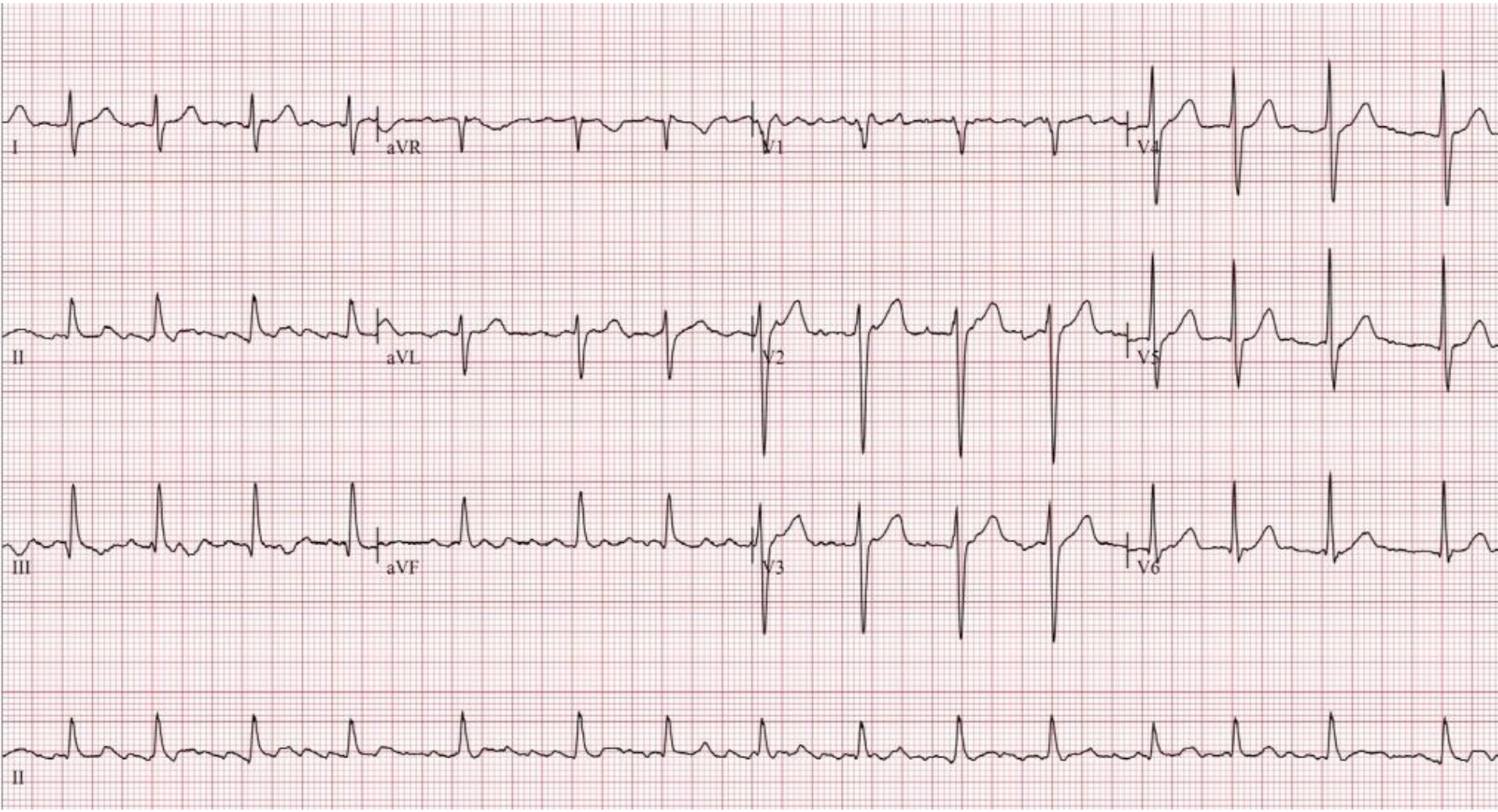
