JCR 2013

Case Study : Ticagrelor

Jung-Won Suh, MD, PhD

Seoul National University Bundang Hospital

P2Y12 inhibitors

	Clopidogrel	Prasugrel	Ticagrelor
Class	Thienopyridine	Thienopyridine	Triazolopyrimidine
Reversibility	Irreversible	Irreversible	Reversible
Activation	Prodrug, limited by metabolization	Prodrug, not limited by metabolization	Active drug
Onset of effect[a]	2–4 h	30 min	30 min
Duration of effect	3–10 days	5–10 days	3–4 days
Withdrawal before major surgery	5 days	7 days	5 days

[a]50% inhibition of platelet aggregation.

ESC Guidelines for the management of ACS in patients without persistent ST-segment elevation. EHJ 2011;32:2999-3054

Recommendation in guidelines

Antiplatelets in ACS

NSTE-ACS

Antiplatelet therapy		Class	Level
	ASA	I	C
	Clopidogrel (with 600-mg loading dose as soon as possible)	I	C
	Clopidogrel (for 9-12 months after PCI)	I	B
	Prasugrel	IIa	B
	Ticagrelor	I	B

STEMI

Antiplatelet therapy		Class	Level
	ASA	I	B
	Clopidogrel (with 600-mg loading dose as soon as possible)	I	C
	Prasugrel	I	B
	Ticagrelor	I	B

