

Association of Renal Function and Platelet Reactivity During DAPT Maintenance Phase after PCI

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Background

- Chronic kidney disease (CKD)
 - A pandemic public health problem. 500 million people worldwide estimated to have some kind of kidney injury.
 - 5% of Korean adults suffer from CKD with eGFR <60 mL/min/1.73 m².
 - The incidence of CKD may increase with population aging and diabetes progression.

Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m ²) for 3 months or longer
RI1	Normal or Increased GFR	>90
RI2	Mild reduction in GFR	60-89
RI3	Moderate reduction in GFR	30-59
RI4	Severe reduction in GFR or kidney failure	<30
RI5	Dialysis	

RI renal impairment, GFR indicates glomerular filtration rate. The RI was defined according to the United States National Kidney Foundation classification

Purpose of Study

- The aim of this study was to assess residual platelet reactivity during chronic DAPT dependent on gradual triaging of RI stage with adverse clinical outcomes in a large cohort of post-PCI Korean patients.

Methods

- Inclusion criteria
 - Age: 18 ~ 80
 - DAPT (aspirin + clopidogrel) \geq 1 month.
 - Percutaneous coronary intervention

Methods

- Exclusion criteria
 - Hemodynamic instability,
 - Malignancies,
 - Active bleeding or bleeding diathesis,
 - Contraindication to antiplatelet agents, concomitant use of warfarin or glycoprotein IIb/IIIa receptor blocker,
 - Platelet count $< 80\,000/\text{mm}^3$ or hematocrit $< 30\%$,
 - An aspartate aminotransferase (AST) concentration or an alanine aminotransferase (ALT) concentration ≥ 3 times the upper normal limit,
 - Significant hepatic dysfunction,
 - A treatment with ticlopidine, prasugrel, ticagrelor,
 - Dipyridamole,
 - Cardiac arrest and cerebrovascular injury with three months.

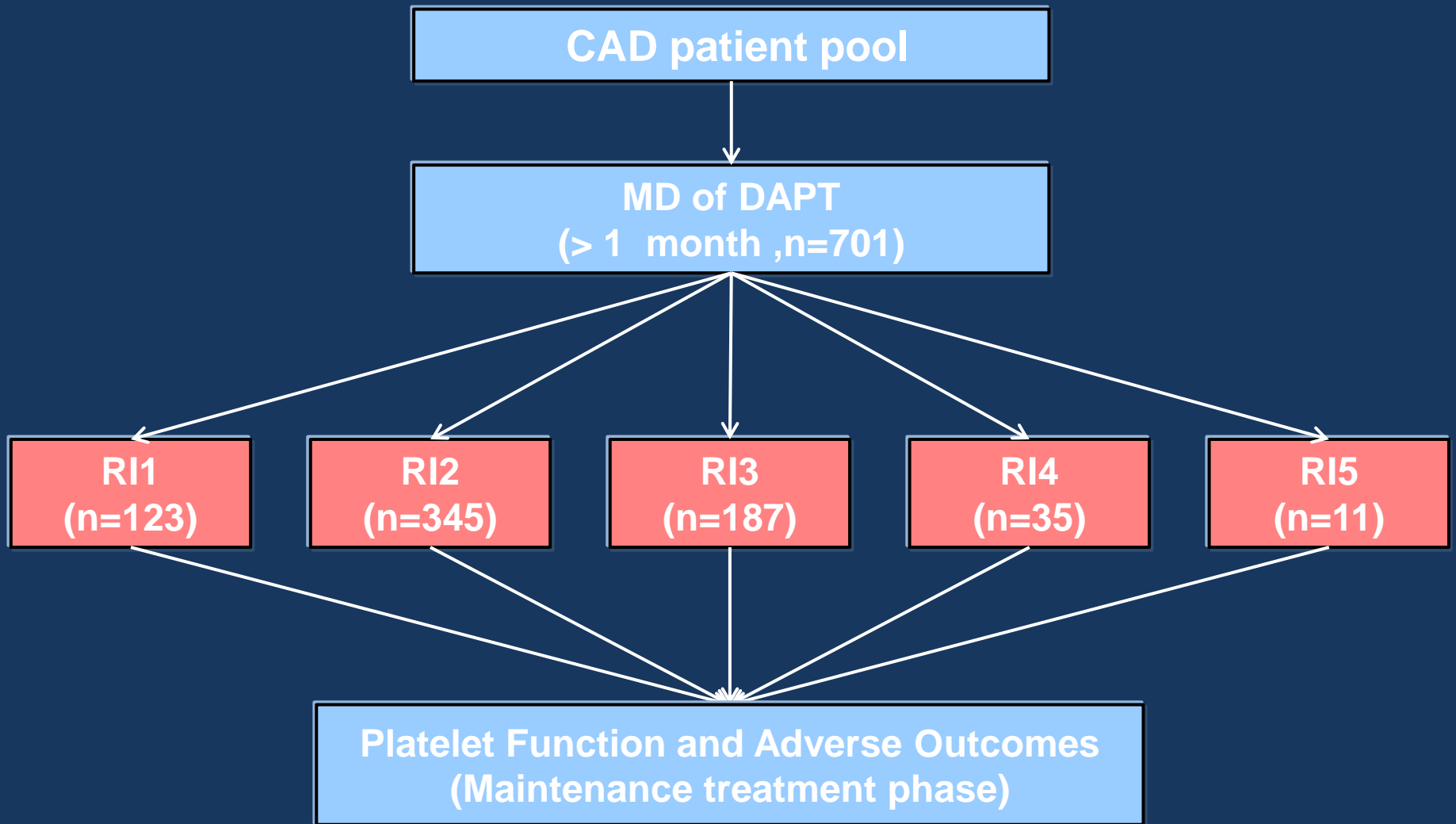
Clinical Outcomes (1 year of follow-up)

