

Measuring and Monitoring - Case Presentation -

원광대학교병원

김 남 호

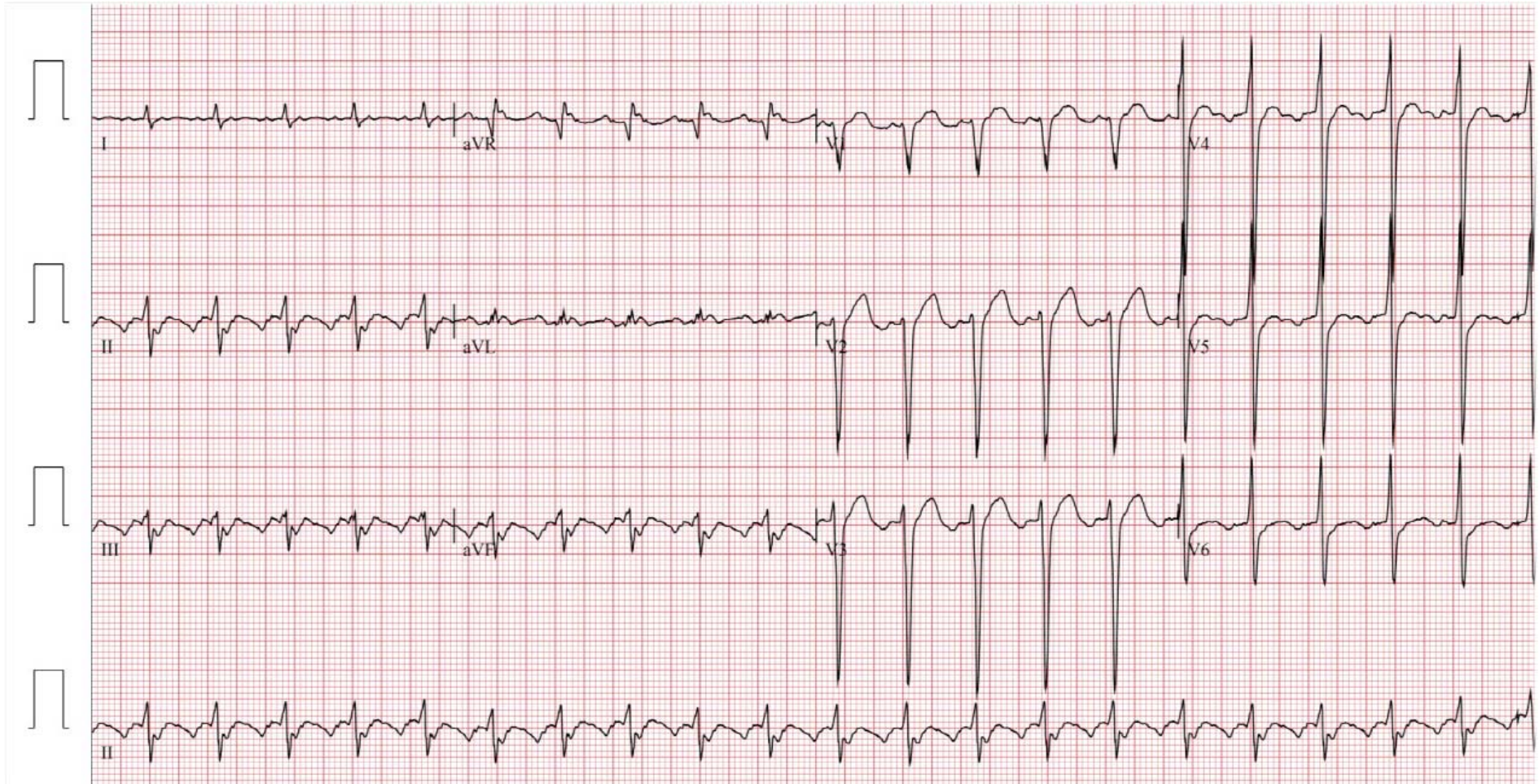
Two Topics

- 1. Difficult monitoring of PT INR**
- 2. Risk and benefit of anticoagulation**

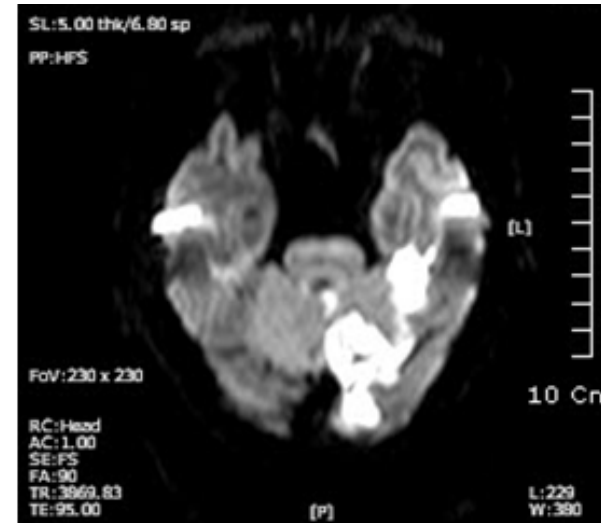
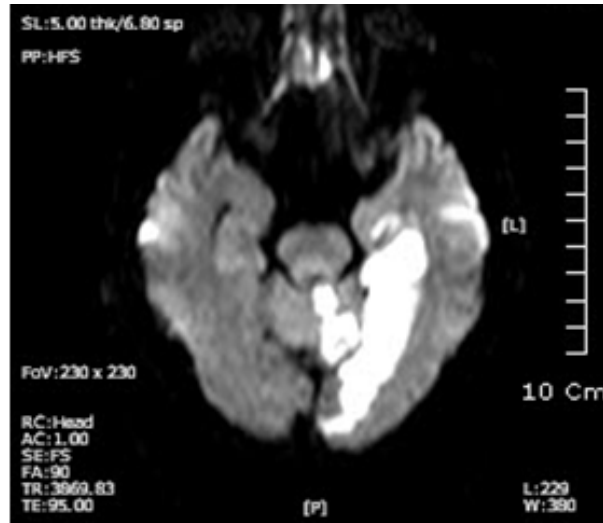
46세 남자 (증례1)

- 주소 : 우측 반신마비 및 언어장애
- 5년전 : Right MCA infarction, AF, DCM (LVEF 30%)
- 항응고제 복용 중 1년전부터 f/u loss됨.
내원 당일 새벽에 상기 주소 발생

46세 남자 (증례1)



46세 남자 (증례1)