Acute Coronary SYNDROMES

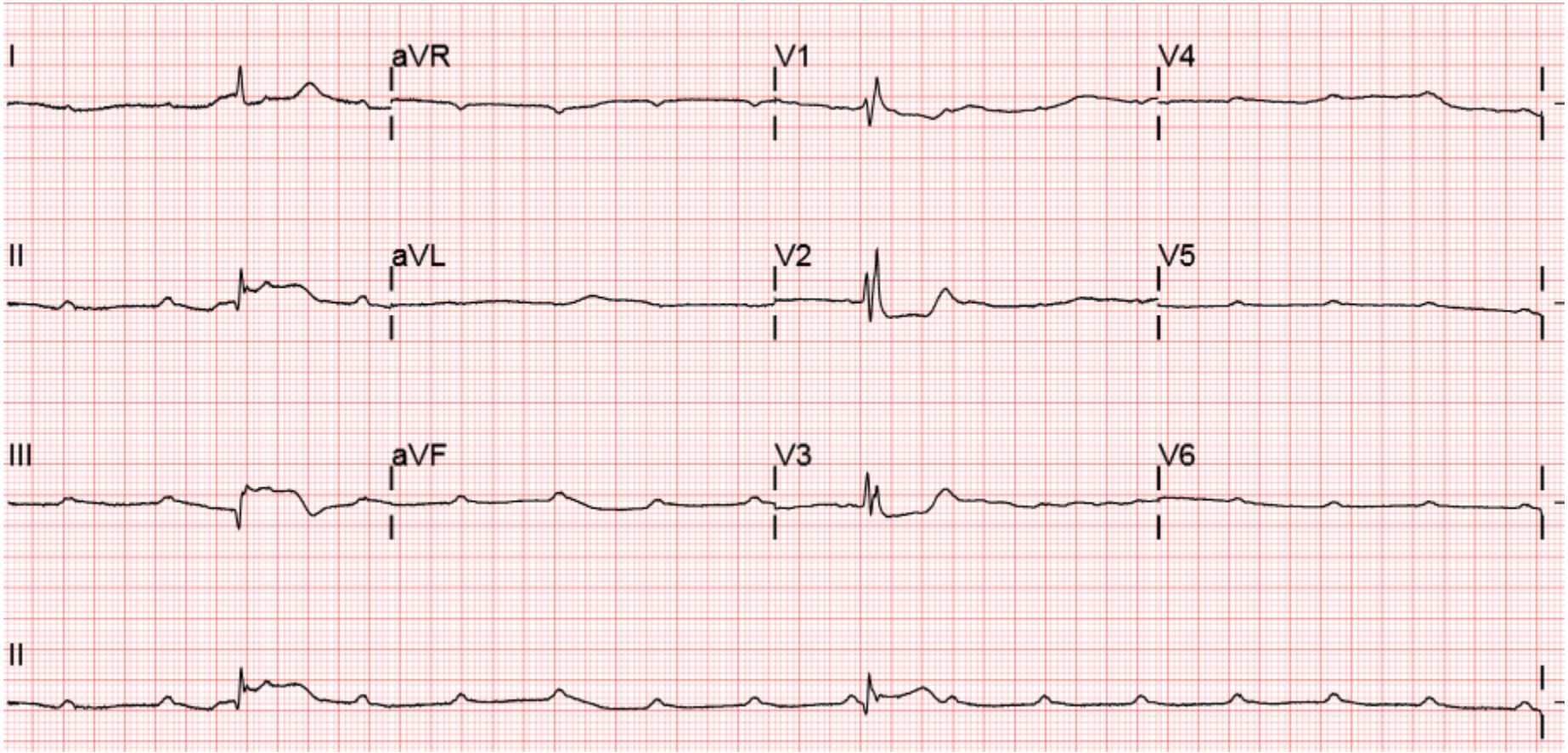
www.escardio.org/guidelines

Wijns W, et al. *Eur Heart J.* 2010 Aug 29. [Epub ahead of print]

theheart.org MedscapeCME

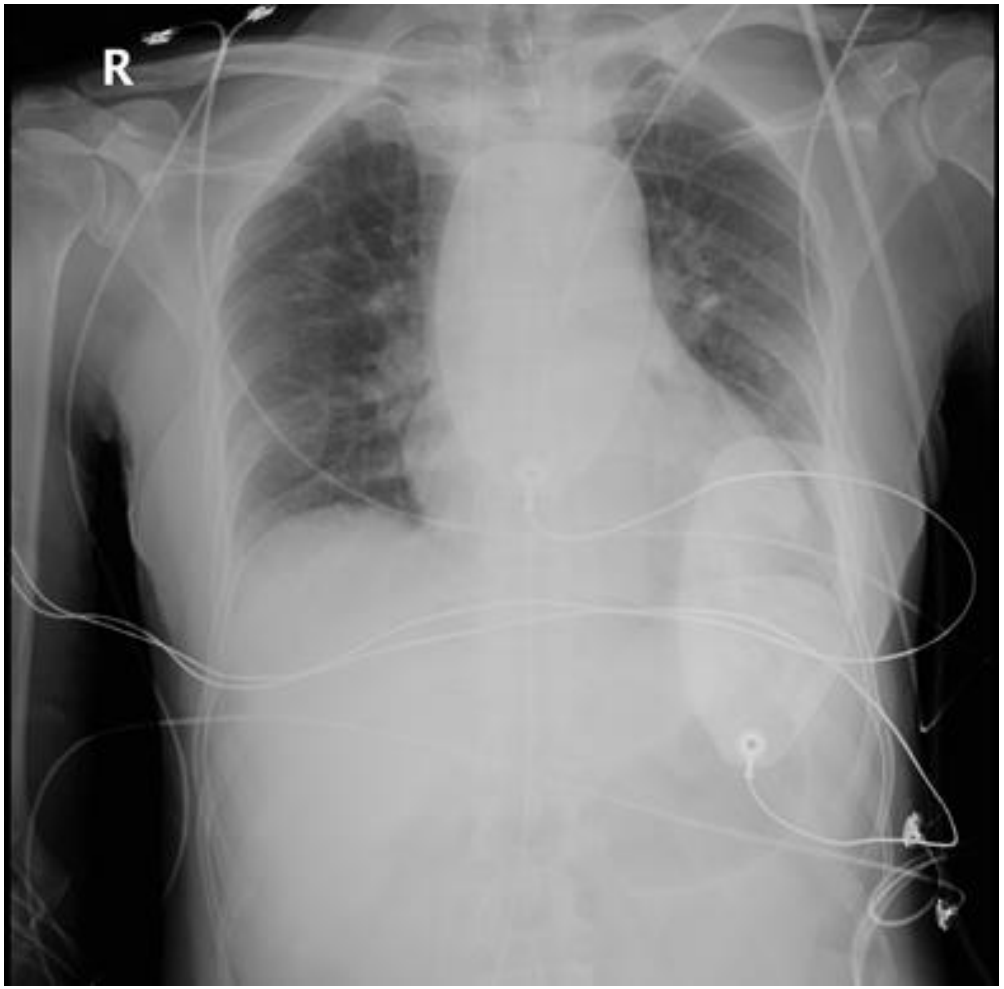
Case (M/74)

