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Original Article

Personalization of clopidogrel therapy based on genetic polymorphism analysis: clinical implications

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Abstract: Objective: This study aimed to evaluate the impact of gene polymorphisms on clopidogrel metabolism and to use this analysis to inform treatment strategy for a population in southern Anhui of China. Methods: The research was conducted from 2019 to 2022, aincluding 430 patients from the Wuhu Hospital, affiliated with East China Normal University who were candidates for clopidogrel therapy. Genes influencing clopidogrel's absorption and metabolism were analyzed to guide treatment. Patient data were collected, and genotype and metabolic type distributions were compared. Patients needing medication adjustments were followed up and divided into two groups based on whether they received adjustments or not, and the re-admission rates for antiplatelet therapy within 12 months were compared. Results: The 430 samples showed the expected genotypes and gene distribution, with no significant correlation to age or sex. The CYP2C19 metabolic phenotype frequency was moderate at 57.44%, fast at 25.12%, slow at 15.58%, and ultra-fast at 1.86%. The ABCB1-3435C>T genotype distribution was wild type in 38.14%, heterozygous in 42.33%, and mutant homozygous in 19.53%, with the TT group being significantly younger. The PON1-576G>A genotype showed no significant baseline differences. Of the 279 patients needing medication advice, 39.07% received it. The adjusted group had a significantly lower re-admission rate within one year. Conclusion: The distribution of gene polymorphisms related to clopidogrel metabolism varied within the study population, indicating a potential for personalized medication approaches. The study provides insight into the clinical application of genetic testing for clopidogrel therapy.

Keywords: Clopidogrel, gene polymorphism, antiplatelet therapy, individualized medication, cardiovascular disease

Introduction

As contemporary lifestyles and diets evolve, the prevalence of cardiovascular diseases has risen sharply on a global scale, with a disproportionate impact on developing nations [1]. The World Health Organization has reported that cardiovascular diseases are responsible for over 17 million deaths annually, accounting nearly one-third of all global deaths [2]. Amidst this quiet epidemic, antiplatelet medications, including clopidogrel, have become indispensable in the prevention of thrombosis and for mitigation of cardiovascular events. Clopidogrel has been instrumental in patients suffering from myocardial infarction or stroke by inhibiting platelet aggregation [3]. Nonetheless, the suitability of clopidogrel varies among individuals, a variability that, in recent years, has been increasingly attributed to genetic polymorphisms [4, 5].

The CYP2C19 gene is pivotal in the metabolic pathway of clopidogrel, with variations in genotype, possibly leading to differences in metabolic rates and, consequently, in the drug's effectiveness [6, 7]. Individuals carrying the CYP2C19*2 or CYP2C19*3 allele may experience slower metabolism of clopidogrel, leading to increased drug concentrations and a heightened risk of bleeding. Conversely, CYP2C19*17 mutation might result in over-metabolism, diminishing the drug's therapeutic efficacy [8]. In addition to CYP2C19, ABCB1 and PON1 genes

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also play significant roles in the pharmacokinetics and pharmacodynamics of clopidogrel [9]. The P-glycoprotein encoded by ABCB1 influences the drug's absorption and excretion, while the PON1 enzyme, implicated in the activation of clopidogrel, has a genotype that is tied to the drug's bioavailability and efficacy [10, 11]. Despite the established link between genetic polymorphisms and clopidogrel's efficacy, clinical application of this knowledge remains limited, possibly due to the complexity and confusion surrounding genetic information among healthcare providers and patients [12].

This study aimed to explore the distribution of related genes in the population in Wuhu area to provide clinicians with more precise and feasible guidance so that they can choose the most optimal treatment for patients according to their genotypes. We believe that through this method, we can further reduce the adverse reactions from clopidogrel treatment and improve its efficacy to meet the expectations of patients and doctors for individualized treatment.

Subjects and methods

Subjects

A total of 430 patients with cardiovascular or cerebrovascular diseases at the Wuhu Hospital Affiliated to East China Normal University were selected for this study. The cohort comprised 268 males and 162 females, with age ranging from 31 to 95 years old.