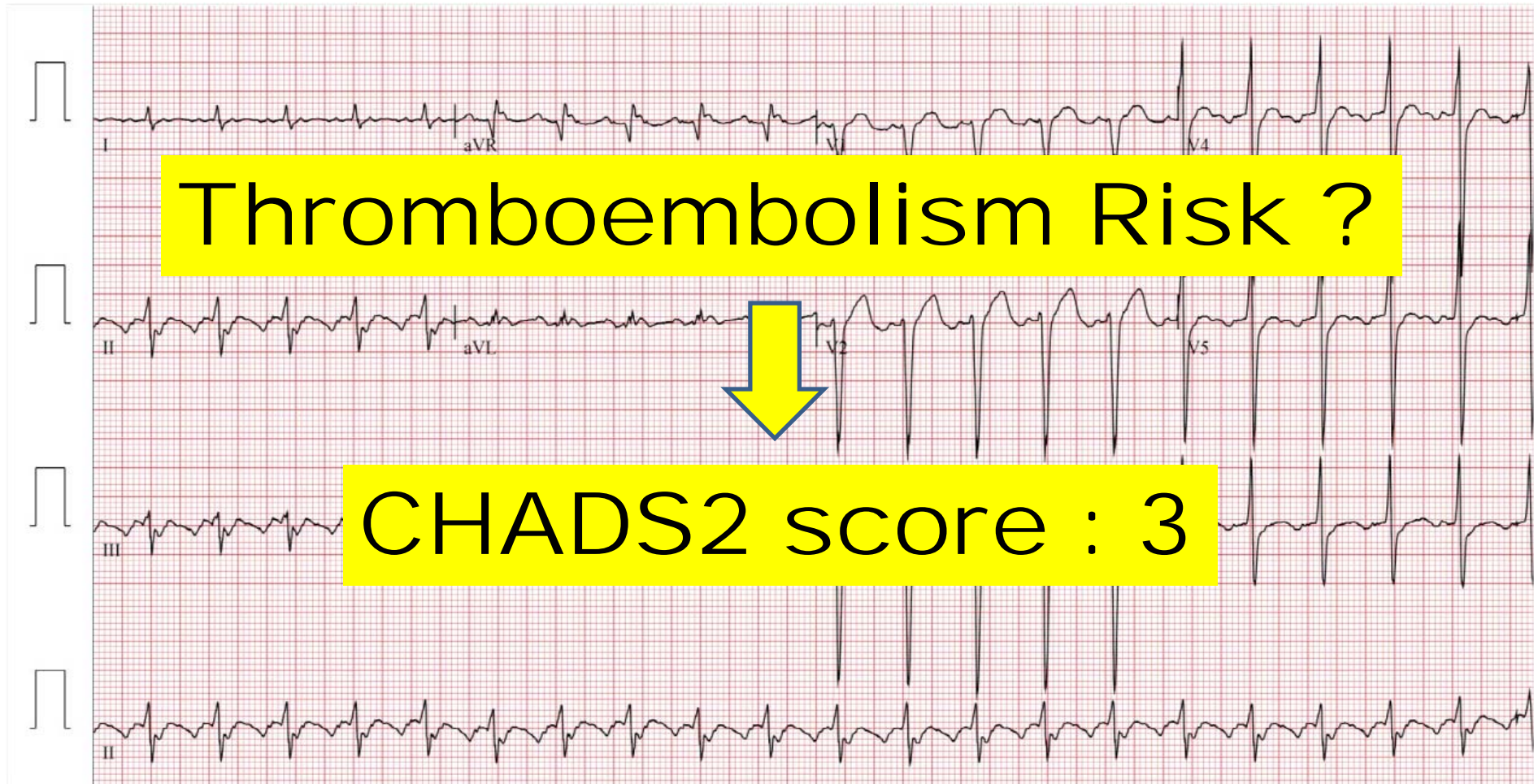


Risk Stratification of Stroke and TE

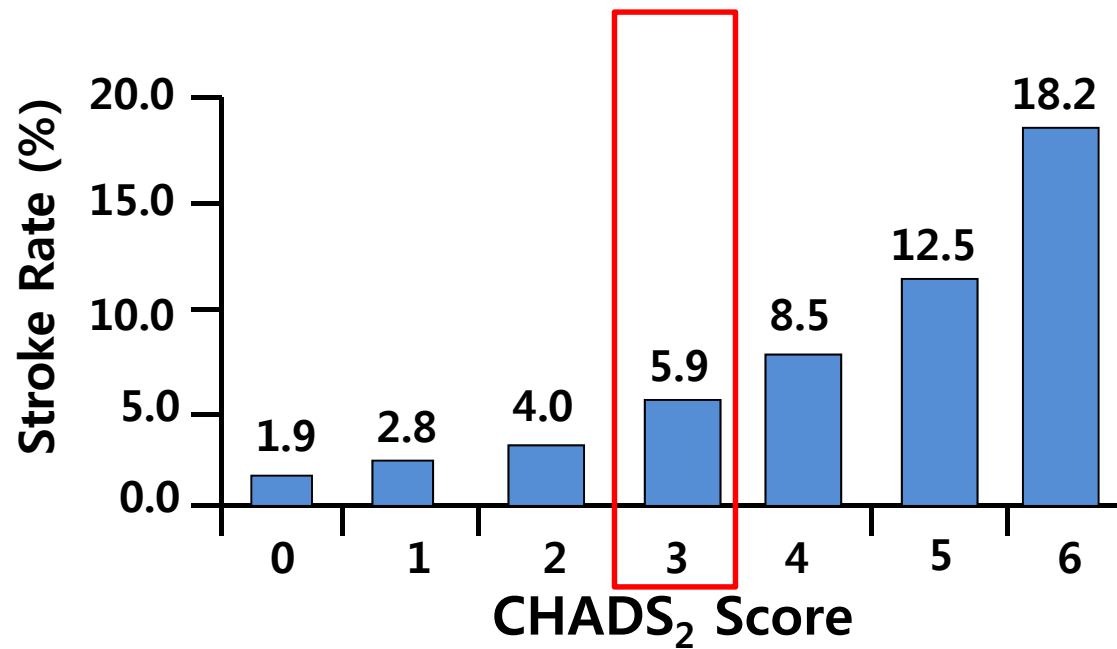
CHADS₂ Score

Risk Factor	Score
Congestive heart failure/ LV dysfunction	1
Hypertension	1
Age \geq 75	1
Diabetes mellitus	1
Stroke/ TIA/ Thrombo-embolism	2
Maximum score	6

46세 남자 (증례1)

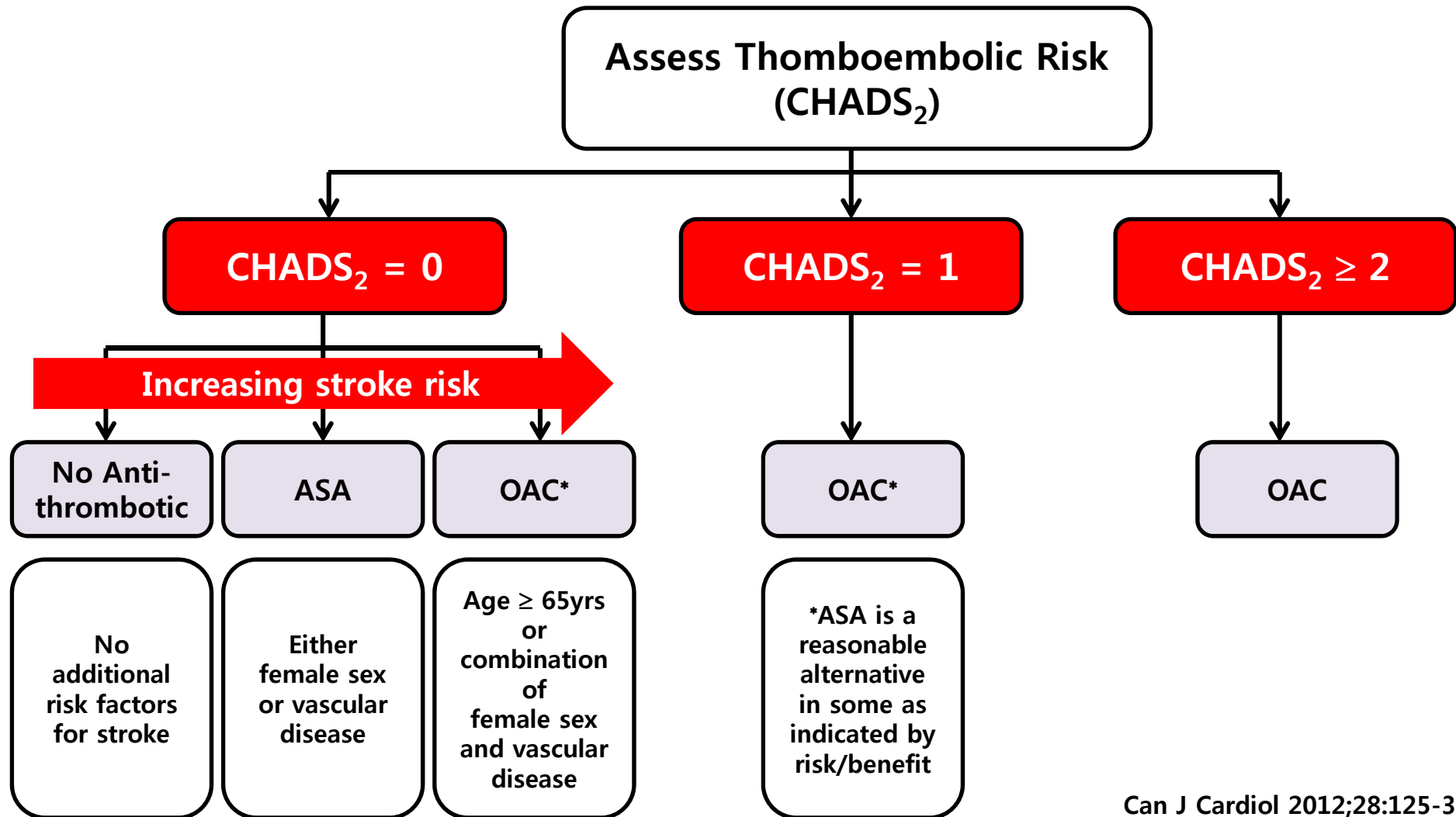


Risk of Stroke



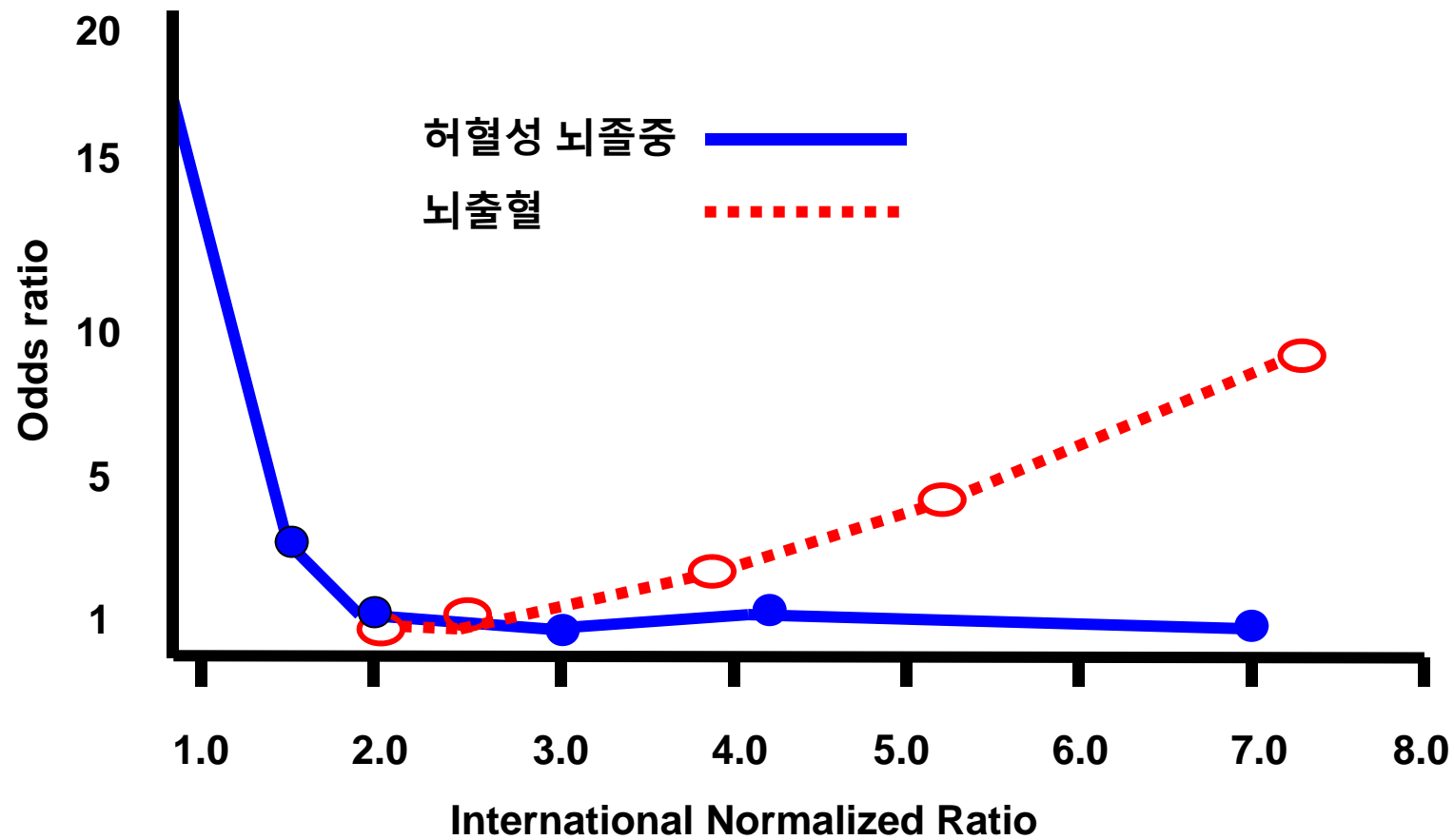
Antithrombotic Therapy

2012 CCS Guideline



Can J Cardiol 2012;28:125-36

Optimal INR



46세 남자 (증례1)