- ✓ Chief complaint : dizziness (3DA)
- ✓ PHx : dyslipidemia



Laboratory findings

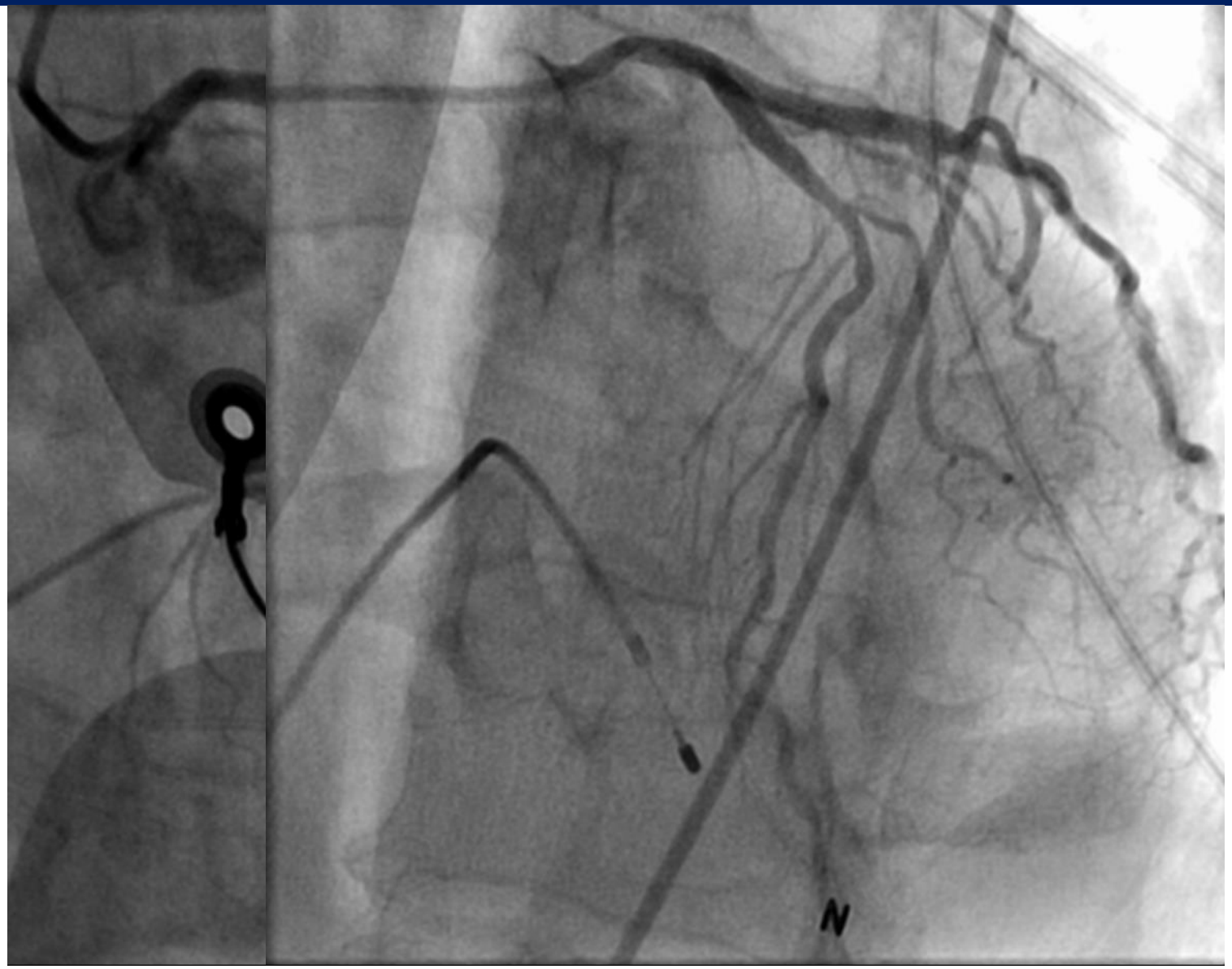
- ✓ At ER,
  - BUN/Cr 47/3.6
  - T-bil : 3.6
  - CK-MB/ Troponin-I/GOT/GPT: 8.2/31.1/1794/1714
  - Hb 12.2, Platelet 121K



