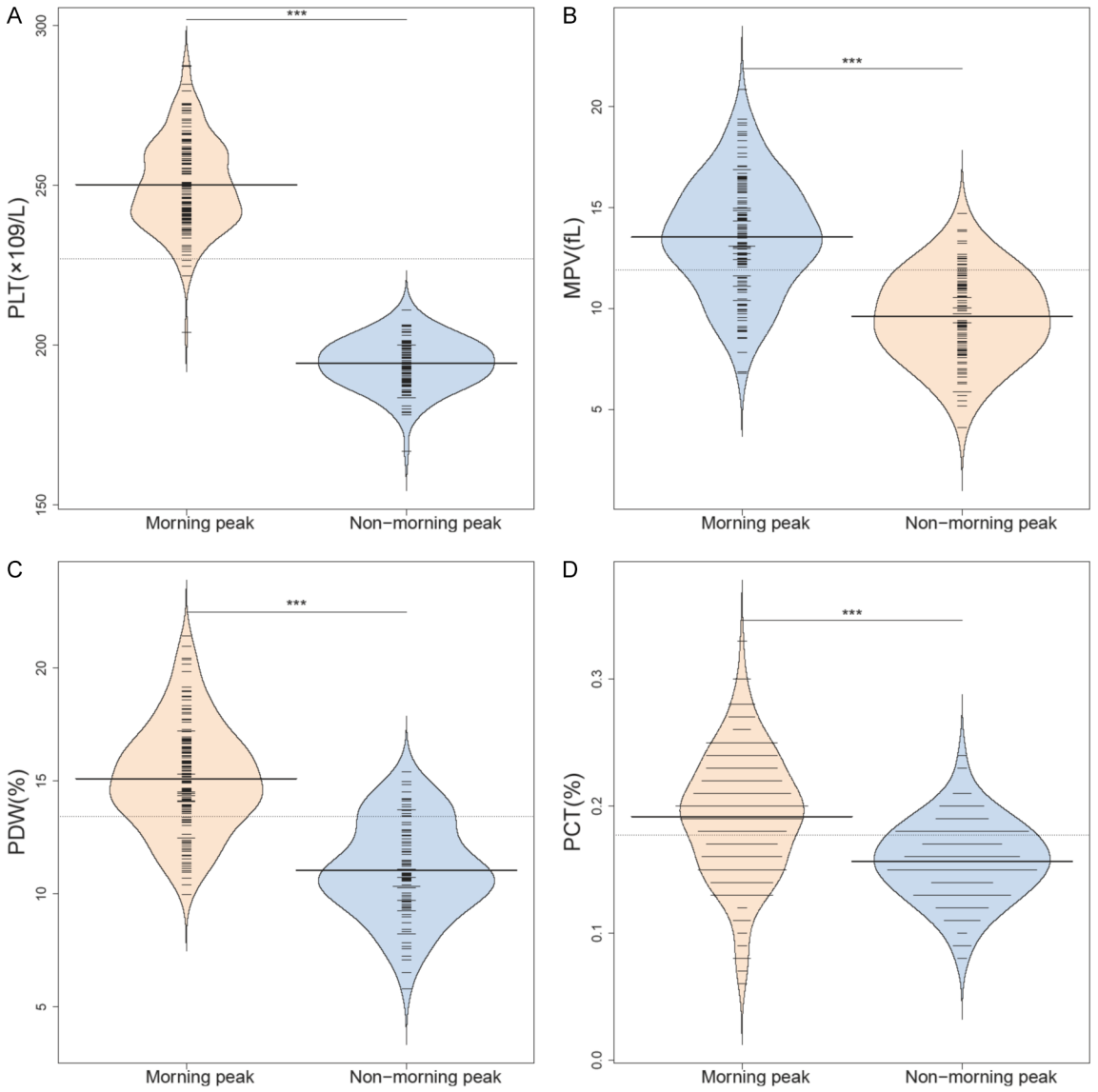


**Figure 2.** Comparison of platelet levels between with morning peak blood pressure and without morning peak blood pressure. ***: *P* < 0.001. A: PLT: platelet count; B: MPV: mean platelet volume; C: PDW: platelet distribution width; D: PCT: plateletcrit.

P < 0.001), while high-sensitivity C-reactive protein (hs-CRP) was also significantly correlated (r = 0.28, P < 0.001). PLT exhibited an exceptionally high correlation with MPBP (r = 0.917, P < 0.001), along with MPV (r = 0.607, P < 0.001), PDW (r = 0.664, P < 0.001), and PCT (r = 0.384, P < 0.001). Additionally, allele frequency showed a significant positive correlation with MPBP (r = 0.223, P < 0.001). Although genotype was negatively correlated with MPBP, and this correlation was weaker (r = -0.124, P = 0.048).