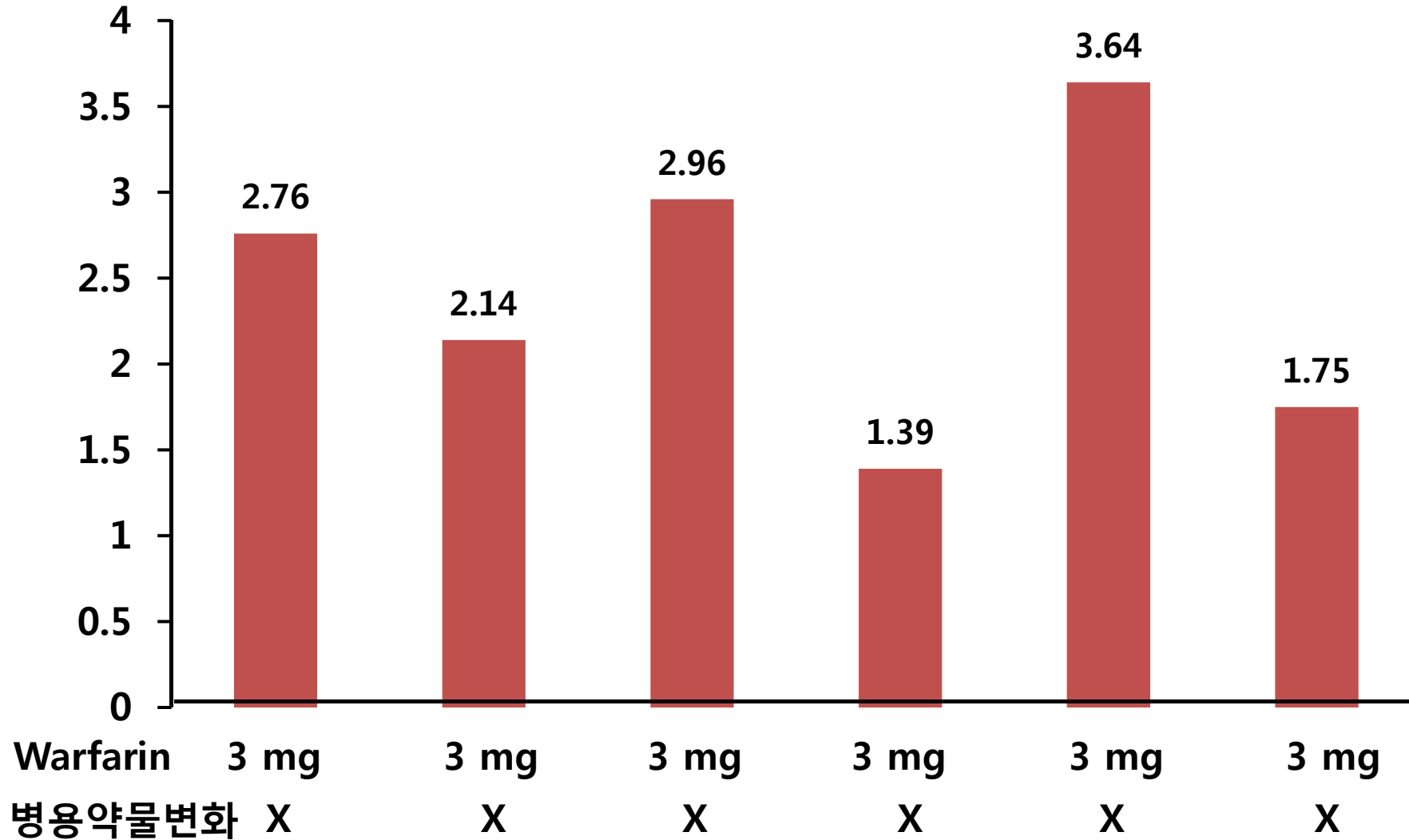


Thromboembolism Risk ?

CHADS2 score : 3

OAC (PT INR 2-3)

PT INR Monitoring



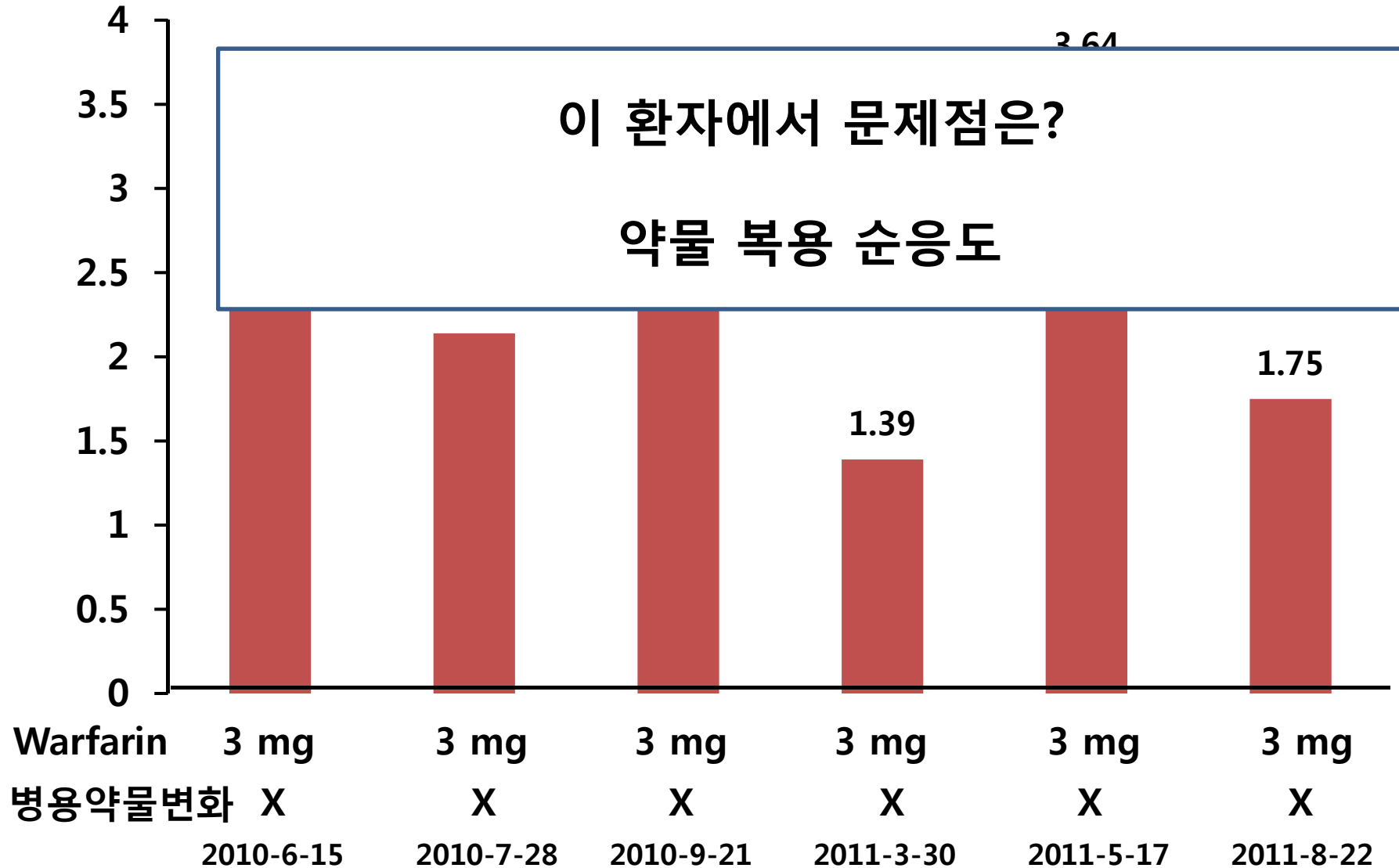
Limitation of Warfarin

Time in Therapeutic Range (TTR)

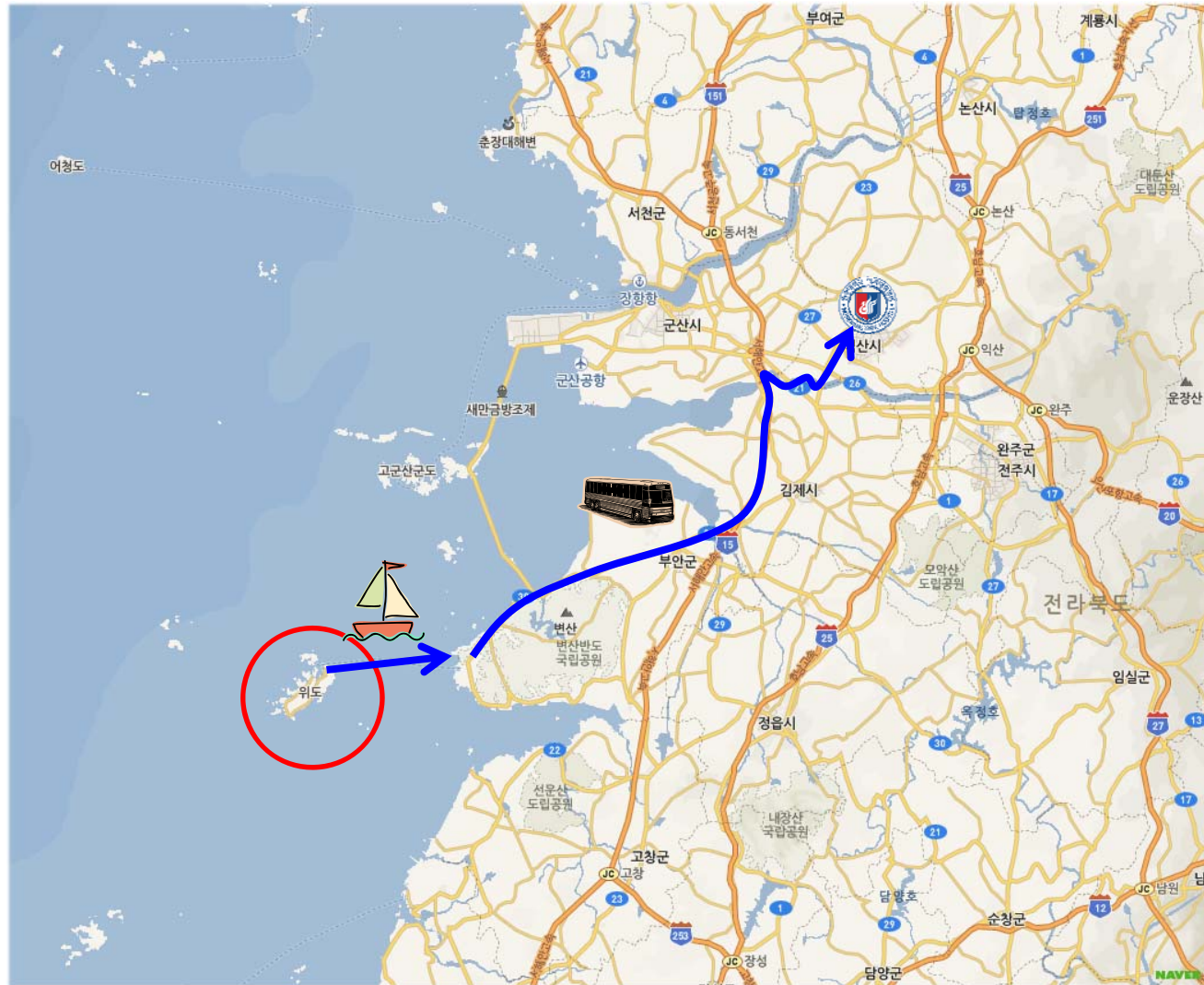
Warfarin	
INR range	Median (25 th , 75 th)
<1.5	2.7 (0.0 – 9.0)
1.5 to <1.8	7.9 (3.5 – 14.0)
1.8 to <2.0	9.1 (5.3 – 13.6)
2.0 to 3.0	57.8 (43.0 – 70.5)
>3.0 to 3.2	4.0 (1.9 – 6.5)
>3.2 to 5.0	7.9 (3.3 – 13.8)
>5.0	0.0 (0.0 – 0.5)