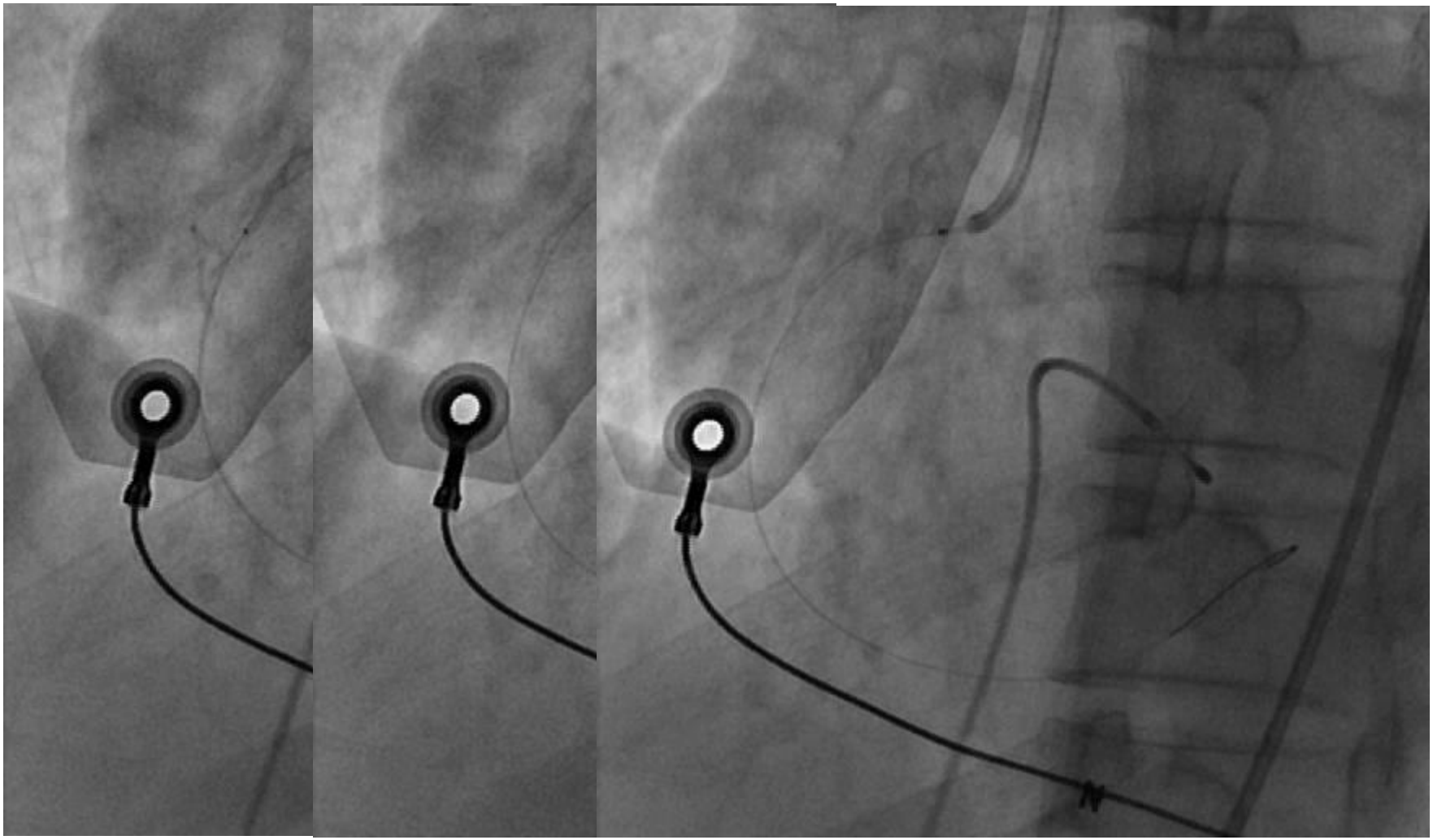
Initial antiplatelet management at ER

- ✓ Aspirin 300mg
- ✓ Clopidogrel 600mg

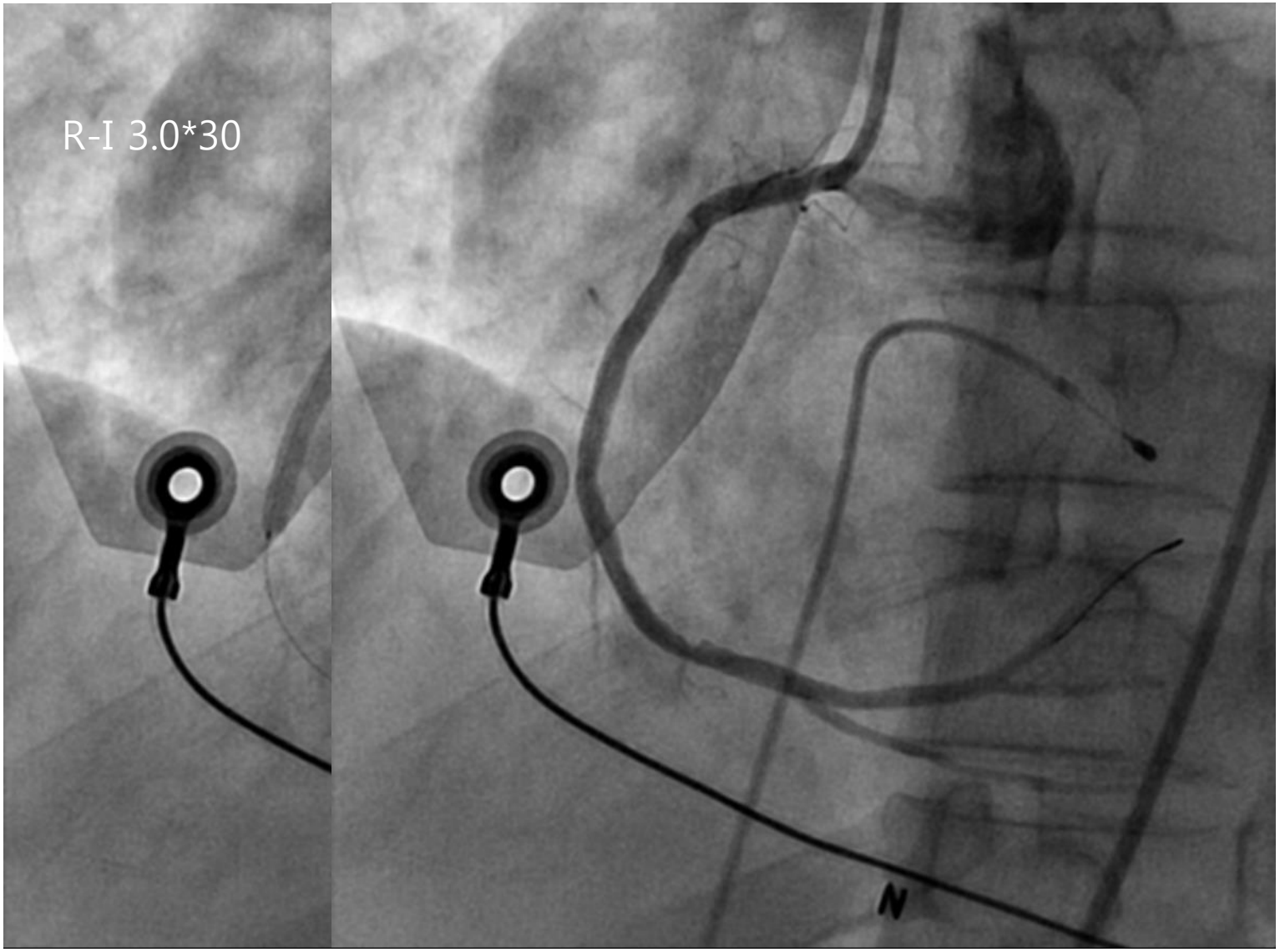
Primary PCI



Primary PCI : thrombus aspiration & IC abciximab