- **MACE**

- CV death, MI, stent thrombosis, stroke (ischemic and hemorrhagic).

- **Bleeding events**

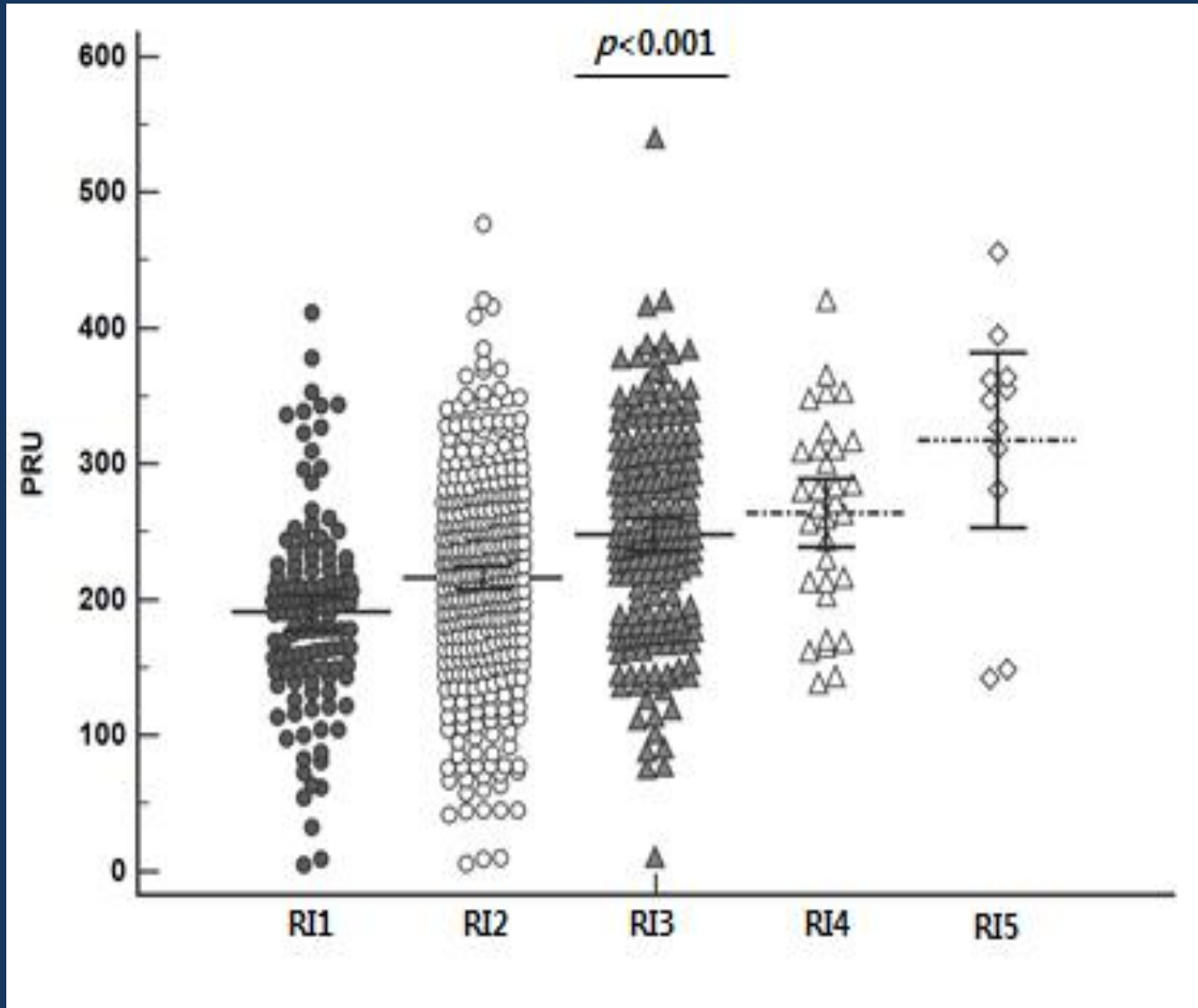