Based on Rosendaal method with all INR values included Based on Safety Population

PT INR Monitoring



46세 남자 (증례1)



46세 남자 (증례 1)

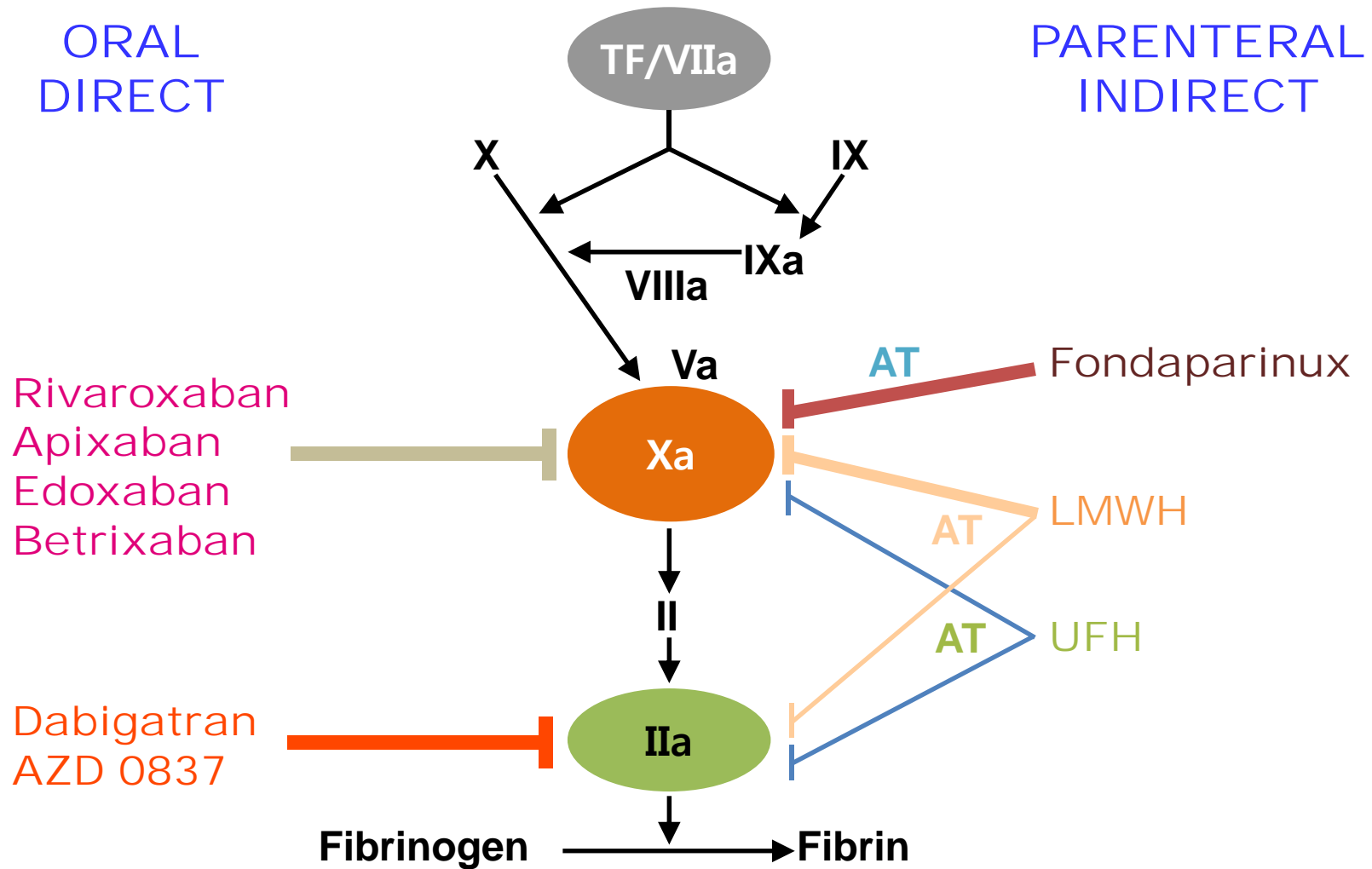
- 해결책은?
 1. 인근 병원으로 전원
 2. 새로운 항응고제로 대체
 3. PT INR Self-monitoring



Limitation of Vitamin K antagonist

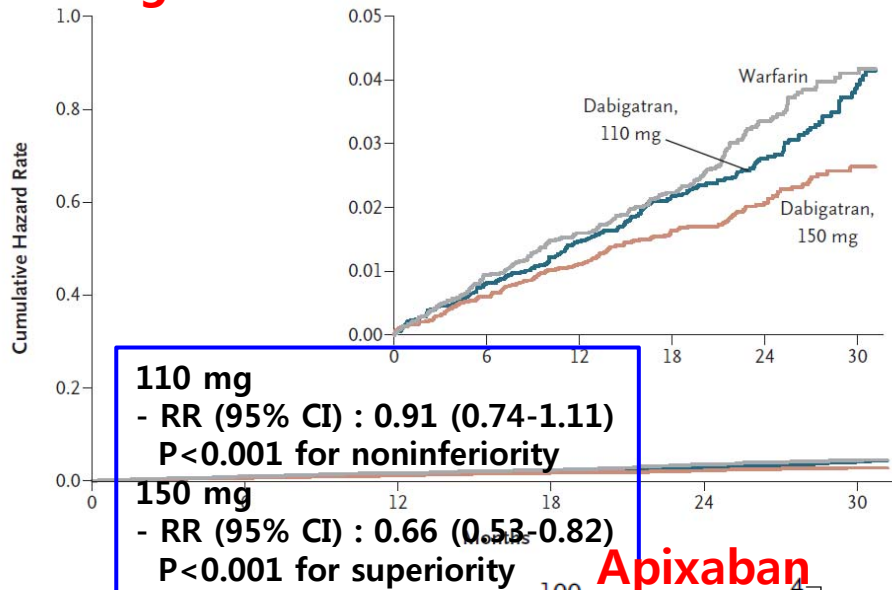
- **Slow onset and offset of antithrombotic effect**
- **Narrow therapeutic range**
- **Many pharmacokinetic and pharmacodynamic interactions**
- **Variable and unpredictable antithrombotic effect**

New Anticoagulants

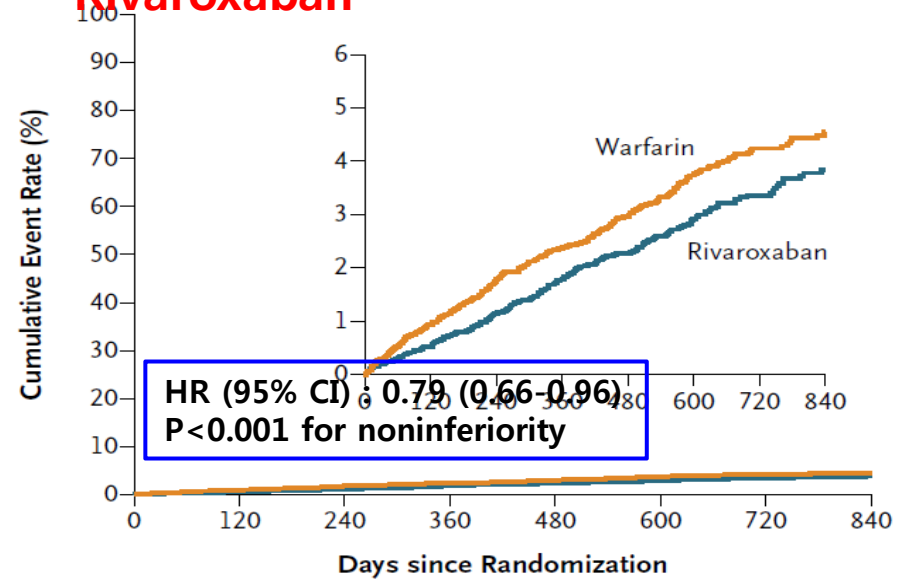


New Anticoagulants

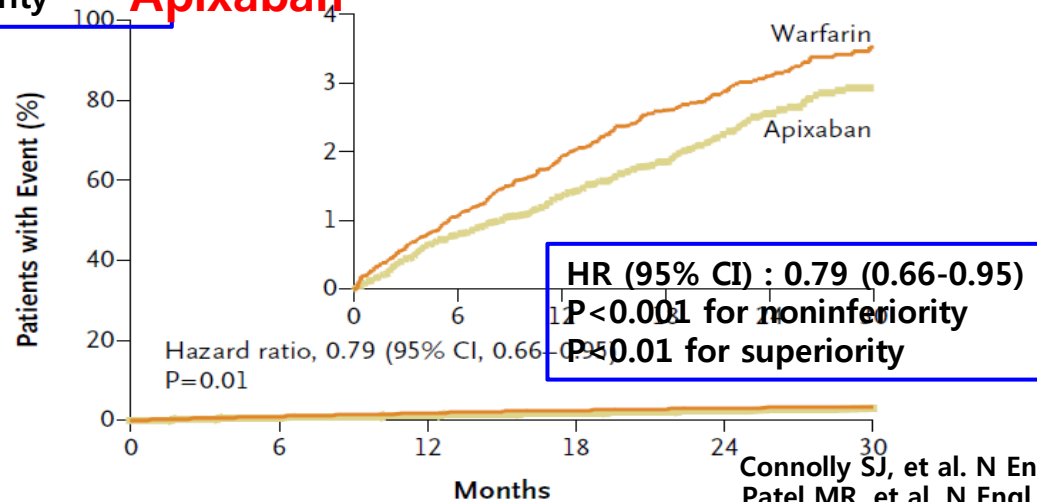
Dabigatran



Rivaroxaban



Apixaban



Connolly SJ, et al. N Engl J Med 2009;361:1139-51
 Patel MR, et al. N Engl J Med 2011;365:883-91
 Granger CB, et al. N Engl J Med 2011;365:981-92