The inclusion criteria were as follows: (1) individuals who were permanent residents of southern Anhui, and not close relatives of other participants; (2) patients with no contraindications to clopidogrel and who were willing to undergo treatment with it; (3) individuals who had undergone genetic testing for CYP2C19*2, *3, *17, ABCB1-3435C>T, and PON1-576G>A, and had available genetic test reports. The exclusion criteria were: (1) patients with a family history of hereditary conditions; (2) those with a recent history of blood transfusion; (3) patients suffering from chronic hematologic disorders. This study was approved by the Ethics Committee of the Wuhu Hospital Affiliated to East China Normal University (2018-KY-B03).

Methods

In situ hybridization and fluorescent staining analysis: Peripheral venous blood (2 mL) was collected from patients using EDTA-K anticoagulant vacuum blood collection tubes [13]. The patient's CYP2C19, ABCB1, and PON1 genotypes were determined using *in situ* hybridization and fluorescent staining analysis. The specific procedures were as follows: (1) A working solution was prepared by diluting ammonium chloride solution with sterile injectable water in a 1:9 ratio; (2) One millilitre of the working solution was added to a 1.5 mL centrifuge tube, followed by the addition of 150 μl of the mixed blood specimen. The solution was then thoroughly mixed and left to stand at room temperature for 5 minutes; (3) The sample was centrifuged at 3,000 rpm for 5 minutes; (4) After centrifugation, the supernatant was removed from the centrifuge tube, leaving a precipitate of enriched white blood cells at the bottom; (5) One hundred microliters of GoldView were added to the centrifuge tube and mixed thoroughly by repeated pipetting. The tube was then left to stand at room temperature for 30 minutes to obtain the white blood cell preservation solution; (6) A 1.5 μl aliquot of the white blood cell preservation solution was added to the corresponding GoldView reagent. The tube cap was closed tightly, and the tube was placed into the fluorescence detection instrument; (7) The fluorescence staining *in situ* hybridization analysis system was used to automatically read the fluorescence signal values, generate the fluorescence curve chart, and perform positive control quality assurance.

Genotype classification: This study employed a retrospective design. The rationale for conducting genotype determination among the selected patients was grounded in substantial evidence presented by the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines and a multitude of studies that have consistently demonstrated a significant influence of gene polymorphisms on clopidogrel's therapeutic efficacy [14-16]. Consequently, our patient cohort was comprised of individuals who had already undergone the recommended genetic testing at the time of their enrollment. The financial support for the genetic testing of these patients was provided by the Anhui Provincial Natural Science Foundation (Grant

No. 1908085MH248) and the Major Projects of Natural Science Research in Anhui Universities (Grant No. KJ2021ZD0101). These grants were instrumental in facilitating a retrospective analysis by enabling access to the essential genetic data, which was a fundamental component of our research. The analysis focused on the varying metabolic kinetics of clopidogrel, influenced by the activity of different enzymes encoded by various genotypes: (1) CYP2C19 was divided into four metabolic phenotypes: fast metabolic type (EM,*1/*1), ultra-fast metabolic type (UM,*1/*17,*17/*17), moderate metabolic type (IM,*1/*2,*1/*3, *17/*2,*17/*3) and slow metabolic type (PM,*2/*2,*2/*3,*3/*3). (2) ABCB1-3435C>T genotype was divided into wild type (CC), mutant heterozygous type (CT), and mutant homozygous type (TT). (3) PON1-576G>A genotype was divided into wild type (GG), mutant heterozygous type (GA), and mutant homozygous type (AA).