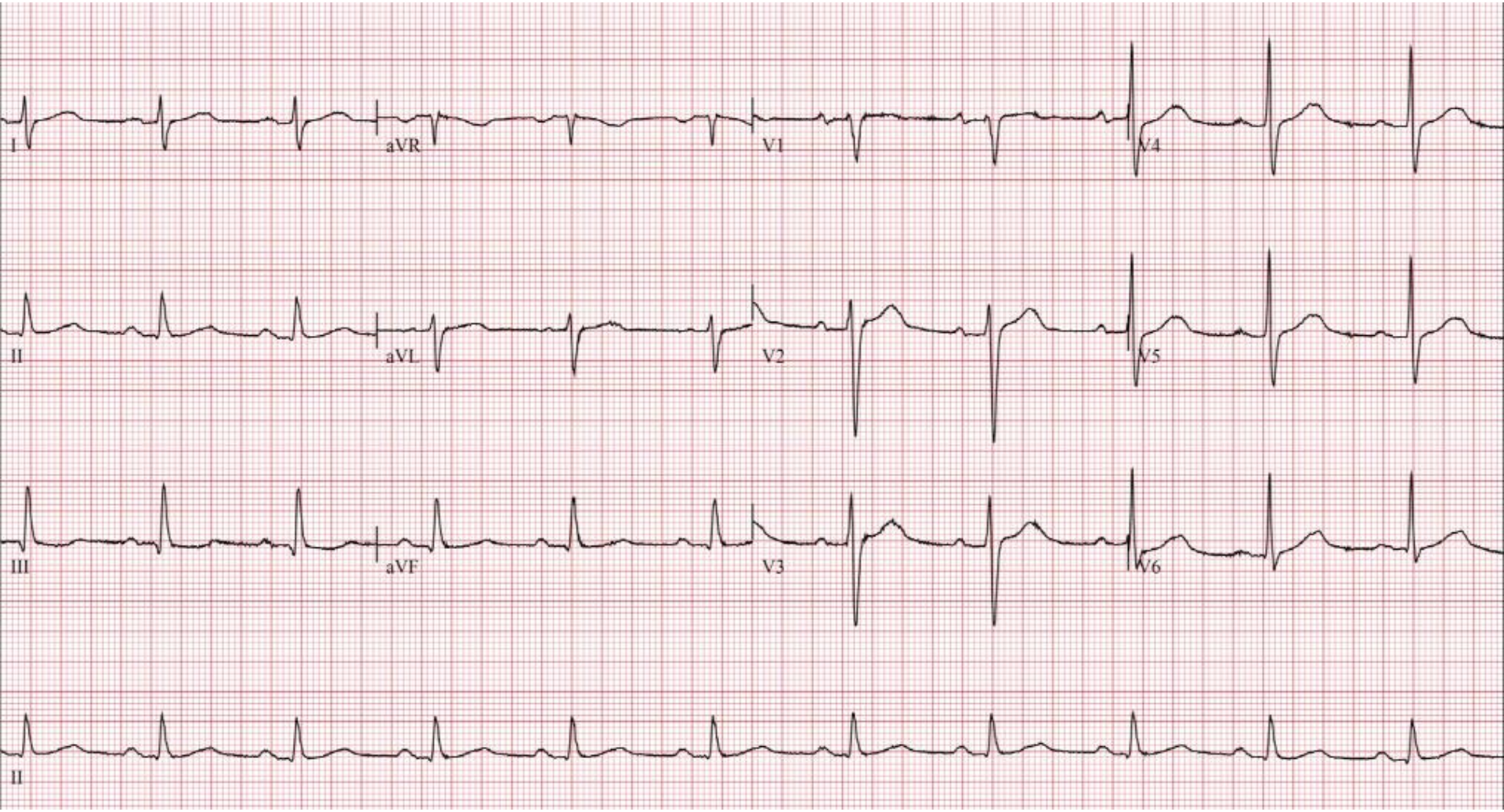
Trend in anticoagulation therapy