- BARC type ≥ 2 scale



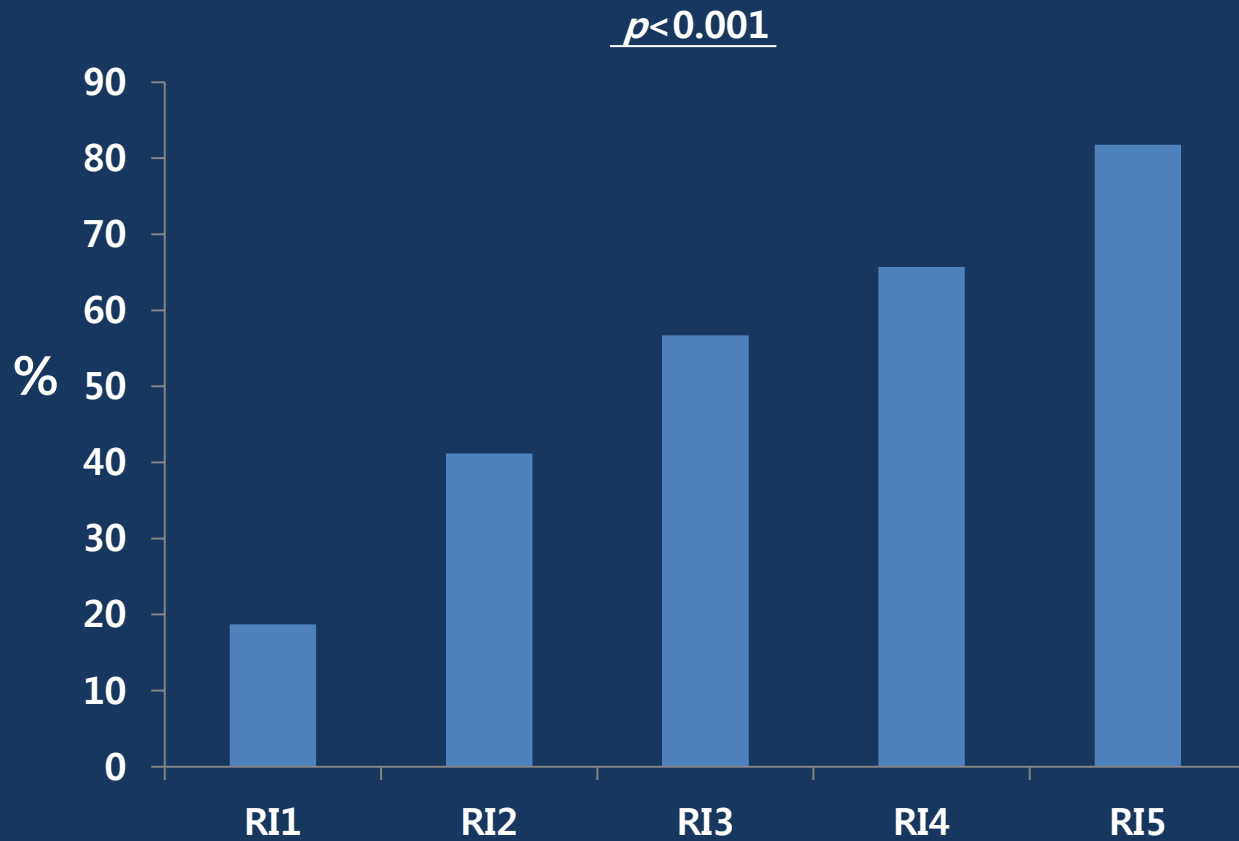
Platelet Function Measurement:
VerifyNow