Medication recommendations: Based on the CPIC guidelines and the results of the TRITON-TIMI 38 study [17, 18], this research used the classification method provided by Beijing Huaxia ShiDai Gene Technology Development Co., Ltd. to divide the risk of clopidogrel resistance into five levels, and adjusted the dosage of clopidogrel accordingly: For type I (EM+CC/CT+GG type), the conventional dose of 75 mg/d was adopted; for type II (IM type, TT type or GA/AA type), the dose was increased to 150-225 mg/d or the drug was substituted by ticagrelor; for type III (IM+TT type, IM+GA/AA type or PM type), the drug was substituted by ticagrelor, or both drugs were used in combination; for type IV (UM+CC/CT+GG type), 50 mg/d clopidogrel was used, and those who could not tolerate it were treated with a dressing change if there was no aspirin resistance. For type V (UM+TT type or UM+GA/AA type), the conventional dose of 75 mg/d was used.

Patients requiring modification to their standard antiplatelet therapy were monitored over a one-year period for subsequent evaluation and analysis. They were categorized into two groups: those who received the proposed adjustments to their treatment regimen, and those who did not. A comparative analysis was conducted to assess the re-admission rates of these two groups within the 12-month time frame, focusing on the impact of the adjusted antiplatelet therapy on their clinical outcome.

Statistical analyses

The Hardy-Weinberg law of genetic equilibrium was applied to determine whether the selected samples represented the population. Statistical analysis was performed using SPSS version 22.0. Categorical data were presented as percentage (%) and analyzed using the chi-square test. Quantitative data were expressed as the mean ± standard deviation ($\bar{x} \pm s$). For intragroup comparisons before and after treatment, a paired sample t-test was used; for comparisons between different groups, an independent sample t-test was applied. $P<0.05$ was considered to indicate a significant difference.

Results

Genotype distribution analysis

Hardy-Weinberg genetic equilibrium test: All 430 patients were tested for the three genotypes: CYP2C19, ABCB1, and PON1. The gene distribution conformed to Hardy-Weinberg genetic equilibrium ($P>0.05$), indicating that the samples were representative of the population (**Table 1**).

CYP2C19 metabolic phenotype distribution: Among the 430 patients, the metabolic phenotype of CYP2C19 was mainly moderate metabolic type, with 247 cases (57.44%). CYP2C19*17/*3 and CYP2C19*3/*3 genotypes were not found. The genotype distribution of different metabolic types is summarized in **Table 2**. In addition, there was no significant difference in age, sex, smoking history, concomitant disease, or combined use of proton pump inhibitor (PPI) among patients with different metabolic types ($P>0.05$). However, the body weight in EM and UM groups was notably lower than that in IM and PM groups ($P<0.05$), but no notable difference was found between EM and UM groups or between IM and PM groups in body weight ($P>0.05$, **Table 3**).

Comparison in baseline data of patients with different ABCB1-3435C>T genotypes: In terms of ABCB1-3435C>T, there were 164 cases of wild type (CC) (38.14%), 182 cases of mutant heterozygous type (CT) (42.33%), and 84 cases of mutant homozygous type (TT) (19.53%).

Table 1. Hardy-Weinberg genetic equilibrium test results of CYP2C19, ABCB1, and PON1 gene distribution

Gene	Genotype	n (%)	Allele	n (%)
CYP2C19*2	GG	148 (34.42)	G	527 (61.28)
	GA	231 (53.72)	A	333 (38.72)
	AA	51 (11.86)		
CYP2C19*3	GG	382 (88.84)	G	811 (94.30)
	GA	47 (10.93)	A	49 (5.70)
	AA	1 (0.23)		
CYP2C19*17	CC	417 (96.98)	C	845 (98.26)
	CT	11 (2.56)	T	15 (1.74)
	TT	2 (0.47)		
ABCB1-3454C>T	CC	164 (38.14)	C	510 (59.30)
	CT	182 (42.33)	T	350 (40.70)
	TT	84 (19.53)		
PON1-576G>A	GG	142 (33.02)	G	506 (58.84)
	GA	222 (51.63)	A	354 (41.16)
	AA	66 (15.35)		

CC, wild type; CT, mutant heterozygous type; TT, mutant homozygous type; GG, wild type; GA, mutant heterozygous type; AA, mutant homozygous type.

