

SUPPLEMENTARY DATA

Supplementary Table 1. Baseline characteristics

Variables	DOUBLE group (n = 39)	TRIPLE group (n = 41)	P
Age, years	62 ± 10	64 ± 10	0.229
Male, n (%)	26 (66.7)	29 (70.7)	0.695
Body mass index, kg/m ²	24.7 ± 3.3	24.7 ± 2.7	0.914
Method of glucose control, n (%)			
Oral hypoglycemic agent	32 (82.1)	34 (82.9)	0.918
Insulin	4 (10.3)	1 (2.4)	0.195
Clinical presentation, n (%)			0.971
Stable angina	12 (30.8)	9 (22.0)	
Unstable angina	9 (23.1)	11 (26.8)	
Acute myocardial infarction	18 (46.1)	21 (51.2)	
Clopidogrel use, n (%)			0.968
300-mg loading	16 (41.0)	17 (41.5)	
Chronic therapy (≥ 5 days)	23 (59.0)	24 (58.5)	
Risk factor, n (%)			
Hypertension	25 (64.1)	31 (75.6)	0.262
Hypercholesterolemia	13 (33.3)	14 (34.1)	0.939
Current smoking	17 (43.6)	17 (41.5)	0.478
Chronic kidney disease	5 (12.8)	4 (9.8)	0.734
History, n (%)			
Previous myocardial infarction	5 (12.8)	6 (14.6)	0.814
Previous PCI	6 (15.4)	10 (24.4)	0.314
Previous bypass surgery	1 (2.6)	2 (4.9)	1.000
Previous stroke	2 (5.1)	4 (9.8)	0.676
Concomitant medications, n (%)			
Statin	37 (94.9)	37 (90.2)	0.676
CYP3A4-metabolized	33 (84.6)	30 (73.2)	0.211
Beta blocker	32 (82.1)	33 (80.5)	0.858
Angiotensin blocker	34 (87.2)	35 (85.4)	0.814
Calcium channel blocker	10 (25.6)	7 (17.1)	0.349
Proton pump inhibitor	2 (5.1)	4 (9.8)	0.676
Glycoprotein IIb/IIIa inhibitor, n (%)	1 (2.6)	2 (4.9)	1.000
LV ejection fraction ≤ 45%, n (%)	5 (12.8)	4 (9.8)	0.734
Hemoglobin, g/dl	13.7 ± 1.7	13.4 ± 1.8	0.370
Platelet count, x10 ³ /mm ³	260 ± 68	275 ± 83	0.356
Hb A _{1c} , %	7.8 ± 1.5	7.4 ± 1.2	0.137
GFR, ml/min/1.73 m ² (MDRD)	89 ± 29	87 ± 28	0.781
Total cholesterol, mg/dl	182 ± 44	170 ± 52	0.274
Target vessel, n (%)			0.079
Left anterior descending	14 (35.9)	21 (51.2)	
Left circumflex artery	9 (23.1)	6 (14.6)	
Right coronary artery	16 (41.0)	12 (29.3)	
Left main	0 (0)	2 (4.9)	
AHA/ACC lesion type B2/C	22 (56.4)	24 (58.5)	0.848
Multivessel intervention, n (%)	12 (30.8)	11 (26.8)	0.697
Intervention method, n (%)			0.611
Drug-eluting stent	37 (94.9)	40 (97.6)	
Paclitaxel-eluting	10 (25.6)	8 (19.5)	
Sirolimus-eluting	25 (64.1)	28 (68.3)	
Zotalimus-eluting	1 (2.6)	0 (0)	
Everolimus-eluting	1 (2.6)	4 (9.8)	
Ballooning only	2 (5.1)	1 (2.4)	
Number of stent	1.6 ± 0.8	1.8 ± 1.3	0.203

PCI = percutaneous coronary intervention; CYP = cytochrome P450; LV = left ventricular; Hb A_{1c} = hemoglobin A_{1c}; GFR = glomerular filtration rate; MDRD = Modification of Diet in Renal Disease; AHA = American heart association; ACC = American college of cardiology.

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Supplementary Table 2. Platelet function measurements