Baseline Characteristics and Laboratory Data Results						
Variable	RI1 (n=123)	RI2 (n=345)	RI3 (n=187)	RI4 (n=35)	RI5 (n=11)	P-value
Age (years)	54.8±7.8	63.2±9.0	71.7±6.4	72.1±9.9	61.2±7.9	<0.001
Sex (Female %)	14(11.4)	71(20.6)	77(41.2)	18(51.4)	6(54.6)	<0.001
Body mass index (kg/m²)	26.1±3.3	24.6±2.8	23.6±3.0	23.0±2.8	23.5±2.1	<0.001
Risk factors						
Hypertension, n (%)	48(39.0)	202(58.6)	128(68.4)	28(80.0)	8(72.7)	<0.001
Diabetes, n (%)	35(28.5)	120(34.8)	77(41.2)	21(60.0)	8(72.7)	0.001
Hyperlipidemia, n (%)	68(55.3)	159(46.1)	100(53.5)	11(31.4)	1(9.1)	0.003
Smoking, n (%)	27(22.0)	49(14.2)	24(12.8)	4(11.4)	0(0.0)	0.097
Hemoglobin (g/dL)	14.3±1.4	13.5±1.6	12.4±1.8	11.5±1.6	10.3±1.5	<0.001
Platelet count, 1000/mm³	244±63	232±137	242±81	244±76	207±57	0.777
Creatinine (g/l)	0.8±0.1	1.0±0.2	1.2±1.0	3.5±3.4	6.4±3.5	<0.001
Hematocrit	41.6±3.8	40.2±20.2	36.7±5.1	34.4±4.1	30.3±4.3	0.001