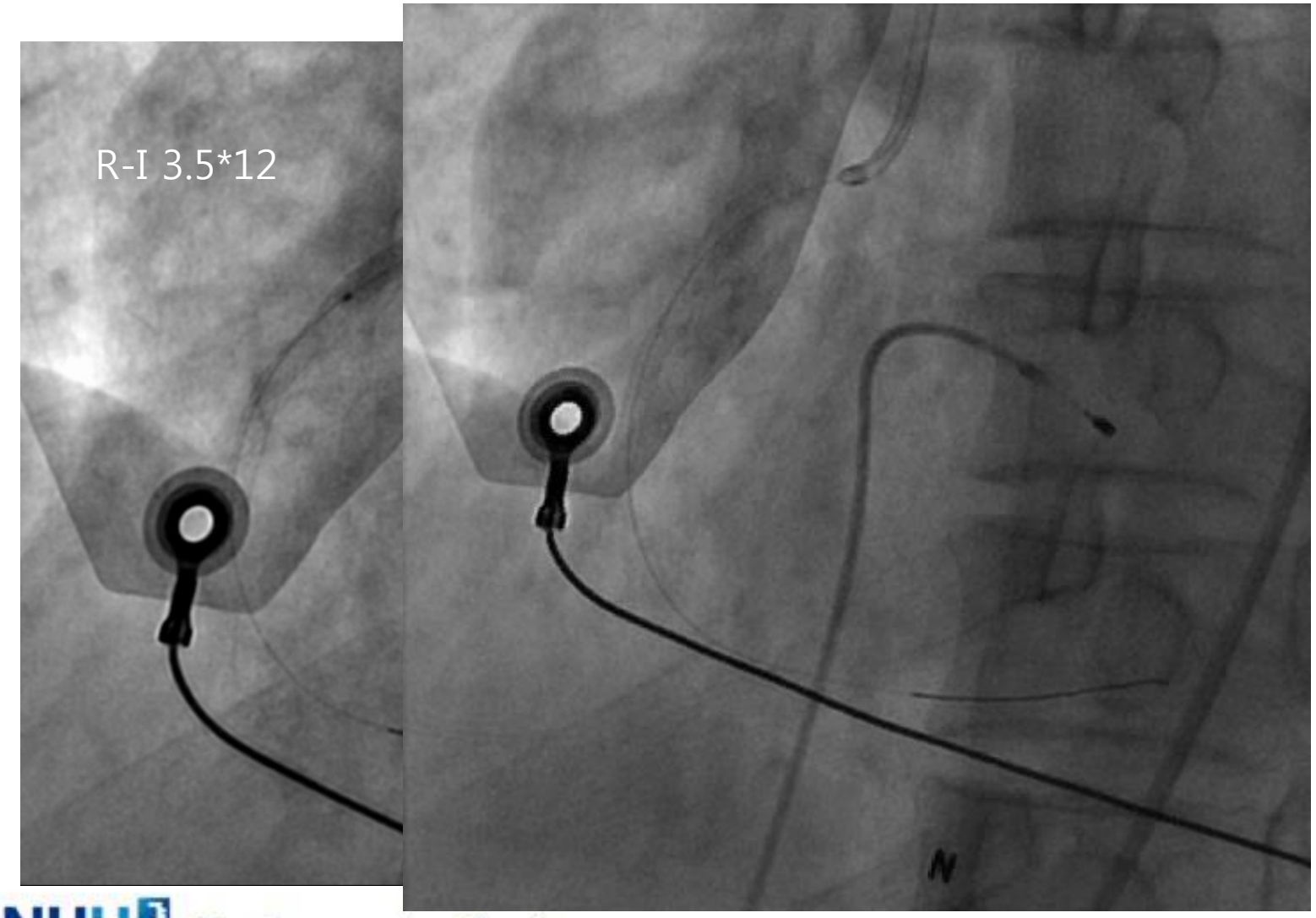


Primary PCI: Stenting



Primary PCI: Stenting

- ✓ Remnant thrombi in proximal edge on IVUS



Progression : D4

- ✓ tPM was maintained for 48hrs
- ✓ Complete AV block → 1st degree AV block
- ✓ EF 39%, RCA territory RWMA, RV dysfunction
- ✓ SCr : 3.6 → 0.8
- ✓ T-bil 3.6 → 1.0

- ✓ Antiplatelet regimen (D1~) : aspirin 100mg +
  - Clopidogrel? Prasugrel? Ticagrelor?