Ko Jum Suk, MD, PhD
Wonkwang university school of medicine and hospital

72/M 3일 전부터 심계항진, 과거력 : 고혈압/당뇨/5년 전 AMI로 PCI(DES)/위궤양, 심초음파 : EF 52%



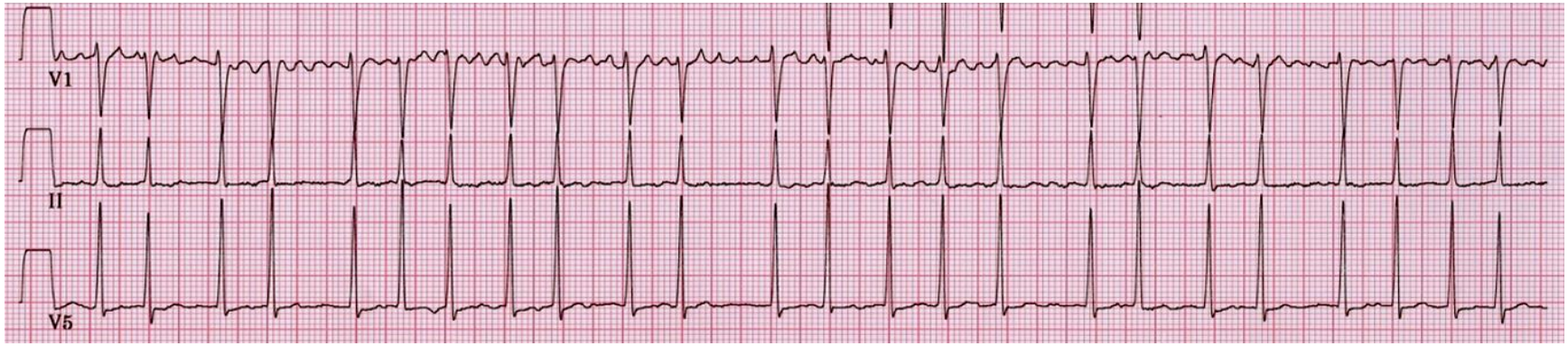
이전 심전도



심방세동 – 심전도 진단

정의

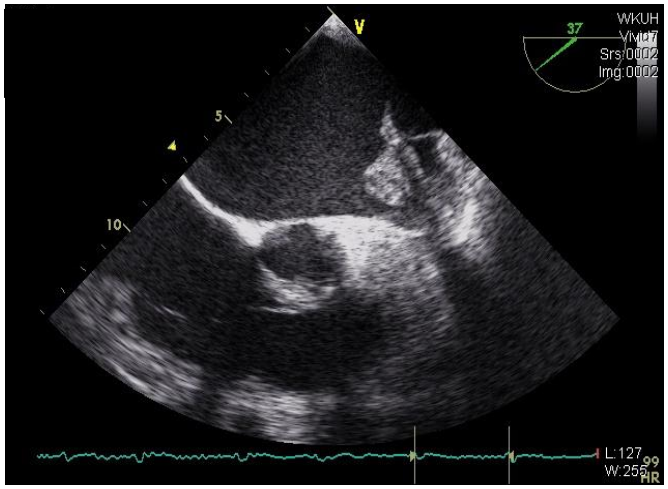
- 명확한 **P**파가 없거나, 기저선이 물결치듯 하거나 **350-600 bpm**의 빈도로 모양이 다양한 심방활동
- 방실전도계가 정상인 경우에는 심실반응이 불규칙