Platelet activity at Maintenance Phase-I



Platelet Inhibition by VerifyNOW



VerifyNow

Logistic Regression for Platelet Inhibition

by VerifyNow

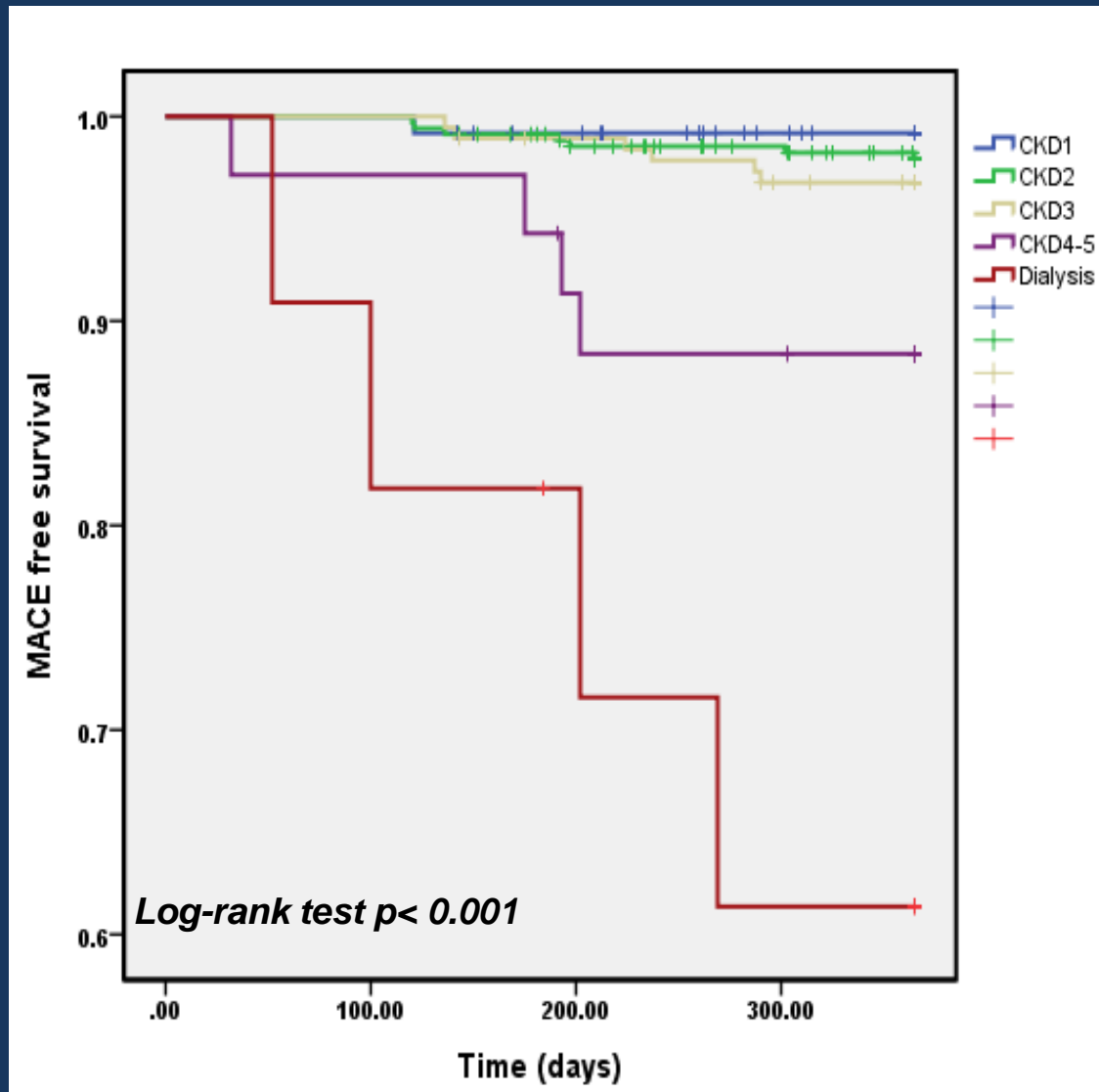
	Multivariate Logistic Regression		
	OR	95%CI	<i>p</i>
Age	1.025	1.002-1.048	0.032
Female sex	1.679	1.125-2.507	0.011
HTN	1.333	0.929-1.912	0.119
Dyslipidemia	2.757	1.924-3.951	<0.001
Smoking	0.609	0.370-1.001	0.050
RI1		reference	
RI2	2.453	1.377-4.370	0.002
RI3	3.195	1.608-6.350	0.001
RI4	4.664	1.725-12.608	0.002
RI5	12.000	2.135-67.444	0.005
p for trend	1.511	1.139-2.004	0.004

Incidence of MACE at 1 year

	RI1 (n=123)	RI2 (n=345)	RI3 (n=187)	RI4 (n=35)	RI5 (n=11)	<i>P</i> -value
CV death, n(%)	0(0.0)	0(0.0)	2(1.1)	2(5.7)	3(27.3)	<0.001
AMI, n(%)	0(0.0)	3(0.9)	0(0.0)	0(0.0)	0(0)	0.541
ST, n(%)	1(0.8)	2(0.6)	2(1.1)	2(5.7)	2(18.2)	<0.001
Stroke, n(%)	0(0.0)	4(1.2)	2(1.1)	1(2.9)	1(9.1)	0.075
MACE, n(%)	1(0.8)	9(2.7)	6(3.3)	5(14.5)	6(36.6)	<0.001