Variables	DOUBLE group (n = 39)	TRIPLE group (n = 41)	P
Maximal PA, %			
20 μ M ADP			
Baseline	57.5 \pm 15.4	60.7 \pm 13.0	0.320
30-day follow-up	44.8 \pm 15.8	37.7 \pm 12.4	0.029
5 μ M ADP			
Baseline	45.6 \pm 16.9	48.6 \pm 13.7	0.393
30-day follow-up	32.8 \pm 13.3	26.8 \pm 9.3	0.023
6 μ g/ml collagen			
Baseline	60.7 \pm 18.1	64.3 \pm 13.4	0.318
30-day follow-up	51.9 \pm 18.6	38.6 \pm 13.2	< 0.001
Final PA, %			
20 μ M ADP			
Baseline	47.7 \pm 22.4	53.5 \pm 16.8	0.188
30-day follow-up	29.1 \pm 20.0	21.6 \pm 12.9	0.049
5 μ M ADP			
Baseline	36.0 \pm 20.4	40.4 \pm 16.4	0.290
30-day follow-up	18.4 \pm 14.2	14.0 \pm 8.5	0.097
6 μ g/ml collagen			
Baseline	59.1 \pm 18.8	62.3 \pm 15.1	0.389
30-day follow-up	49.9 \pm 19.8	36.0 \pm 15.5	0.001
VerifyNow P2Y12 assay			
P2Y12 reaction units			
Baseline	255 \pm 79	262 \pm 74	0.666
30-day follow-up	182 \pm 76	154 \pm 66	0.088
HPR prevalence, n (%)			
5 μ M ADP-maximal PA > 46%			
Baseline	16 (41.0)	25 (61.0)	0.117
30-day follow-up	8 (20.5)	0 (0)	0.002
P2Y12 reaction units > 235			
Baseline	23 (59.0)	29 (70.7)	0.270
30-day follow-up	10 (25.6)	5 (12.2)	0.124

PA = platelet aggregation; ADP = adenosine diphosphate; HPR = high on-treatment platelet reactivity

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Supplementary Table 3. Distributions of allele, genotype and metabolic phenotype

Gene	Allele	Frequency (%)	HWE, X^2 -test	Genotype	Predicted phenotype	Distribution, n (%)		
						Total n, (%)	DOUBLE group n, (%)	TRIPLE group n, (%)
<i>CYP2C19</i>	*1	56.9	-	*1/*1	Extensive metabolizer	26 (32.5)	14 (35.9)	12 (29.3)
	*2	32.5	0.079	*1/*2	Intermediate metabolizer	28 (35.0)	11 (28.2)	17 (41.4)
	*3	10.6	1.126	*1/*3	Intermediate metabolizer	11 (13.8)	7 (17.9)	4 (9.8)
				*2/*2	Poor metabolizer	9 (11.2)	4 (10.3)	5 (12.2)
				*2/*3	Poor metabolizer	6 (7.5)	3 (7.7)	3 (7.3)
				*3/*3	Poor metabolizer	0 (0)	0 (0)	0 (0)
<i>CYP3A5</i>	*1	22.5	-	*1/*1	Expresser	5 (6.2)	3 (7.7)	2 (4.9)
	*3	77.5	0.371	*1/*3	Expresser	26 (32.5)	14 (35.9)	12 (29.3)
				*3/*3	Non-expresser	49 (61.3)	22 (56.4)	27 (65.8)
<i>ABCB1</i>	*C	63.1	-	CC	High expression	34 (42.5)	17 (43.6)	17 (41.5)
<i>C3435T</i>	*T	36.9	1.017	CT	Intermediate expression	33 (41.2)	15 (38.5)	18 (43.9)
				TT	Poor expression	13 (16.3)	7 (17.9)	6 (14.6)

HWE = Hardy-Weinberg equilibrium; *CYP* = cytochrome P450; *ABCB1* = adenosine 5'-triphosphate-binding cassette gene B1.

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Supplementary Table 4. Effect of double-dose clopidogrel: determinants of decrease in 20 μ M ADP-induced maximal platelet aggregation (n = 39)

Variables	Univariate analysis			Multivariate analysis		
	β coefficient			β coefficient		
	Value	SE	<i>P</i>	Value	SE	<i>P</i>
<i>CYP2C19</i> loss-of-function allele	-7.8	3.1	0.015	-7.9	2.8	0.008
1 loss-of-function allele carriage	-5.4	5.1	0.301	-5.4	4.7	0.162
2 loss-of-function alleles carriage	-8.3	2.7	0.006	-8.3	2.7	0.007
<i>ABCB1</i> 3435 <i>TT</i> vs. <i>CC/CT</i> type	-9.3	6.0	0.128	-4.8	5.5	0.391
Platelet count (per $10^3/\text{mm}^3$)	-0.1	0.0	0.080	-0.1	0.0	0.066

ADP = adenosine diphosphate; SE = standard error, *CYP* = cytochrome P450; *ABCB1* = adenosine 5'-triphosphate-binding cassette gene

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Supplementary Table 5. Effect of adding cilostazol: determinants of decrease in 20 μ M ADP-induced maximal platelet aggregation (n = 41)

Variables	Univariate analysis			Multivariate analysis		
	β coefficient			β coefficient		
	Value	SE	<i>P</i>	Value	SE	<i>P</i>
Age \geq 60 years	9.3	3.6	0.014	5.4	3.6	0.149
Hypercholesterolemia	-5.8	3.8	0.131	-5.5	3.4	0.109
Current smoking	-7.7	3.5	0.035	-6.8	3.5	0.058
CYP3A4-metabolized statin	6.3	4.0	0.124	6.6	3.6	0.079
LV ejection fraction \leq 45%	-8.5	6.1	0.167	-8.0	5.5	0.152

ADP = adenosine diphosphate; SE = standard error, CYP = cytochrome P450; LV = left ventricular.