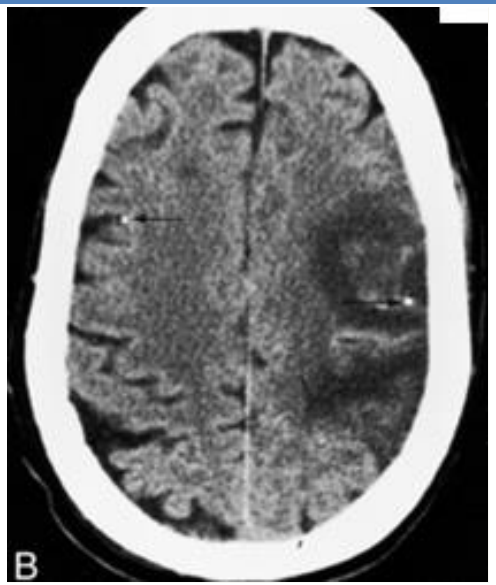


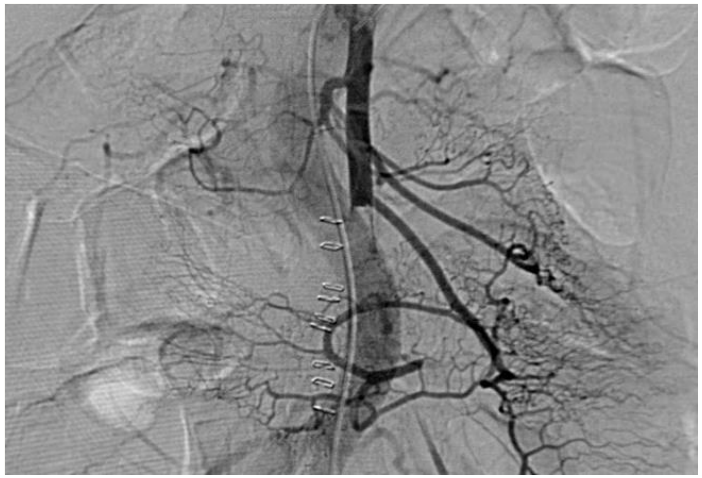
심방세동 – 임상적 의미

- 빠른 심박수 → 저혈압, 폐울혈, 협심증
- 종료 후 휴지 → 실신
- 심박출량에 심방 수축의 기여 소실 → 심부전
- 심계항진 → 불안
- 좌심방 혈전 및 전신 색전

심방세동 – 전신 색전 **(embolization)**



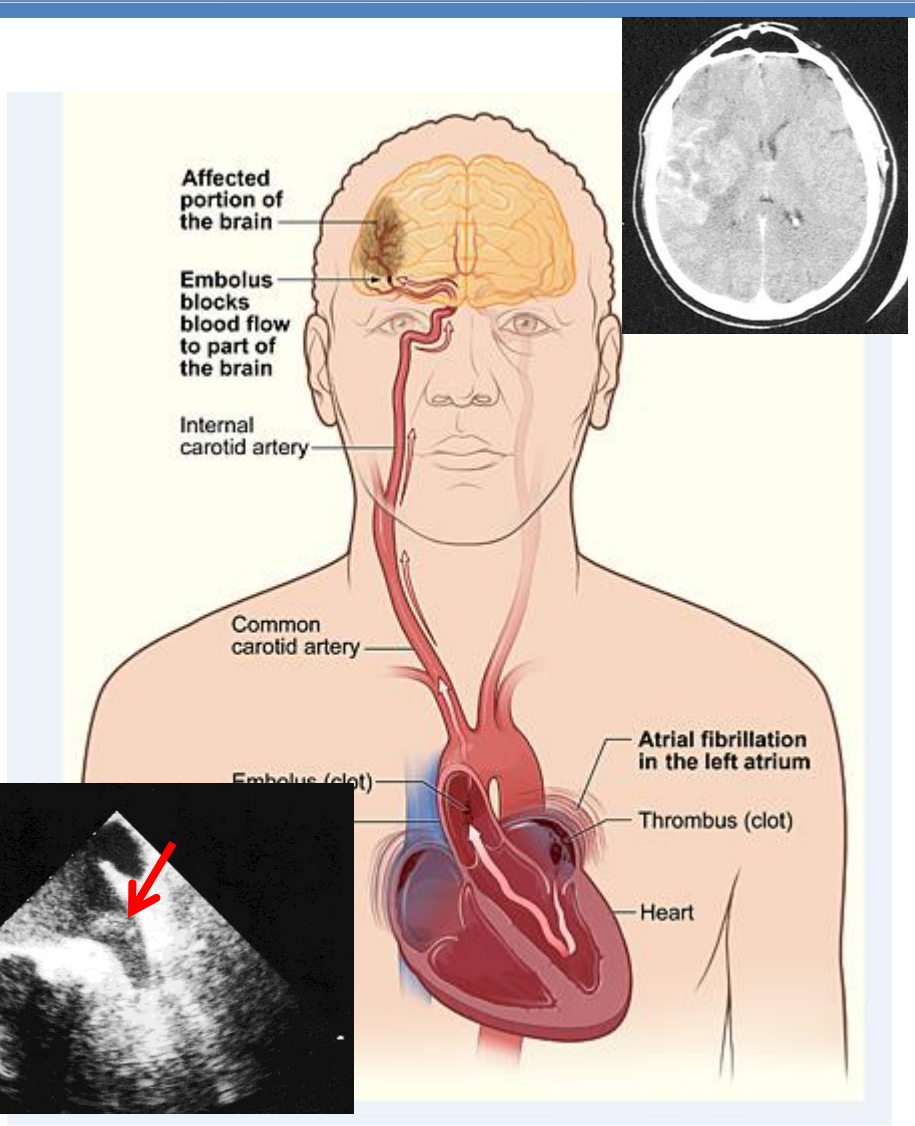




이 환자에서 가장 염려되는 것은?