Dichotomous data are shown as n (%). RI=renal impairment; MACE=major adverse clinical events; CV= Cardiovascular; MI=myocardial infarction; ST=stent thrombosis

Cumulative Kaplan–Meier estimates for MACE dependent on eGFR



RI1: 0.8%
RI2: 2.7%
RI3: 3.3%
RI4: 14.5%
RI5: 36.6%

Incidence of MACE Dependent on eGFR by Multivariate Cox Hazard Regression Analyses

	Multivariate Cox Hazard Regression		
	HR	95%CI	P-value
RI1		Reference	
RI2	2.046	0.246-16.991	0.508
RI3	3.465	0.417-28.786	0.250
RI4	13.896	1.553-124.334	0.019
RI5	31.898	2.891-351.945	0.005

MACE=major adverse clinical events; HR=hazards ratio; CI=confidence interval; RI=renal impairment;

Incidence of Bleeding events at 1 year

	RI1 (n=123)	RI2 (n=345)	RI3 (n=187)	RI4 (n=35)	RI5 (n=11)	P-value
Bleeding, n(%)	3(2.4)	4(1.2)	1(0.5)	2(5.7)	0(0)	P= 0.143

Dichotomous data are shown as n (%). RI=renal impairment;

Summary of individual bleeding events

Patients	Sex	Age	DAPT duration (day)	BARC type	Bleeding site	RI
1	F	64	225	3a	GI	RI4
2	M	70	320	3a	Hb drop	RI3
3	M	52	309	3b	GI	RI2
4	M	43	270	3b	Minor surgery	RI1
5	M	63	212	3b	GI	RI2
6	M	74	310	3b	GI	RI4
7	M	80	186	3a	Heavy bruising	RI2
8	F	60	301	2	Mouth	RI2
9	M	52	12	3a	Right arm hematoma	RI1
10	M	51	363	3a	GI	RI1

Cumulative Multivariate Cox Hazard Regression estimates for Bleeding Events.

	Multivariate Cox Hazard Regression		
	HR	95%CI	P-value
Age	0.958	0.894-1.027	0.226
Dyslipidemia	0.256	0.053-1.228	0.088
Smoking	0.0	0.0	0.982
RI1	reference		
RI2	0.522	0.109-2.500	0.416
RI3	0.376	0.030-4.727	0.449
RI4	3.091	0.407-23.491	0.275
RI5	0.0	0.0	0.996

MACE=major adverse cardiac events; HR=hazards ratio; CI=confidence interval; RI=renal insufficiency.

Cumulative Multivariate Cox Hazard Regression estimates for MACE and Bleeding Events.

	Multivariate Cox Hazard Regression		
	HR	95%CI	P-value
Dyslipidemia	0.473	0.216-1.038	0.062
Smoking	0.207	0.028-1.527	0.122
RI1	reference		
RI2	0.907	0.292-2.820	0.866
RI3	0.974	0.285-3.335	0.967
RI4	4.225	1.180-15.127	0.027
RI5	9.149	2.226-37.602	0.002

MACE=major adverse cardiac events; HR=hazards ratio; CI=confidence interval; RI=renal insufficiency.

DISCUSSION

- **MD** of Clopidogrel
 - Higher PRU according to decreased renal function
 - Higher incidence of HPR according to decreased renal function
 - Higher MACE follow decreased renal function
 - But, not with bleeding events

Study limitations

- Insufficient numbers of enrolled CKD R14-5 and dialysis patients
- Relatively short follow-up
- No data on CYP2C19 polymorphism