Table 2. Gene frequency distribution of different metabolic phenotypes of CYP2C19 (n=430)

Metabolic phenotype	n (%)	Genotype	n	%
Fast metabolic type (EM)	108 (25.12)	CYP2C19*1/*1	108	25.12%
Ultra-fast metabolic type (UM)	8 (1.86)	CYP2C19*1/*17	6	1.40%
		CYP2C19*17/*17	2	0.47%
Moderate metabolic type (IM)	247 (57.44)	CYP2C19*1/*2	211	49.07%
		CYP2C19*1/*3	32	7.44%
		CYP2C19*17/*2	4	0.93%
		CYP2C19*17/*3	-	-
Slow metabolic type (PM)	67 (15.58)	CYP2C19*2/*2	51	11.86%
		CYP2C19*2/*3	16	3.72%
		CYP2C19*3/*3	-	-

According to the comparison of baseline data among patients with different genotypes, the age of patients in the TT group was significantly younger than that of the CC and CT groups (P<0.05). However, no notable difference was found in age between the CC and CT groups (P>0.05), and there were no statistical differences among groups regarding other data (P>0.05, **Table 4**).

Comparison in baseline data of patients with different PON1-576G>A genotypes: In terms of PON1-576G>A, there were 142 cases of wild type (GG) (33.02%), 222 cases of mutant heterozygous type (GA) (51.63%), and 66 cases of mutant homozygous type (AA) (15.35%). No notable differences were found in the baseline data among patients with different genotypes (P>0.05, **Table 5**).

Clinical implications of genotype-based drug adjustment

Comparison of re-admission between adjusted and not adjusted groups: According to genetic testing results, 279 patients were suggested to adjust the medication regimen, of which 109 patients received adjustment. All these patients were followed up for one year. The follow-up results showed that in the adjusted group, 5 patients were re-admitted for drug adjustment and 104 patients were not, while in the not

Table 3. Comparison of basic data of patients with CYP2C19 metabolic phenotype

Item	Total (n=430)	EM (n=108)	UM (n=8)	IM (n=247)	PM (n=67)	P
Sex (male), n (%)	268 (62.33)	66 (61.11)	3 (37.50)	157 (63.56)	42 (62.69)	0.506
Age (years), $\bar{x} \pm s$	69.80±11.99	68.89±13.57	71.38±11.19	70.04±11.18	70.16±12.15	0.809
Weight (kg), $\bar{x} \pm s$	65.47±9.53	62.44±9.73	61.38±7.52	66.45±9.33	67.25±8.88	0.008
Complicated with hypertension, n (%)	323 (75.12)	80 (74.07)	7 (87.50)	179 (72.47)	57 (85.07)	0.157
Complicated with diabetes mellitus, n (%)	139 (32.33)	40 (37.04)	4 (50.00)	80 (32.39)	15 (22.39)	0.153
Smoking history, n (%)	124 (28.84)	30 (27.78)	4 (50.00)	75 (30.36)	15 (22.39)	0.328
Combined use of PPI, n (%)	193 (44.88)	38 (35.19)	2 (25.00)	121 (48.99)	32 (47.76)	0.063

EM, Fast metabolic type; UM, Ultra-fast metabolic type; IM, Moderate metabolic type.

Table 4. Comparison of baseline data of patients with ABCB1-3435C>T genotype

Item	Total (n=430)	CC (n=164)	CT (n=182)	TT (n=84)	P
Sex (male), n (%)	268 (62.33)	94 (57.32)	114 (62.64)	60 (71.43)	0.094
Age (years), $\bar{x} \pm s$	69.80±11.99	71.81±11.45	69.47±11.63	66.56±12.98	0.004
Weight (kg), $\bar{x} \pm s$	65.47±9.53	65.20±9.62	65.57±9.04	65.80±10.33	0.881
Complicated by hypertension, n (%)	323 (75.12)	126 (76.83)	136 (74.73)	61 (72.62)	0.758
Complicated by diabetes mellitus, n (%)	139 (32.33)	59 (35.98)	52 (28.57)	28 (33.33)	0.331
Smoking history, n (%)	124 (28.84)	49 (29.88)	50 (27.47)	25 (29.76)	0.902
Combined use of PPI, n (%)	193 (44.88)	77 (46.95)	82 (45.05)	34 (40.48)	0.623

CC, wild type; CT, mutant heterozygous type; TT, mutant homozygous type.