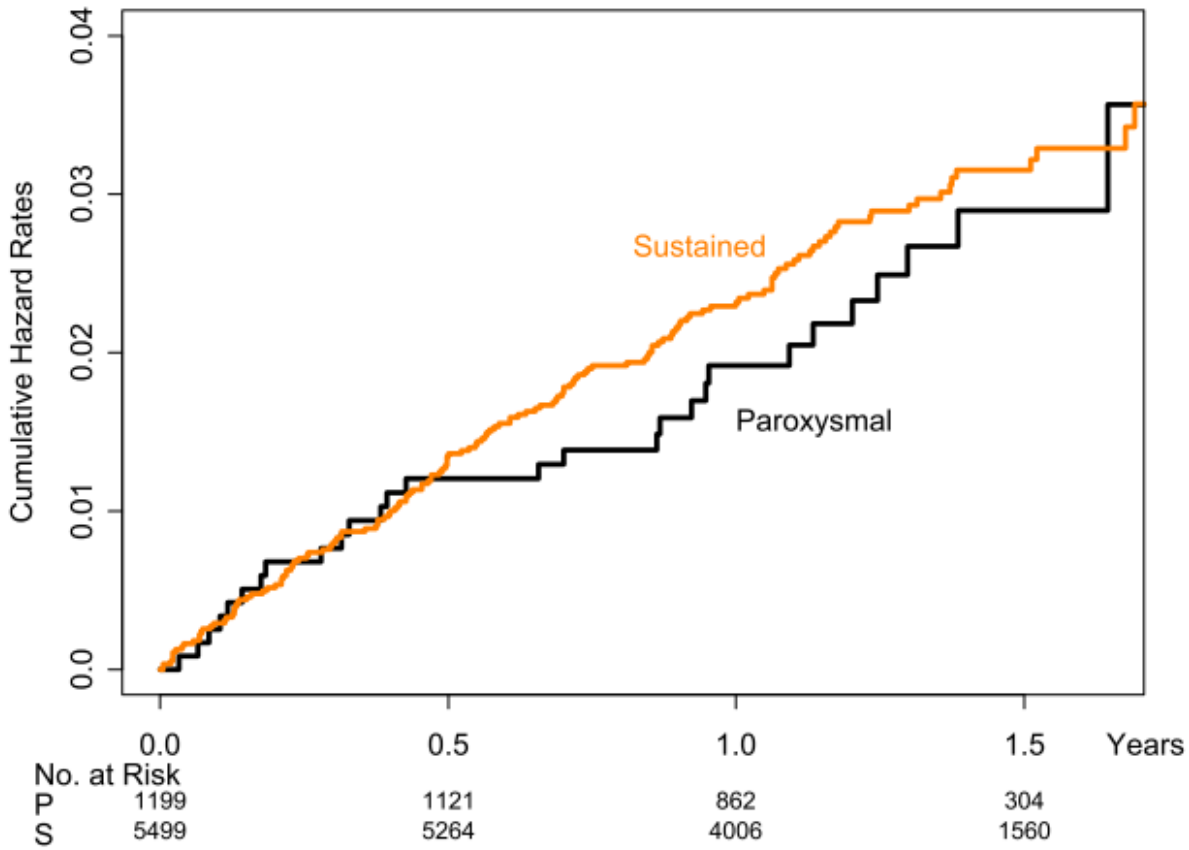
- 빈맥으로 인한 불편감
- 심부전 발생
- 심근경색증 재발
- **뇌졸중 발생(!!!)**

Facts about stroke in atrial fibrillation



- AF patients have a near 5 fold increased risk of stroke
- 1 in every 6 strokes occurs in a patient with AF
- Ischemic stroke associated with AF is typically more severe than stroke due to other etiologies
- Stroke risk persists even in asymptomatic AF

Paroxysmal AF는 위험하지 않다?



An ACTIVE W Substudy JACC 2007;50:2156-2161.