*The factors influencing the occurrence of MPBP in hypertension: multiple logistic regression analysis*

The dependent variable in this study was MPBP in hypertensive patients. Independent variables included statistically significant indicators (TC, LDL-C, HDL-C, hs-CRP, PLT, MPV, PDW, PCT, allele frequency and Genotype), ACE genotype and platelet parameters. A multivariate logistic regression model was developed to analyze the factors influencing MPBP. Results

**Table 6.** Correlation analysis

| Parameters | r | P |
|---|---|---|
| HDL-C (mmol/L) | 0.289 | < 0.001 |
| LDL-C (mmol/L) | 0.169 | 0.008 |
| TC (mmol/L) | 0.526 | < 0.001 |
| hs-CRP (mg/L) | 0.28 | < 0.001 |
| PLT (× $10^9$/L) | 0.917 | < 0.001 |
| MPV (fL) | 0.607 | < 0.001 |
| PDW (%) | 0.664 | < 0.001 |
| PCT (%) | 0.384 | < 0.001 |
| Allele frequency | 0.223 | < 0.001 |
| Genotype | -0.124 | 0.048 |

Note: HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; hs-CRP: high-sensitivity C-reactive protein; PLT: platelet count; MPV: mean platelet volume; PDW: platelet distribution width; PCT: plateletcrit.

indicated that TC, LDL-C, HDL-C, hs-CRP, PLT, MPV, PDW, PCT, allele frequency, and genotype are independent risk factors for early morning peak hypertension, with significant differences observed across groups (all $P < 0.05$; **Table 7**).

## Discussion

Hypertension, a chronic condition with high incidence and disability rates, is characterized by blood pressure exceeding normal ranges, potentially causing functional changes in the heart, blood vessels, lungs, kidneys and other organs, impacting prognosis [17]. Blood pressure control is important for hypertension management. However, due to circadian rhythm fluctuations, blood pressure peaks within a short time after waking, as the body transitions from a sleeping to an upright position, rapidly rising to its daily maximum, or morning peak, within 24 hours [18].

While a morning peak in blood pressure is physiologically normal within certain limits, excessively high MPBP in hypertensive patients can worsen blood pressure control, aggravate target organ damage, and increase the risk of cardiovascular and cerebrovascular events [19]. Research by Johansson et al. highlighted a strong association between elevated MPBP and cardiovascular and cerebrovascular complications in hypertensive patients, noting that complications frequently occur between 4:00 and 5:00 a.m., with each 1 mmHg increase in MPBP raising the risk of these events by 3.3% [20]. Therefore, understanding the pathogenesis of MPBP and establishing effective control strategies are crucial for improving hypertension management and preventing cardiovascular and cerebrovascular complications.

The occurrence of MPBP in hypertension is significantly associated with unstable plaques in large arteries, where activation of the renin-angiotensin-aldosterone system and blood rheology changes can contribute to plaque instability [21]. Therefore, this study investigates the relationship between morning peak hypertension, platelet levels, and ACE gene polymorphisms to explore its preliminary mechanisms, providing a foundation for future hypertension and cardiovascular disease interventions.

Most studies suggest that the phenomenon of MPBP in hypertensive patients is linked to abnormal sympathetic stimulation and increased activity of the renin-angiotensin-aldosterone system upon waking [22, 23]. In hypertensive patients, arterial elasticity decreases, central nervous function weakens, and sympathetic excitability increases, leading to rapid blood pressure elevations during morning postural changes. ACE, a crucial component of the renin-angiotensin-aldosterone system, is considered a candidate gene for investigating the pathophysiological mechanisms of essential hypertension. Located on chromosome 17q23, ACE is a key enzyme that catalyzes angiotensin I into angiotensin II, which induces vasoconstriction, promotes vascular smooth muscle cell proliferation, and regulates water and sodium balance through angiotensin II receptors, ultimately controlling arterial blood pressure [24].

ACE gene polymorphisms exist naturally in populations and can be classified into three types based on the presence of a 287 bp fragment: II, DD, and ID, with significant geographical and ethnic variations in allele and genotype frequencies [25]. Su et al. conducted in-depth studies and found a strong association between ACE gene polymorphism and cerebral small vessel disease, noting that the allele D significantly increases the incidence of cerebrovascular disease [26].