New Anticoagulants

- **Advantages**
 - Rapid onset of action
 - Predictable anticoagulant effect
 - Specific coagulation enzyme target
 - Low potential for food interactions
 - Low potential for drug interaction

No routine monitoring required
No dose adjustment required

PT INR Self-monitoring



CoaguChek XS Plus System (Roche)

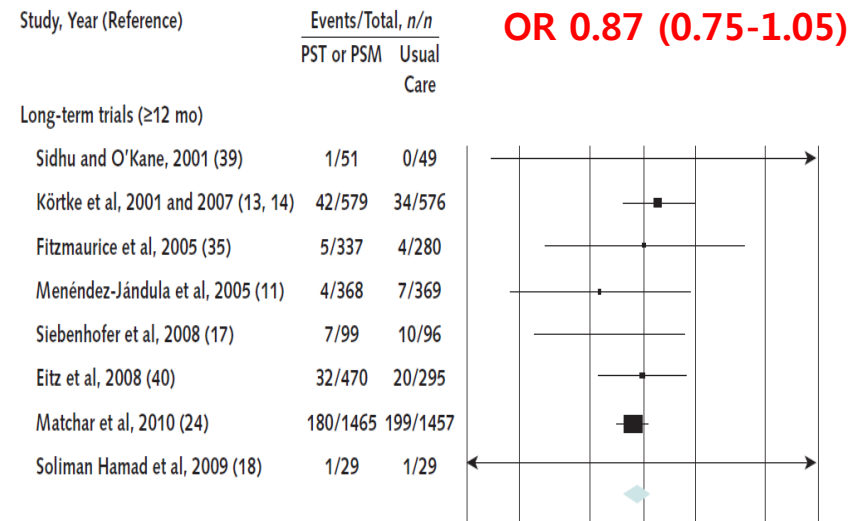
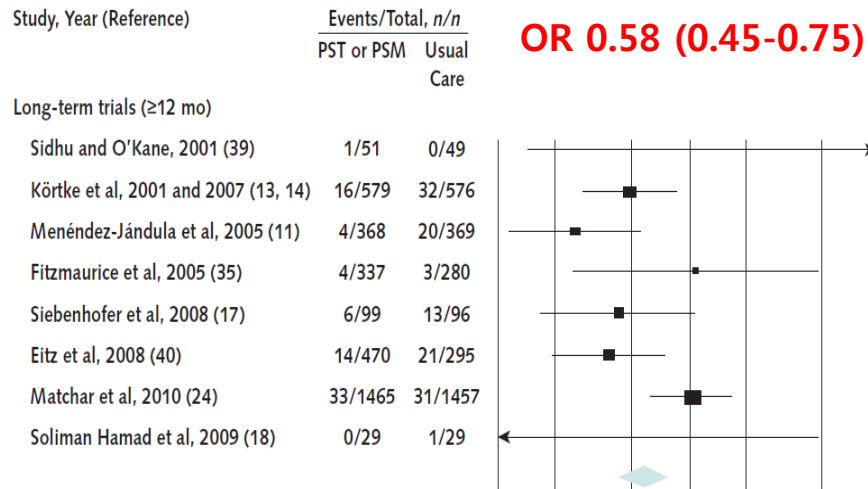


INRatio 2 (HemoSense)

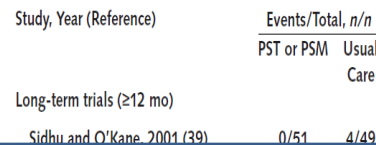
PT INR Self-monitoring

Thromboembolic events

Major bleeding events



All-cause mortality
OR 0.74 (0.63-0.87)



Compared with usual care, PST with or without PSM is associated with significantly fewer deaths and thromboembolic events, without increased risk for a serious bleeding event, for a highly selected group of motivated adult patients requiring long term anticoagulation with vitamin K antagonists.

Bloomfield HE, et al. Ann Intern Med 2011;154:472-482

46세 남자 (증례1)

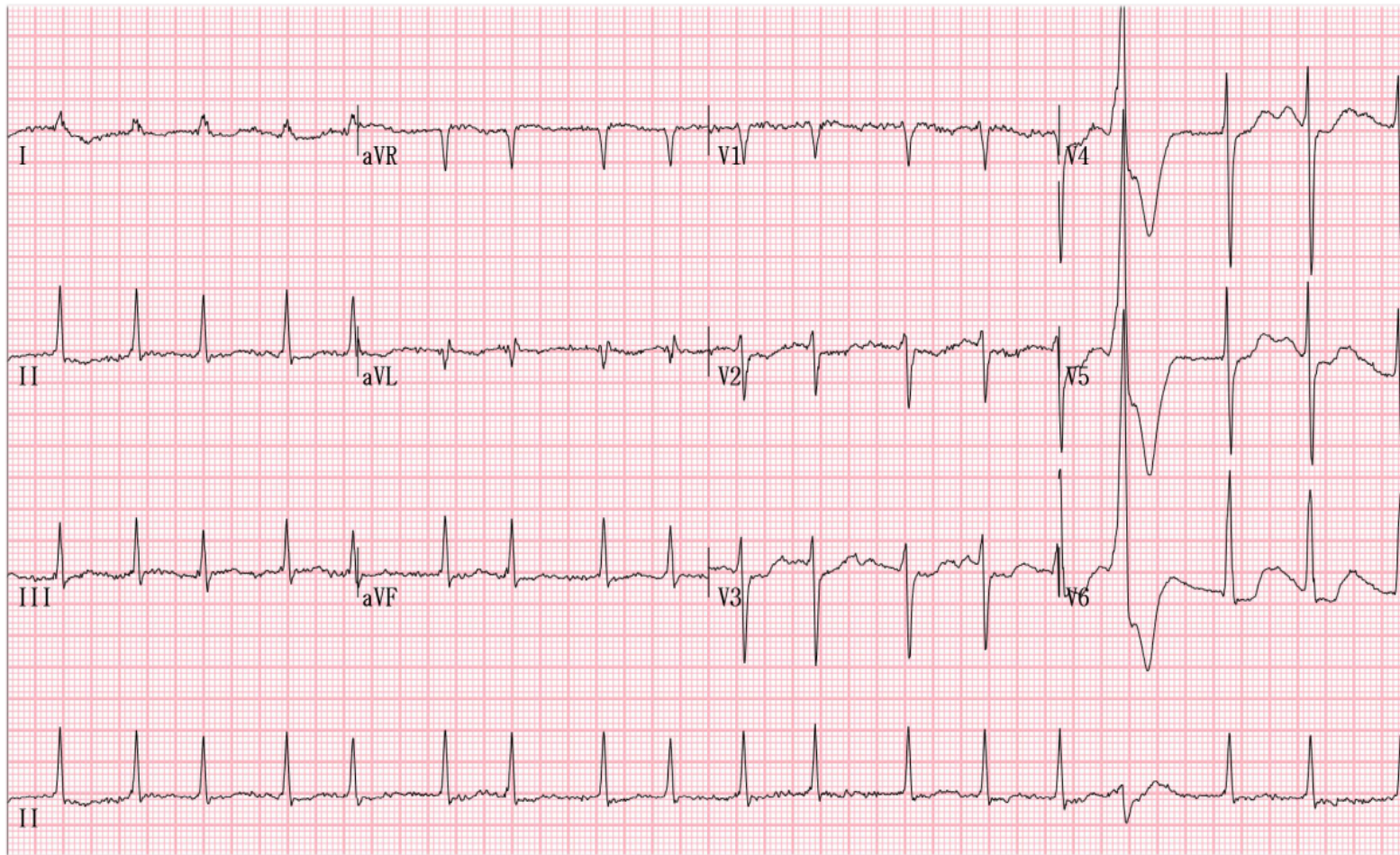
- 해결책은?

1. 근처 (1시간) 병원으로 전원
2. 새로운 항응고제로 대체
3. PT INR Self-monitoring



68세 남자 (증례2)