Table 5. Comparison of baseline data of patients with PON1-576G>A genotype

Item	Total (n=430)	GG (n=142)	GA (n=222)	AA (n=66)	P
Sex (male), n (%)	268 (62.33)	83 (58.45)	143 (64.41)	42 (63.64)	0.504
Age (years), $\bar{x} \pm s$	69.80±11.99	70.15±11.26	69.24±12.37	70.88±12.11	0.565
Weight (kg), $\bar{x} \pm s$	65.47±9.53	65.57±8.56	65.63±9.75	64.74±10.65	0.792
Complicated by hypertension, n (%)	323 (75.12)	106 (74.65)	163 (73.42)	54 (81.82)	0.378
Complicated by diabetes mellitus, n (%)	139 (32.33)	50 (35.21)	64 (28.83)	25 (37.88)	0.257
Smoking history, n (%)	124 (28.84)	33 (23.24)	73 (32.88)	18 (27.27)	0.134
Combined use of PPI, n (%)	193 (44.88)	62 (43.66)	98 (44.14)	33 (50.00)	0.659

GG, wild type; GA, mutant heterozygous type; AA, mutant homozygous type.

Table 6. Comparison of the second admission between the adjusted group and no adjustment group (n)

Group	Re-admission	No re-admission	Total	X^2	P
Adjustment	5	104	109	42.07	<0.0001
No adjustment	67	103	170		
Total	72	207	279		

adjusted group, 67 patients were re-admitted for drug adjustment, and 103 patients did not receive adjustment again. According to genetic testing results, patients who received their initial adjustment were more stable and less likely to need to be re-admitted for medication adjustment. There was a significant difference in the number of secondary admissions between the two groups (P<0.0001, **Table 6**). The 279 patients who were suggested for medication adjustment included 136 patients with type II, 137 patients with type III, 2 with type IV, and 4 with type V. Comparing the number of re-admissions, we found that the re-admission rate in patients with type III who received the initial adjusted medication was significantly reduced (P<0.0001, **Table 7**), while there was

Table 7. Pairwise comparison in patients with the same genotype (n)

Genotype	Drug adjustment	Re-admission	No re-admission	Total	X^2	P
Type II	Adjustment	2	28	136	0.55	0.46
	No adjustment	12	94			
Type III	Adjustment	2	71	137	97.16	<0.0001
	No adjustment	55	9			
Type IV	Adjustment	1	1	2	-	-
	No adjustment	0	0			
Type V	Adjustment	0	4	4	-	-
	No adjustment	0	0			
Total		72	207	279		

Table 8. Comparison of baseline data between the two groups (n)

Item	Total (n=279)	Adjustment (n=109)	No adjustment (n=170)	P
Sex (male), n (%)	182 (65.23)	70 (64.22)	112 (61.54)	0.776
Age (years), $\bar{x} \pm s$	69.07±11.81	68.54±10.67	69.41±12.48	0.548
Weight (kg), $\bar{x} \pm s$	66.06±10.04	65.50±9.60	66.42±10.30	0.455
Complicated by hypertension, n (%)	213 (76.34)	80 (73.39)	133 (78.24)	0.353
Complicated by diabetes mellitus, n (%)	90 (32.26)	36 (33.03)	54 (31.76)	0.825
Smoking history, n (%)	85 (30.47)	39 (35.78)	46 (27.06)	0.122
Combined use of PPI, n (%)	128 (45.88)	60 (55.05)	68 (40.00)	0.013

Table 9. Comparison of re-admission among patients with different genotype combinations (n)

Genotype	Re-admission	No re-admission	Total	X^2	P
Type II	36	157	193	4.357	0.225
Type III	58	171	229		
Type IV	1	2	3		
Type V	0	5	5		
Total	95	335	430		

no difference in type II, and the number of types IV and V was too small to be counted. The above data collectively indicate that gene sequencing-guided drug use significantly reduces the number of re-admissions of patients.