환자가 뇌졸중 증상이 없으면 **no problem?**

Previous studies

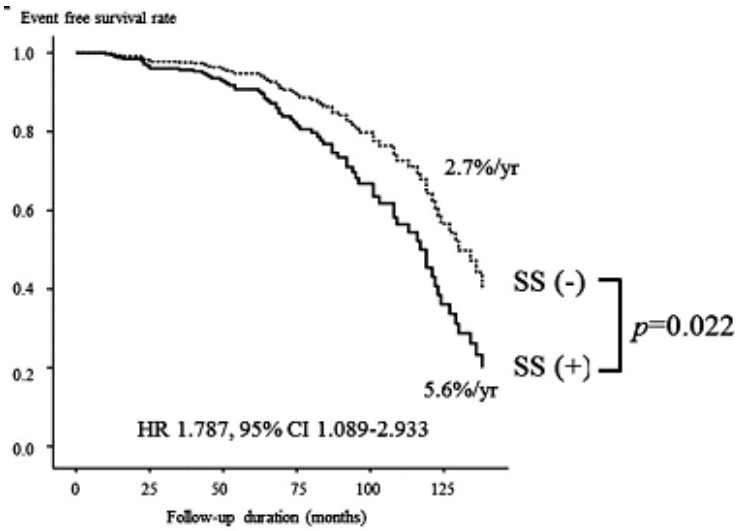
Year	Authors	AF	NSR	Method	SS Prevalence
1987	Petersen et al[2]	29	29	CT	14:8 (48%:28%)
1988	Kempster et al[6]	54	168	CT	7:7 (13%:4%)
1989	Petersen et al[7]	30	30	CT	4:3 (13%:10%)
1990	Feinberg et al[8]	141	—	CT	36 (26%)
1995	Ezekowitz et al[9]	516		CT	76 (14.7%)
1995	Hara et al[10]	72		MRI	32%
2012	Kobayashi et al[11]	71	71	MRI	74.6%:57.7%

28.3%

6.6%

Variable	AF (n = 400)	SR (n = 800)	p Value
Age, yrs (range)	66.60 ± 10.1 (26–90)	65.83 ± 9.3 (26–88)	0.228
20–39	3 (0.8%)	6 (0.8%)	
40–49	22 (5.5%)	40 (5.0%)	
50–59	70 (17.5%)	139 (17.4%)	
60–69	137 (34.3%)	300 (37.5%)	
70–79	134 (33.5%)	277 (34.6%)	
>80	34 (8.5%)	38 (4.8%)	
Women	131 (32.8%)	274 (34.3%)	0.650
Hypertension	229 (57.3%)	479 (59.9%)	0.384
DM	95 (23.8%)	184 (23.0%)	0.772
Dyslipidemia	72 (18.0%)	128 (16.0%)	0.411
CKD	68 (17.0%)	86 (10.8%)	0.003
CHF (ejection fraction ≤35%)	28 (7.0%)	1 (0.1%)	<0.001