2002년 MVR(#St Jude 27 mm) and modified MAZE



Risk Stratification of Stroke and TE

2010 ESC Guideline

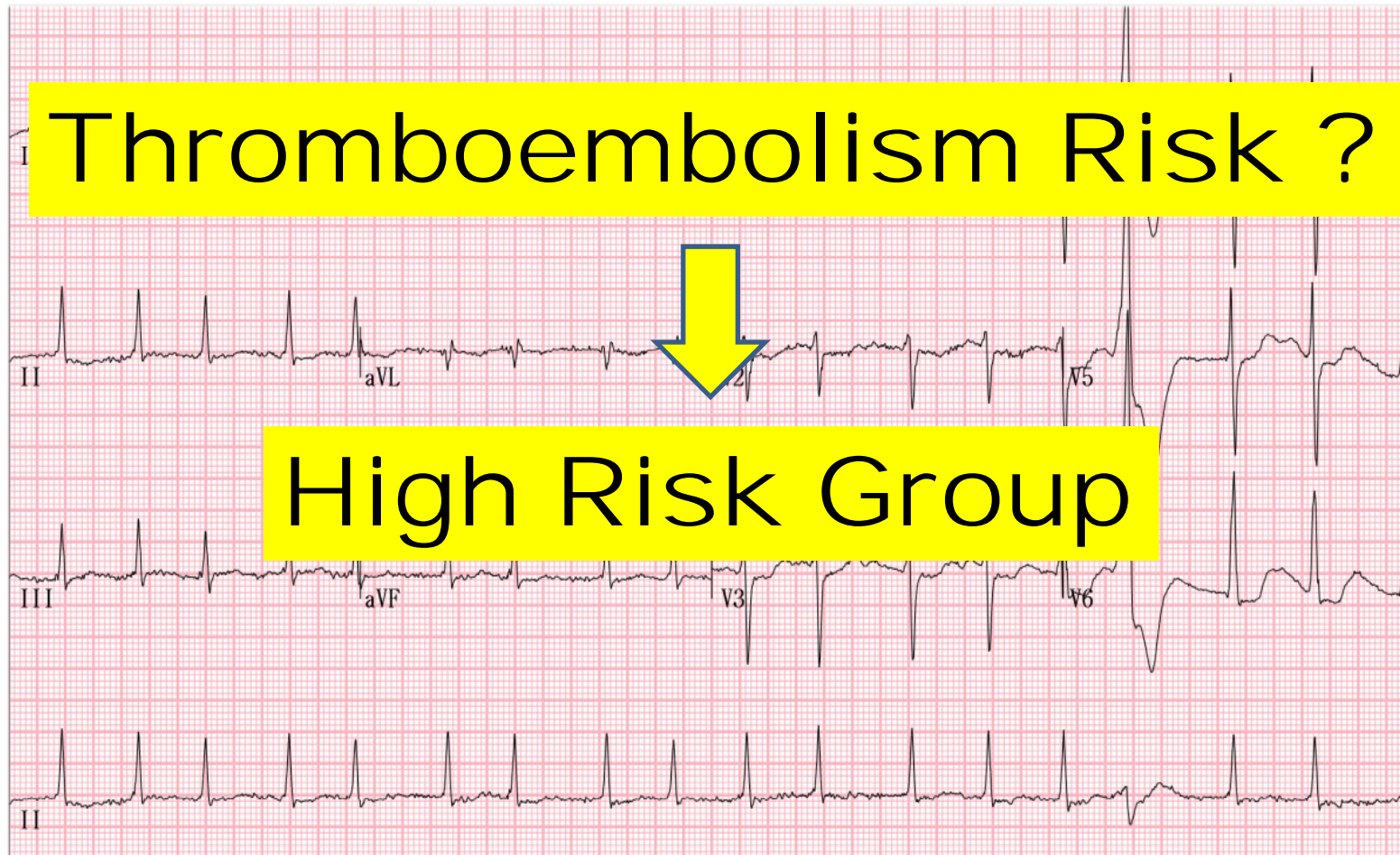
Major Risk Factors (High Risk)	Clinically relevant non-major risk factors
<p>Non-valvular AF</p> <ul style="list-style-type: none">• Previous stroke• TIA• Systemic embolism• Age ≥ 75 years <p>Valvular AF</p> <ul style="list-style-type: none">• MS• Prosthetic heart valve	<ul style="list-style-type: none">• Heart failure or Moderate to severe LV systolic dysfunction (e.g. LV EF $\leq 40\%$)• Hypertension• Diabetes mellitus• Female sex• Age 65-74 years• Vascular disease

Europace 2010;12:1360-1420



68세 남자 (증례2)

2002년 MVR(#St Jude 27 mm) and modified MAZE



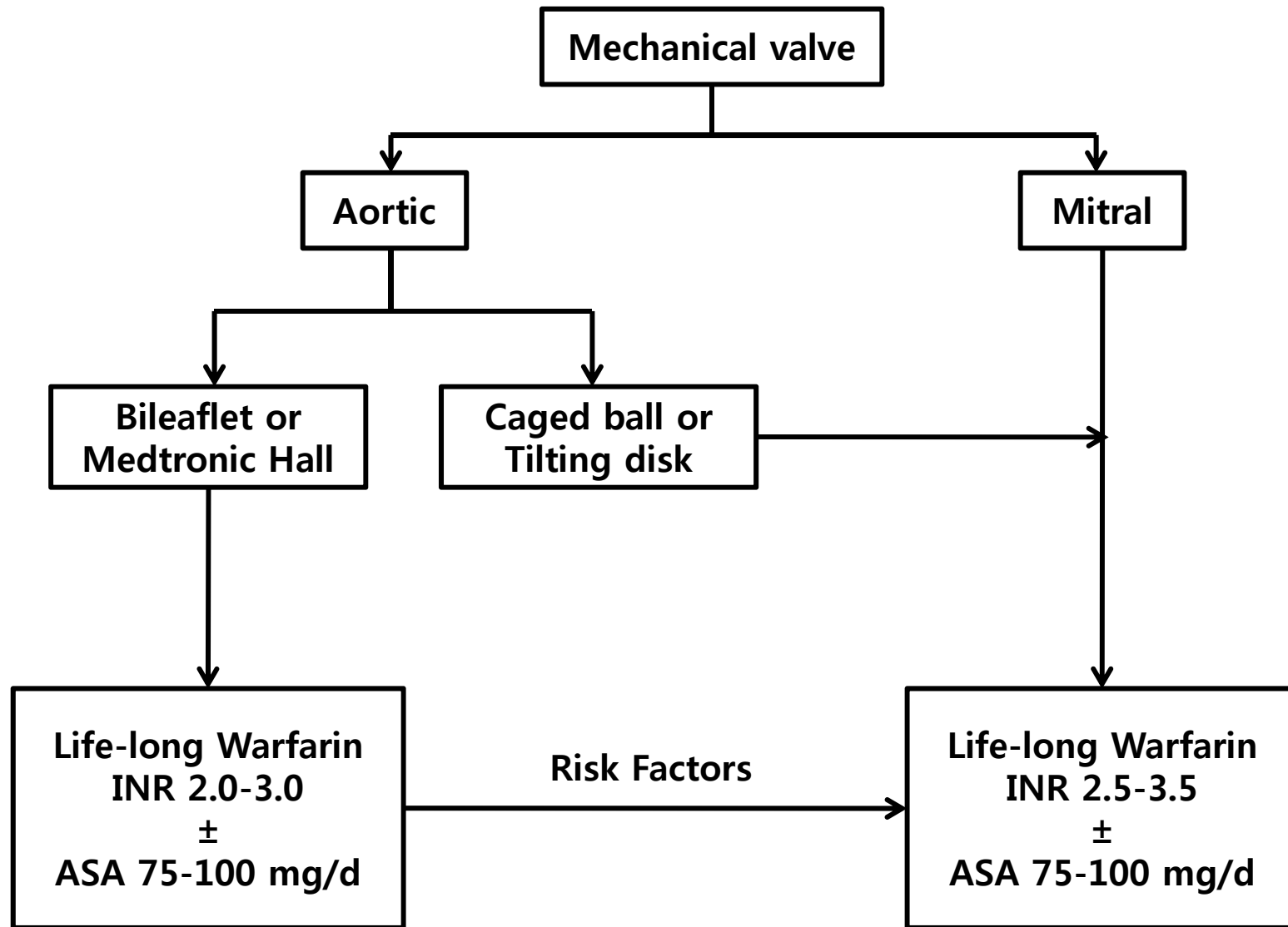
Antithrombotic Therapy

Approach to Thromboprophylaxis

Risk category	CHA2DS2-VASc score	Recommended antithrombotic therapy
One major risk factor or ≥ 2 clinically relevant non-major risk factors	≥ 2	OAC
One clinically relevant non-major risk factors	1	Either OAC or aspirin 75-325 mg daily. Preferred : OAC rather than aspirin
No risk factors	0	Either aspirin 75-325 mg daily or no antithrombotic therapy. Preferred : no antithrombotic therapy rather than aspirin

Europace 2010;12:1360-1420

Optimal INR in Mechanical Valve



68세 남자 (증례2)

2002년 MVR(#St Jude 27 mm) and modified MAZE

Thromboembolism Risk ?