According to a comparison of baseline data between the two groups, the adjusted group had more patients with the combined use of PPI than the no adjustment group (P=0.013), and no notable differences were found in the other clinical baseline data between the two groups (P>0.05, **Table 8**).

Comparison of re-admission in patients with different genotype combinations: According to a comprehensive analysis of all patients (including the patients who were initially advised to adjust their medications and those who were not), the study identified no type I patients, 193 type II patients, and 229 type III patients. Three patients with type IV demonstrated an increased production of active metabolites, enhanced inhibition of platelet aggregation, and a higher risk of bleeding, so these patients required a reduction of dosage or a change in treatment. There were also 5 type V patients, who showed varying responses to clopidogrel, with some genotypes showing increased efficacy and others showing decreased efficacy. As a result, the conventional dose was maintained after a comprehensive assessment. The patients were followed up for one year, and there were no significant differences in outcome among those with different genotype combinations after adjustment of antiplatelet therapy during one year of follow-up (P>0.05, **Table 9**).

Discussion

Genomics and precision medicine have made remarkable progress, leading to a surge of

interest in studying CYP2C19 gene polymorphism [19]. The significance of CYP2C19 in drug efficacy and interactions cannot be overstated, especially regarding cardiovascular medications. The influence of this enzyme is profound, underscoring the need for genotyping patients to tailor treatments effectively [20]. Clopidogrel, a cornerstone of antiplatelet therapy, is subject to various efficacy-determining factors, notably the patient's genetic makeup [21]. The future of medicine is likely to embrace individualized treatment approaches. By identifying a patient's genotype, clinicians can anticipate their response to clopidogrel, allowing for preemptive dosage adjustments or alternative therapeutic strategies. This proactive approach can mitigate potential side effects and enhance treatment efficacy [22]. Consequently, genotyping for CYP2C19 gene polymorphism is indispensable for patients on medications such as clopidogrel.

This study focused on the CYP2C19 gene polymorphism in over 400 patients from the Wuhu region. The findings revealed a high prevalence of heterozygous mutations associated with functional impairments. Clinical vigilance is warranted: the predominant CYP2C19 enzyme type in the Wuhu population is moderate in metabolic activity, with reduced enzymatic function, possibly diminishing the body's ability to metabolize clopidogrel effectively. Standard dosing regimens, such as the conventional 75 mg/day, may only partially convert clopidogrel into its active form, thereby diminishing its antiplatelet effects and increasing the risk of cardiovascular adverse events. It is recommended that thromboelastography be conducted during treatment to assess the drug's efficacy and tailor the therapeutic plan based on the patient's clinical presentation and other diagnostic findings. Furthermore, the study did not find any significant differences in the distribution of CYP2C19 genotypes and metabolic phenotypes among patients of different genders and ages in the Wuhu area, suggesting that the CYP2C19 gene polymorphism, as it relates to clopidogrel metabolism, is not affected by age or sex in this region. These findings align with reports from other geographic areas [23, 24]. Studies have shown that the allele mutation frequencies of CYP2C19*2, yp2c19*3 and CYP2C19*17 in Asian populations are 28%-35%, 2%-7%, and 0.5%-4%, respectively, which are similar to the gene frequency in this study [25, 26].