This study found that, compared with patients without MPBP, those with MPBP showed significantly higher levels of TC, HDL-C and other indicators. They also had significantly elevated 24-hour SBP and DSBP. The ACE genotypes in

**Table 7.** Results of multiple logistic regression analysis on the factors contributing to the occurrence of early peak blood pressure in hypertensive patients

| | Coefficient | Std Error | Wald | *P* Value | OR | CI Lower | CI Upper |
|---|---|---|---|---|---|---|---|
| HDL-C (mmol/L) | 2.484 | 0.572 | 4.346 | < 0.001 | 11.993 | 4.043 | 38.292 |
| LDL-C (mmol/L) | 0.507 | 0.194 | 2.615 | 0.009 | 1.660 | 1.143 | 2.450 |
| TC (mmol/L) | 0.584 | 0.082 | 7.146 | < 0.001 | 1.793 | 1.541 | 2.125 |
| hs-CRP (mg/L) | 4.017 | 0.951 | 4.224 | < 0.001 | 55.554 | 9.098 | 383.442 |
| PLT (× $10^9$/L) | 0.366 | 0.125 | 2.928 | 0.003 | 1.442 | 1.238 | 2.189 |
| MPV (fL) | 0.617 | 0.079 | 7.787 | < 0.001 | 1.853 | 1.603 | 2.189 |
| PDW (%) | 0.837 | 0.104 | 8.055 | < 0.001 | 2.31 | 1.912 | 2.879 |
| PCT (%) | 1.202 | 0.811 | 2.563 | < 0.001 | 1.678 | 1.624 | 1.753 |
| Allele frequency | 0.930 | 0.269 | 3.451 | < 0.001 | 2.534 | 1.503 | 4.328 |
| Genotype | -0.301 | 0.155 | 1.938 | 0.053 | 0.74 | 0.543 | 1.000 |

Note: HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; hs-CRP: high-sensitivity C-reactive protein; PLT: platelet count; MPV: mean platelet volume; PDW: platelet distribution width; PCT: plateletcrit.

both groups fell into three categories, including type I, DD, and ID-with significant differences in genotype composition. Patients with MPBP had a markedly higher proportion of the DD genotype and a significantly higher frequency of the D allele compared to those without MPBP, consistent with previous research findings suggesting that the allele D activates, while the allele I inhibits ACE gene expression. High expression of the DD genotype promotes increased renin-angiotensin-aldosterone system activity, enhancing the conversion rate of angiotensin I, thereby affecting water and sodium metabolism, vasoconstriction, vascular smooth muscle hyperplasia, and the occurrence of morning hypertension. Therefore, hypertensive patients with the ACE DD genotype should consider more intensive antihypertensive therapy to prevent cardiovascular events [27].

When MPBP occurs in hypertensive patients, the rapid blood pressure increase causes hemorheological changes, aggravating endothelial rupture and exposing subendothelial collagen and fibrous tissue. This exposure promotes the release of vasoactive substances, leading to abnormal platelet morphology and function, overexpression of active substances, and increased platelet adhesion and aggregation on vessel walls, which heightens the risk of thrombosis and cardiovascular events, potentially becoming life-threatening [28]. The morning peak phenomenon in hypertension is closely related to platelet aggregation activity; elevated blood pressure enhances platelet aggregation while reducing short-term platelet consumption, temporarily lowering PLT levels in circulation. However, prolonged platelet activation leads to increased (MPV) and PDW as new platelets form, displaying more vigorous metabolism and greater collagen adhesion. The compensatory increase in newly formed platelets also raise the total platelet volume, leading to elevated PCT levels and an increased risk of hypertension complications [29, 30].

Data from this study revealed that patients with MPBP had significantly higher PLT, MPV, PDW, and PCT levels than those without MPBP. Multiple linear regression analysis indicated that PLT, MPV, PDW, and PCT are independent risk factors for MPBP, although not in hypertensive patients. Thus, the occurrence of cardiovascular and cerebrovascular diseases associated with MPBP is not only related to ACE gene polymorphisms but is also closely linked to platelet activity. For hypertensive patients with abnormal platelet parameters, tailored treatment is crucial to improve blood pressure control and reduce the risk of cardiovascular events.

This study has certain limitations, including a relatively small sample size, sample heterogeneity, and potential biases among different data sources. Additionally, only one ACE gene polymorphism site was analyzed in relation to MPBP, and the influence of other biochemical indicators, such as TC and HDL-C levels, on MPBP was not fully examined. When analyzing different ACE gene polymorphism loci, multiple linear regression was used, but specific pathophysiological mechanisms between platelet parameters and MPBP in hypertension were

not addressed. Further research is necessary to better understand the relationships between MPBP, ACE gene polymorphisms, and platelet parameters in hypertensive patients, and to clarify their mechanisms of action.

In conclusion, in hypertensive patients, the likelihood of morning hypertension is high, which can increase the risk of cardiovascular and cerebrovascular diseases. Early attention to platelet parameter levels and ACE gene polymorphisms in these patients, along with a strengthened antihypertensive treatment plan to control morning blood pressure peaks, is essential to preventing cardiovascular and cerebrovascular complications.

## Disclosure of conflict of interest

None.

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