Risk of overt stroke

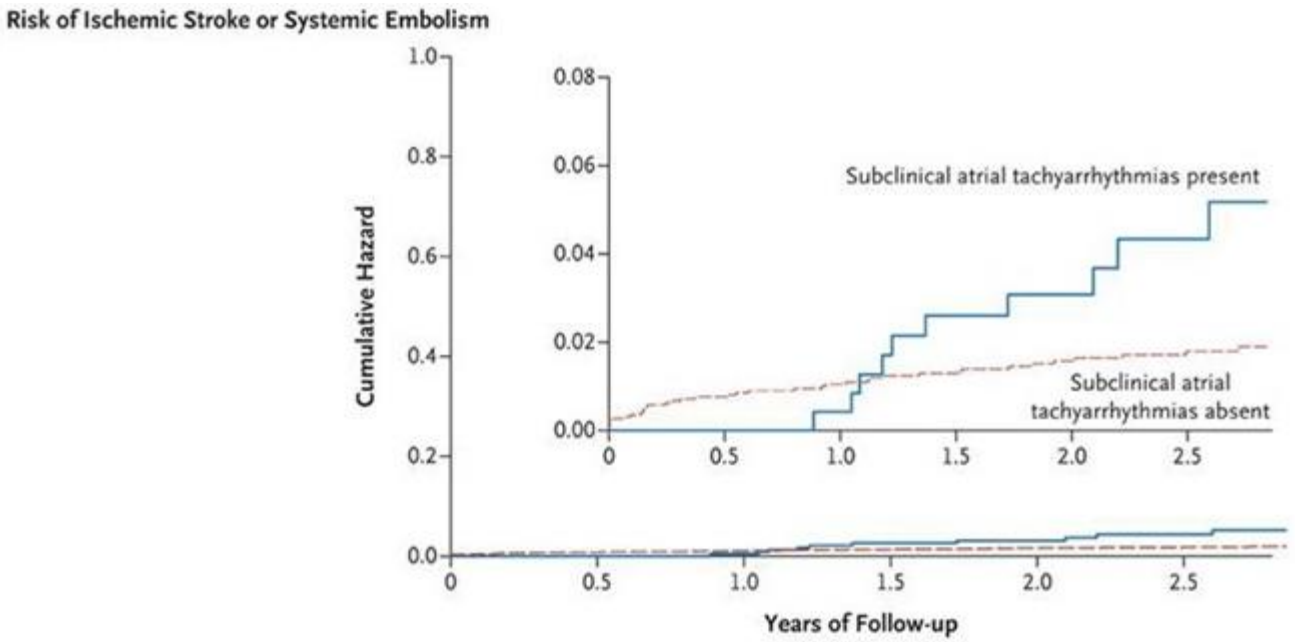


Risk Factors	p Value	OR	95% CI
Age (per 10-yr increase)	<0.001	1.609	1.237–2.091
Men	0.983	1.005	0.613–1.649
Valvular AF	0.012	3.157	1.287–7.741
Congestive heart disease	0.330	0.629	0.248–1.598
Hypertension	0.016	1.849	1.122–3.045
DM	0.889	0.963	0.565–1.640
Vascular disease	0.390	0.689	0.295–1.611
CKD	0.467	1.252	0.683–2.294
Dyslipidemia	0.014	2.062	1.155–3.682
Left atrial size	0.202	1.007	0.996–1.017

Cha et al. Am J Cardiol 2014;113:655-661)

심방세동 증상이 없으면 **OK?**

Subclinical AF and CVA risk



N Engl J Med 2012; 366:120-129

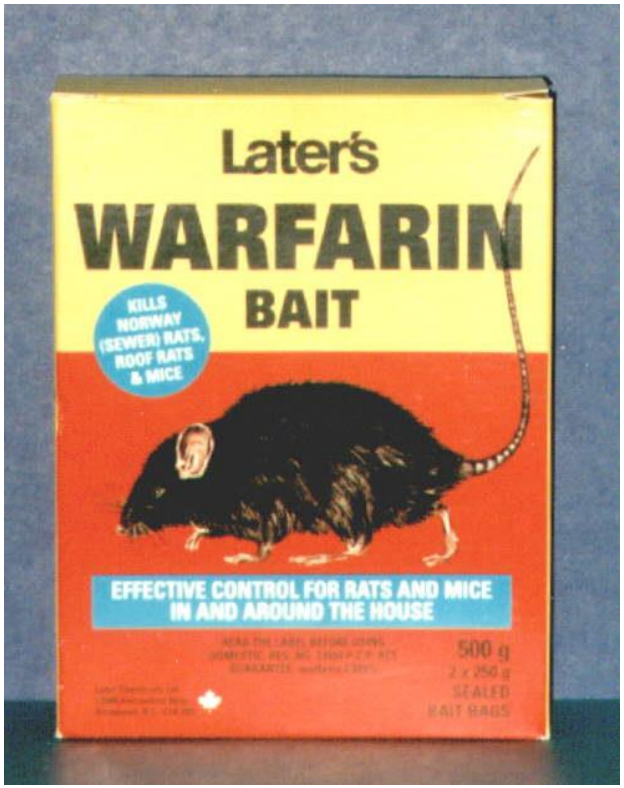
뇌졸중 예방을 위한 선택은?