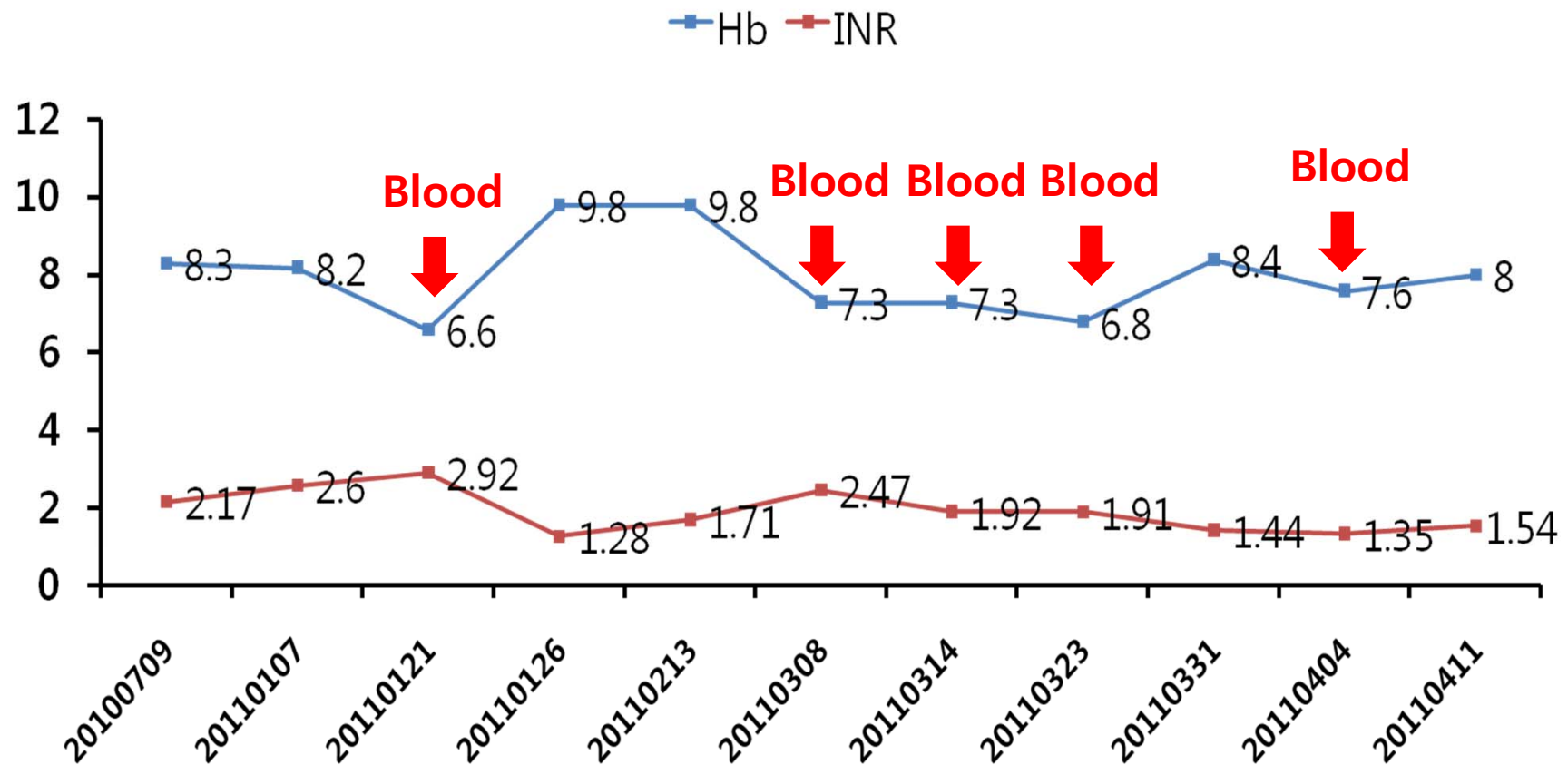
High Risk Group

Oral Anticoagulation
Target INR 2.5-3.5

68세 남자 – PT INR Monitoring

진료일자	BP(S)	BP(D)	맥박	FBS	PP		PT INR	warfarin (mg)	비고
					시간	값			
2011-03-02	114	56	96				2.1	2	WT:59.5
2011-02-16	100	50	64				1.71	2	wt:60.75kg
2011-01-21	100	60	104				2.92	2	
2011-01-18	100	60	50				3.02	2.5	
2011-01-07	130	50	42				2.6	3	120/57-49
2010-12-15	119	41	61				2.01	2	WT:65kg
2010-12-01	120	50	100				2.98	3	WT:64.2kg
2010-11-17	118	59	53				2.51	3	WT:64kg
2010-10-29	110	50	104						
2010-10-22	129	82	110				1.55	1.5	WT:65.9kg
2010-10-01	114	65	102				1.55	1.5	WT:62.2
2010-09-17	120	53	60						WT:65kg
2010-09-10	119	53	54				1.8	1.5	
2010-08-09	110	50	80						
2010-07-23	130	60	60				2.17	3	
2010-07-22	130	80	51						
2010-07-16	115	50	44						
2010-07-09	110	52	44				2.58	3	
2010-06-30	125	50	44				2.12	3	
2010-06-16	100	50	88				1.39	3	
2010-06-01	120	60	84				2	3	
2010-05-19	120	60	93						

68세 남자 (증례2)



Risk of Bleeding

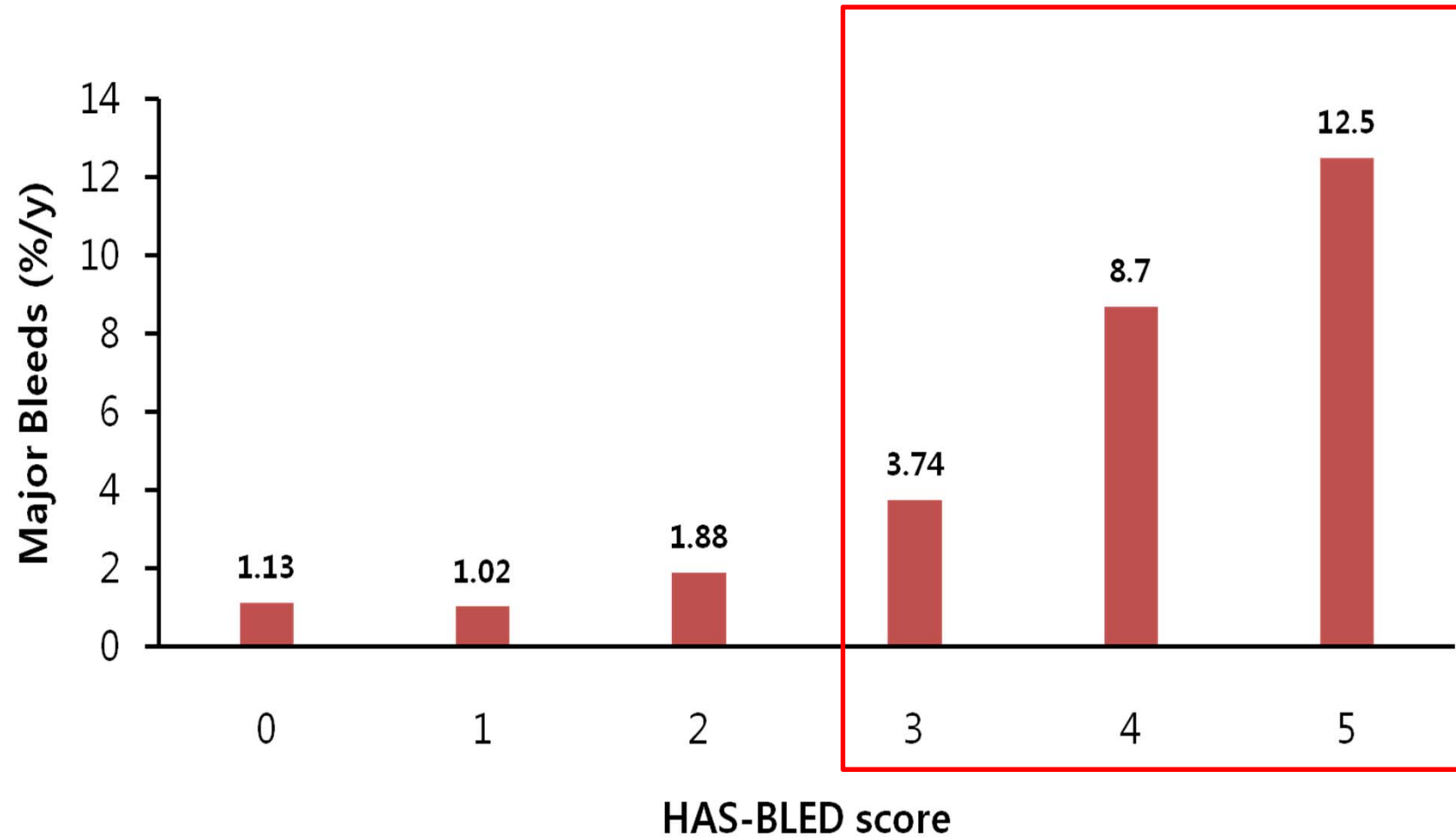
HAS-BLED Bleeding Risk Score

Letter	Clinical characteristic	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g., age > 65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Hypertension is defined as systolic blood pressure > 160 mmHg. Abnormal kidney function is defined as the presence of chronic dialysis or renal transplantation or serum creatinine \geq 200 μ mol/L. Abnormal liver function is defined as chronic hepatic disease (e.g., cirrhosis) or biochemical evidence of significant hepatic derangement (e.g., bilirubin > 2X upper limit of normal, in association AST/ALT > 3X upper limit normal, etc). Bleeding refers to previous bleeding history and/or predisposition to bleeding, e.g., bleeding diathesis, anemia, etc. Labile INR refers to unstable/high INRs or poor time in therapeutic range (e.g., < 60%). Drugs/alcohol use refers to concomitant use of drugs, such as antiplatelet agents, NSAID, or alcohol abuse, etc.

Europace 2010;12:1360-1420

Risk of Bleeding



Pisters R, et al. Chest 2010;138:1093-100

68세 남자 (증례2)

- **HAS-BLED score : 4 points**
 - Abnormal liver and renal function : 2
 - Bleeding : 1
 - Elderly : 1
- **Major bleeding : 8.7%/y**

Optimal Therapy



Lowering of Hemorrhage

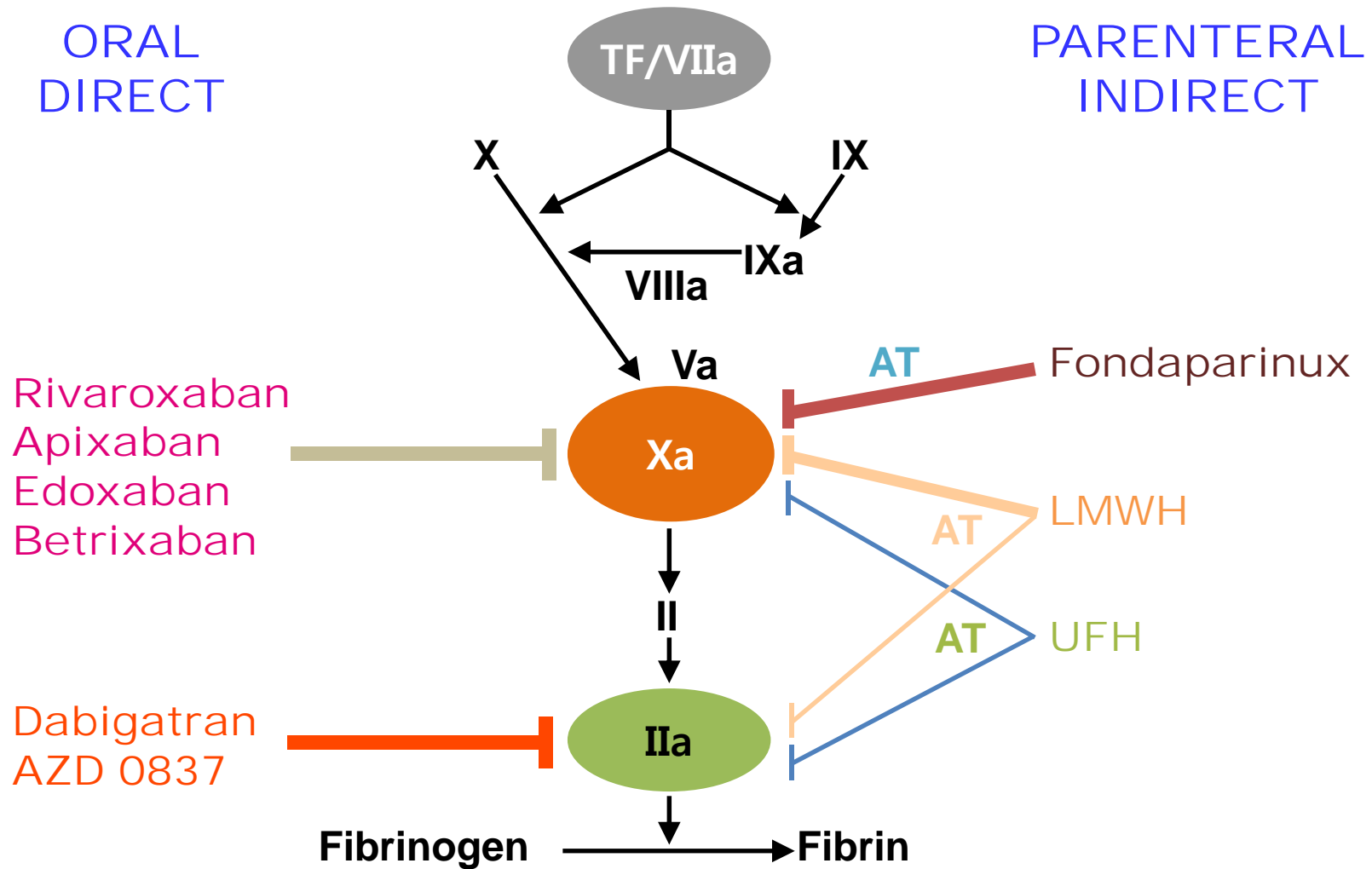
1. Lower target INR range
2. New Anticoagulants