Aspirin 100mg qd / Ticagrelor 90mg bid

Questions for the selection of antiplatelet agents

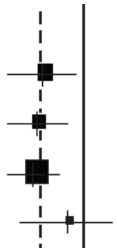
- ✓ 74yr-old man without bleeding history
- ✓ High thrombus burden at presentation
- ✓ Problem lists
  - Renal / hepatic dysfunction at presentation
  - High grade AV block at presentation
  - IC abciximab was loaded in the primary PCI

74 yr-old man without bleeding history

✓ PLATO subgroup analysis

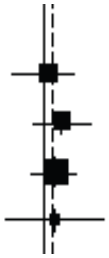
HR and rates (% at 12months) of the primary efficacy point in subgroups

Characteristic	Hazard Ratio (95% CI)	Total Patients	KM % at Month 12 Ti.	KM % at Month 12 CI.	HR (95% CI)	*P* value (Interaction)
Age Group						
<65 Years		10643	7.2	8.5	0.85 (0.74, 0.97)	0.86
≥65 Years		7979	13.2	16.0	0.83 (0.74, 0.94)	
<75 Years		15744	8.6	10.4	0.82 (0.74, 0.91)	0.22
≥75 Years		2878	16.8	18.3	0.94 (0.78, 1.12)	



HR and rates (% at 12months) of the primary safety results in subgroups

Characteristic	Hazard Ratio (95% CI)	Total Patients	KM % at Month 12 Ti.	KM % at Month 12 CI.	HR (95% CI)	*P* value (Interaction)
Age Group						
<65 Years		10528	9.5	9.5	1.00 (0.87, 1.13)	0.42
≥65 Years		7892	14.4	13.6	1.07 (0.95, 1.22)	
<75 Years		15574	11.1	10.8	1.04 (0.94, 1.15)	1.00
≥75 Years		2846	14.2	13.3	1.04 (0.84, 1.29)	



Renal dysfunction at presentation

- ✓ The primary route of ticagrelor is hepatic metabolism (CYP3A)

- ✓ No dosage adjustment is needed in patients with renal impairment. Patients receiving dialysis have not been studied.

Hepatic dysfunction at presentation

- ✓ GOT/GPT elevation mostly due to myocardial damage.
- ✓ Secondary hepatic congestion due to acute myocardial (especially RV) dysfunction

Coadministered GP2b3a inhibitor

✓ PLATO subgroup analysis

HR and rates (% at 12months) of the primary efficacy point in subgroups

Characteristic	Hazard Ratio (95% CI)	Total Patients	KM % at Month 12 Ti.	KM % at Month 12 CI.	HR (95% CI)	*P* value (Interaction)
GPIIb/IIIa (IE to End of Index Hosp.)						0.41
No		13562	9.7	11.9	0.82 (0.74, 0.92)	
Yes		5062	10.0	11.1	0.90 (0.76, 1.07)	

HR and rates (% at 12months) of the primary safety results in subgroups

Characteristic	Hazard Ratio (95% CI)	Total Patients	KM % at Month 12 Ti.	KM % at Month 12 CI.	HR (95% CI)	*P* value (Interaction)
GPIIb/IIIa (IE to End of Index Hosp.)						0.57
No		13393	12.1	11.6	1.05 (0.95, 1.17)	
Yes		5028	10.1	10.1	0.99 (0.83, 1.19)	

High grade AV block at presentation

✓ PLATO analysis

End Point	Ticagrelor Group	Clopidogrel Group	Hazard or Odds Ratio for Ticagrelor Group (95% CI)†	P Value
Bradycardia — no./total no. (%)				
Pacemaker insertion	82/9235 (0.9)	79/9186 (0.9)		0.87
Syncope	100/9235 (1.1)	76/9186 (0.8)		0.08
Bradycardia	409/9235 (4.4)	372/9186 (4.0)		0.21
Heart block	67/9235 (0.7)	66/9186 (0.7)		1.00

Progression : D6

- ✓ The patient discharged without complications
- ✓ Antiplatelet regimen was maintained with
  - Aspirin 100mg qd
  - Ticagrelor 90mg bid

Thank you for your attention!