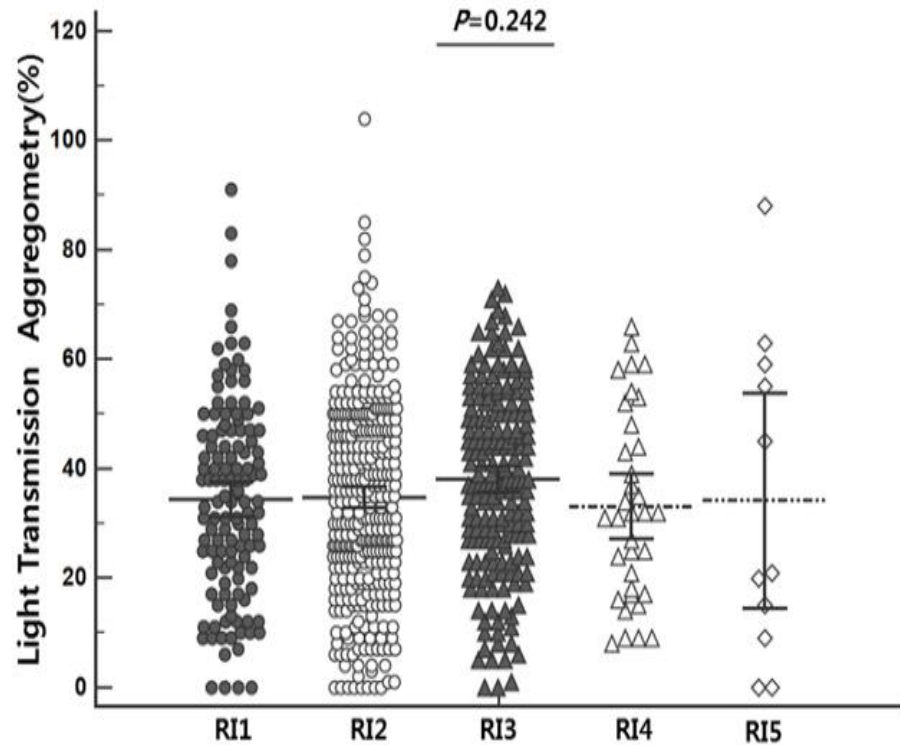
Conclusions

- Changes in GFR directly impact platelet inhibition during maintenance DAPT
- Renal impairment gradually increase adverse vascular events on top of DAPT
- Renal impairment was not associated with bleeding events.
- Large randomized trial is needed to confirm these findings

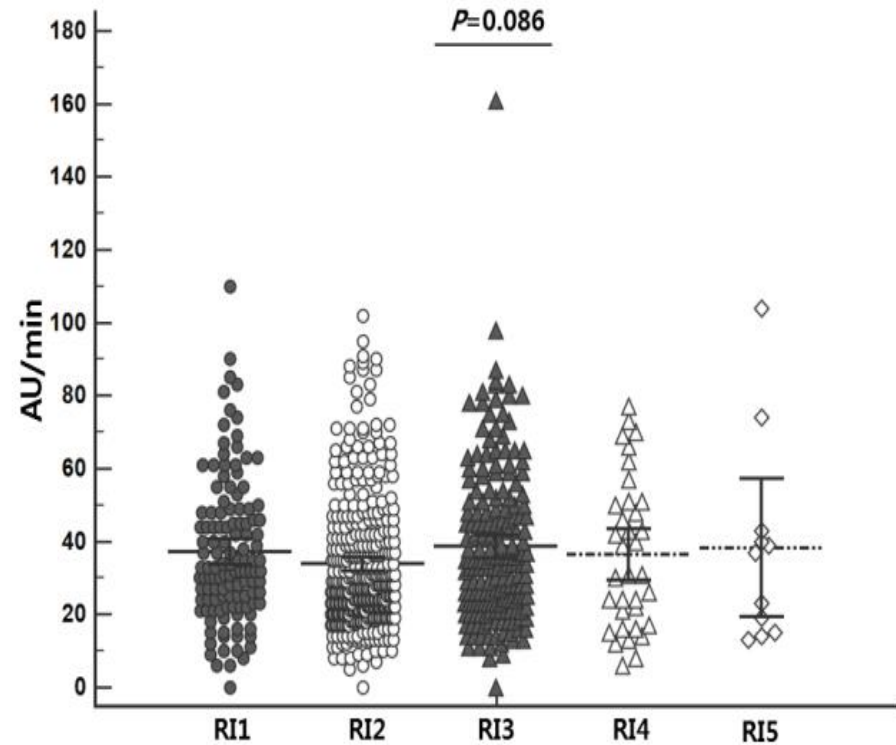


THANK YOU FOR YOUR ATTENTION

Platelet activity at Maintenance Phase-II



LTA



MEA

Platelet functions after Maintenance Dose