The ABCB1 gene primarily encodes MDR1, a pivotal protein involved in the intestinal absorption of numerous drugs, including the antiplatelet agent clopidogrel [27]. During clopidogrel therapy, individuals carrying the T allele at the 3435C>T locus were found to be at an elevated risk for cardiovascular events compared to non-carriers [28]. The ABCB1-3435C>T polymorphism is another genetic marker that warrants consideration when tailoring clopidogrel dosing regimens. In this study, although the prevalence of TT homozygous mutations was low among patients in the Wuhu area, the T allele's frequency was notably high. Patients with the TT homozygous mutation exhibit reduced intestinal absorption of clopidogrel. Even in the presence of a wild-type CYP2C19 enzyme, a standard dose of clopidogrel (75 mg/day) may not achieve optimal antiplatelet effects. Consequently, increasing the dosage or exploring alternative antiplatelet treatment strategies may be advisable. However, findings by Park et al. suggested that the ABCB1-3435C>T genetic variant did not significantly influence clopidogrel's antiplatelet responsiveness in the Asian population, indicating that further research is needed to elucidate the role of ABCB1 gene polymorphism in the formulation of clopidogrel treatment plans [29]. The study found that among patients treated with clopidogrel, carriers of the ABCB1 3435T allele were closely associated with clopidogrel resistance and higher incidence of major adverse cardiovascular events [30]. This genotype affects the absorption of clopidogrel *in vivo*, which has a certain impact on the antiplatelet activity of clopidogrel. We should pay attention to the clinical efficacy of clopidogrel in such patients and achieve a clinical therapeutic effect by adjusting the dose of clopidogrel.

PON1, a liver protein instrumental in the bioactivation of clopidogrel into its active metabolite, plays a crucial role in the drug's clinical efficacy. This study observed no significant variation in the genotype and allele frequency of PON1-576G>A among patients of different genders and ages. The impact of PON1 gene mutations on clopidogrel activity and cardiovascular risk remains an area of ongoing investigation [31]. PON1 is one of the key enzymes in the oxida-

tive metabolism of clopidogrel. PON1 Q192R gene polymorphism is an important part affecting PON1 enzyme activity, which is significantly associated with the efficacy of clopidogrel [32]. The study found that the PON1 Q192R polymorphism was closely related to platelet reactivity and the occurrence of ischemic events [33]. It was found that the PON1 A allele was an independent risk factor for platelet hyperreactivity in patients after PCI [34]. This study revealed that approximately 60% of patients in the Wuhu area possessed GA and AA genotypes, underscoring the need for further research into the correlation between PON1 gene polymorphism and the efficacy and safety of clopidogrel.

Additionally, this research highlighted the impact of re-formulating medication regimens. Data indicated that 279 patients with specific genotypes required medication adjustments, with 109 accepted the proposed changes. Over a one-year follow-up period, 72 patients were re-hospitalized for drug adjustments. There was a marked difference in re-admission rates between the adjusted group and the no adjustment group. This finding underscores the significance of personalized medication strategies, particularly for antiplatelet therapy. Furthermore, it is noteworthy that patients who accepted the adjusted regimen had a significantly higher rate of concomitant use of proton pump inhibitors (PPIs) compared to those on the original regimen, attributing to PPIs' influence on CYP2C19, potentially affecting clopidogrel metabolism. However, other clinical baseline data did not show significant differences between the two groups, suggesting that factors beyond PPI use had minimal impact on these outcomes.

This study recognizes its limitations, including an inpatient-only sample that may not represent the general population and a predominantly Han Chinese demographic that limits ethnic comparison. The single-center design and constrained follow-up duration also restricted the generalizability and depth of analysis regarding clopidogrel's efficacy and safety in genetic testing outcomes.

Conclusion

Assessment of clopidogrel-related absorption and metabolic genotypes in the Wuhu region revealed significant individual variability. This genetic diversity may translate into varying enzymatic activities among patients with distinct genotypes, influencing the efficacy and safety of clopidogrel treatment. Clinical pharmacists should consider a patient's genetic profile in crafting personalized antiplatelet therapy protocols to optimize therapeutic benefits while minimizing adverse effects.

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Disclosure of conflict of interest

None.

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