Lower Target INR Range

INR	Person-yr†	Stroke (95% CI) (N=152)	Person-yr†	Intracranial Hemorrhage (95% CI) (N=58)
		<i>rate/100 person-yr</i>		<i>rate/100 person-yr</i>
<1.5	556	7.7 (5.7–10.4)	561	0.5 (0.2–1.7)
1.5–1.9	2847	1.9 (1.4–2.4)	2867	0.3 (0.1–0.6)
2.0–2.5	5357	0.4 (0.3–0.7)	5400	0.3 (0.2–0.4)
2.6–3.0	2388	0.9 (0.6–1.4)	2409	0.5 (0.3–0.9)
3.1–3.5	834	0.7 (0.3–1.6)	843	0.6 (0.3–1.4)
3.6–3.9	243	0.4 (0.1–2.9)	247	0.4 (0.1–2.9)
4.0–4.5	144	1.4 (0.4–5.5)	147	2.7 (1.0–7.3)
>4.5	115	2.6 (0.8–8.1)	118	9.4 (5.2–16.9)

Hylek EM, et al. N Engl J Med 2003;349:1019-26

New Anticoagulants



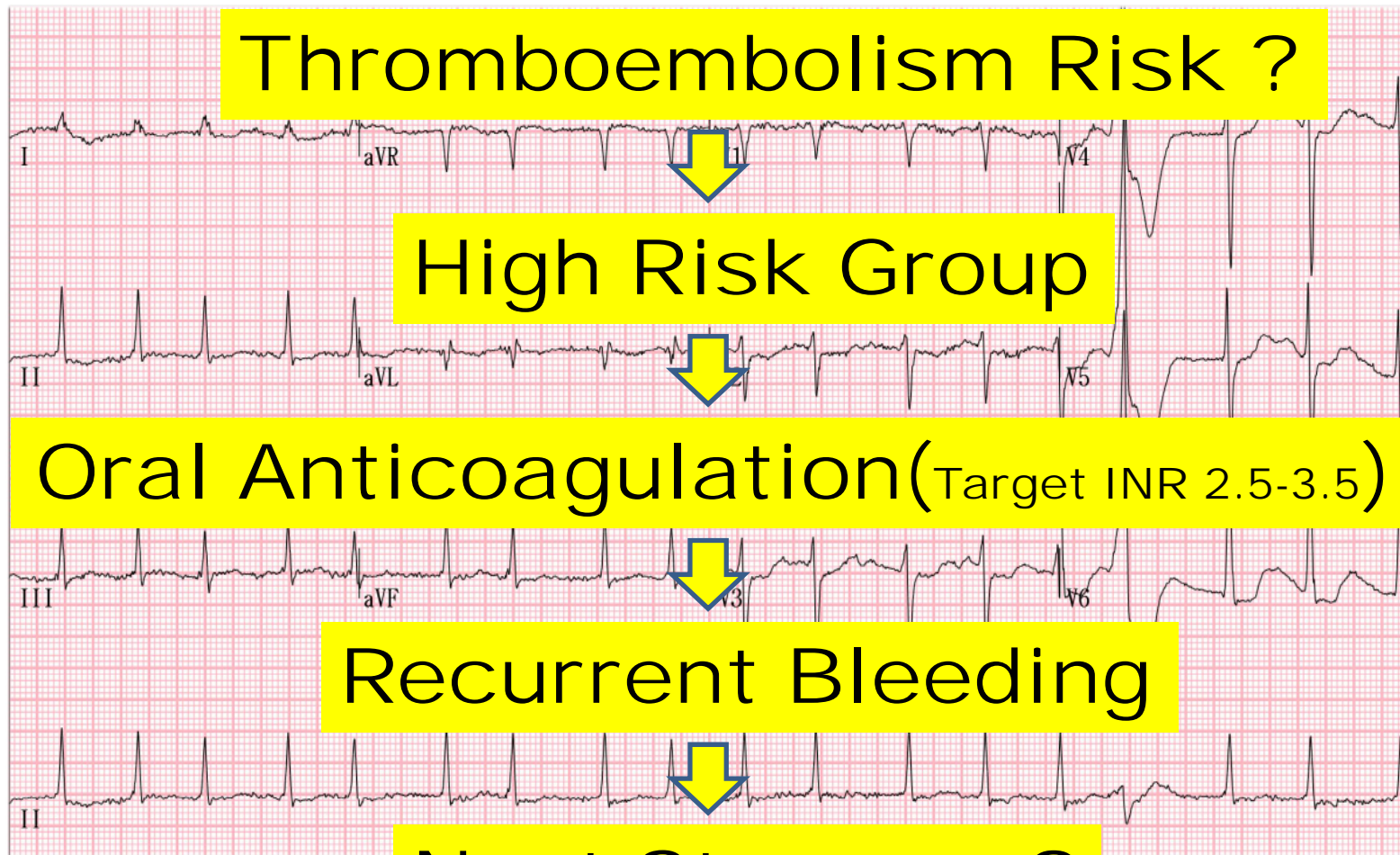
New Anticoagulants

	Major Bleeding			ICH			GI bleeding		
	Event Rate	HR	P value	Event Rate	HR	P value	Event Rate	HR	P value
Dabigatran 110 mg	2.71	0.80 (0.69-0.93)	0.003	0.23	0.31 (0.20-0.47)	<0.001	1.12	1.10 (0.86-1.41)	0.43
Dabigatran 150 mg	3.11	0.93 (0.81-1.07)	0.31	0.30	0.40 (0.27-0.60)	<0.001	1.51	1.50 (1.19-1.89)	<0.001
Rivaroxaban	3.60	1.04 (0.90-1.20)	0.58	0.50	0.67 (0.47-0.93)	0.02			
Apixaban	2.13	0.69 (0.60-0.80)	<0.001	0.33	0.42 (0.30-0.58)	<0.001	0.76	0.89 (0.70-1.15)	0.37

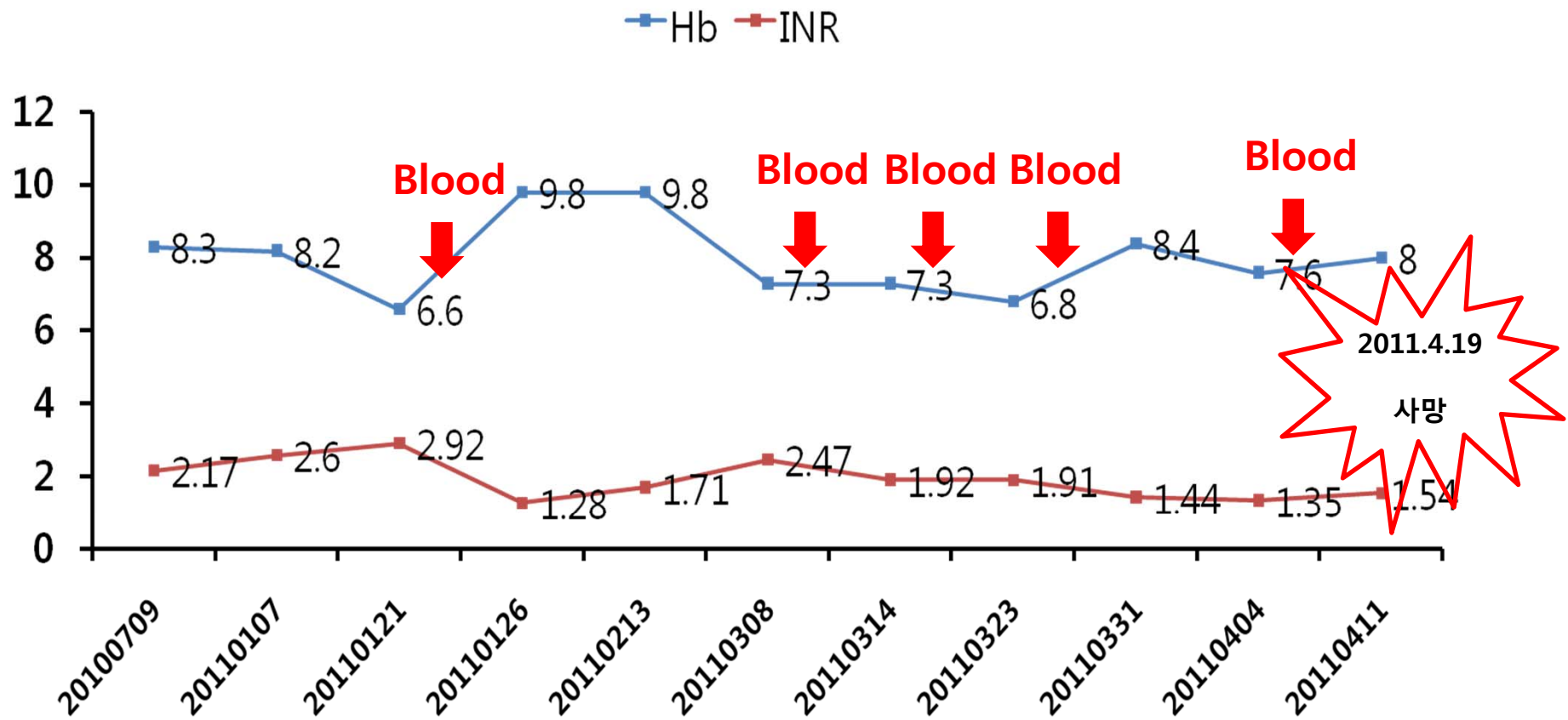
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68세 남자 (증례 2)

2002년 MVR(#St Jude 27 mm) and modified MAZE



68세 남자 (증례2)



Conclusion

1. Difficult monitoring of PT INR

- New anticoagulants
- PT INR Self-monitoring

2. Risk and benefit of anticoagulation

- New anticoagulants
- Lower target INR (?)

경청해주셔서 감사합니다 !!!