- **Aspirin**
- **Aspirin + Clopidogrel**
- **Warfarin**
- **NOAC (Novel oral anticoagulation agent)**
- **Device**

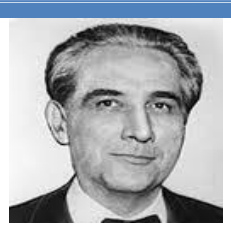
Warfarin

Cow bleeding with sweet clover (1920)

Rodenticide (1950)



항응고제 발전의 역사



Anticoagulant in spoiled sweet clover (K.P. Link)

First clinical use of 4-hydroxycoumarin

Warfarin mechanism elucidated (J. Suttie)

Warfarin dosing/INR

Warfarin clinical trials

***Oral thrombin and Xa** inhibitors*

1910 1920 1930 1940 1950 1960 1970 1980 1990 2000 2010

Heparin discovered by medical student (McLean)

Clinical use of heparin

Requirement for plasma cofactor discovered (K. Brinkhous)

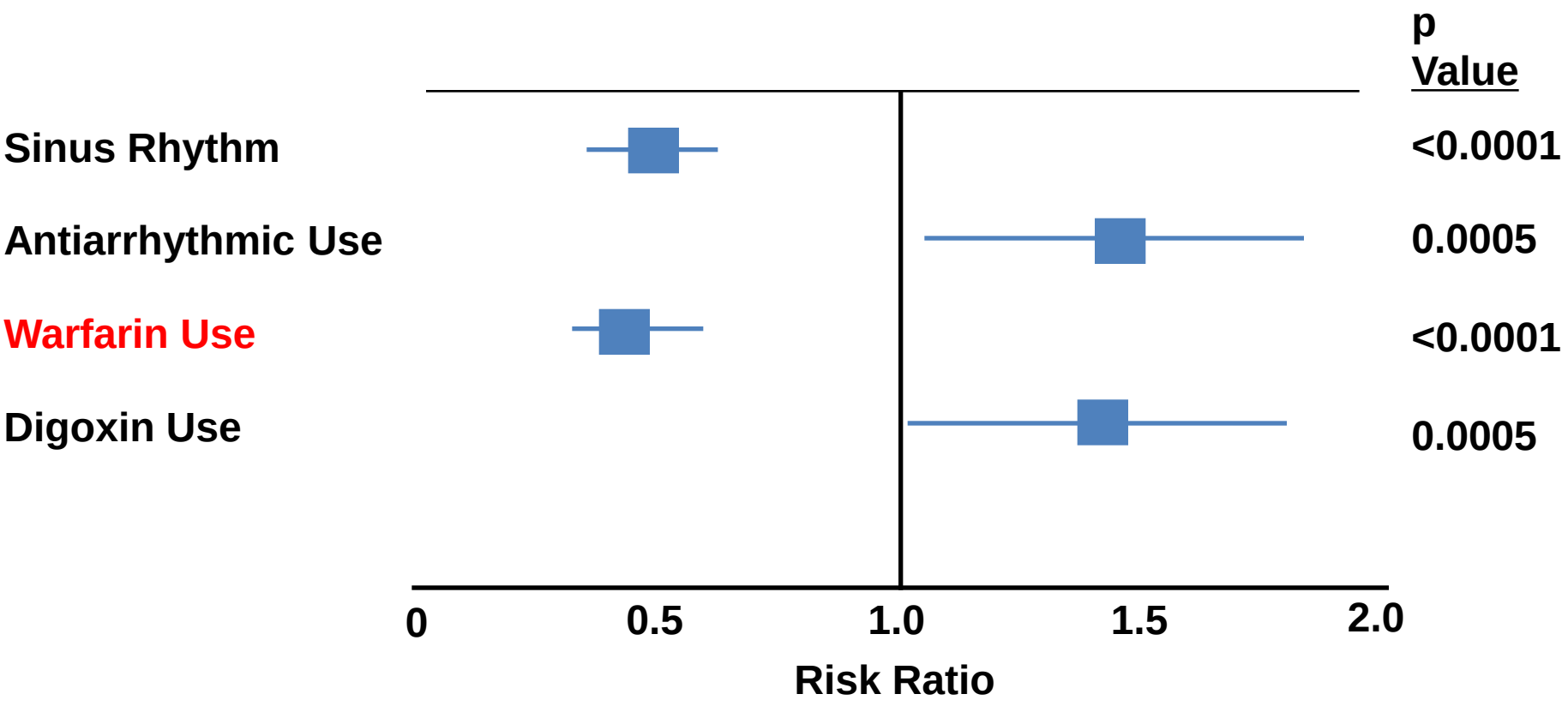
Cont infusion of heparin; aPTT monitoring

LMWH (J. Hirsch)

LMWH trials

Fondaparinux trials

Affirm trial



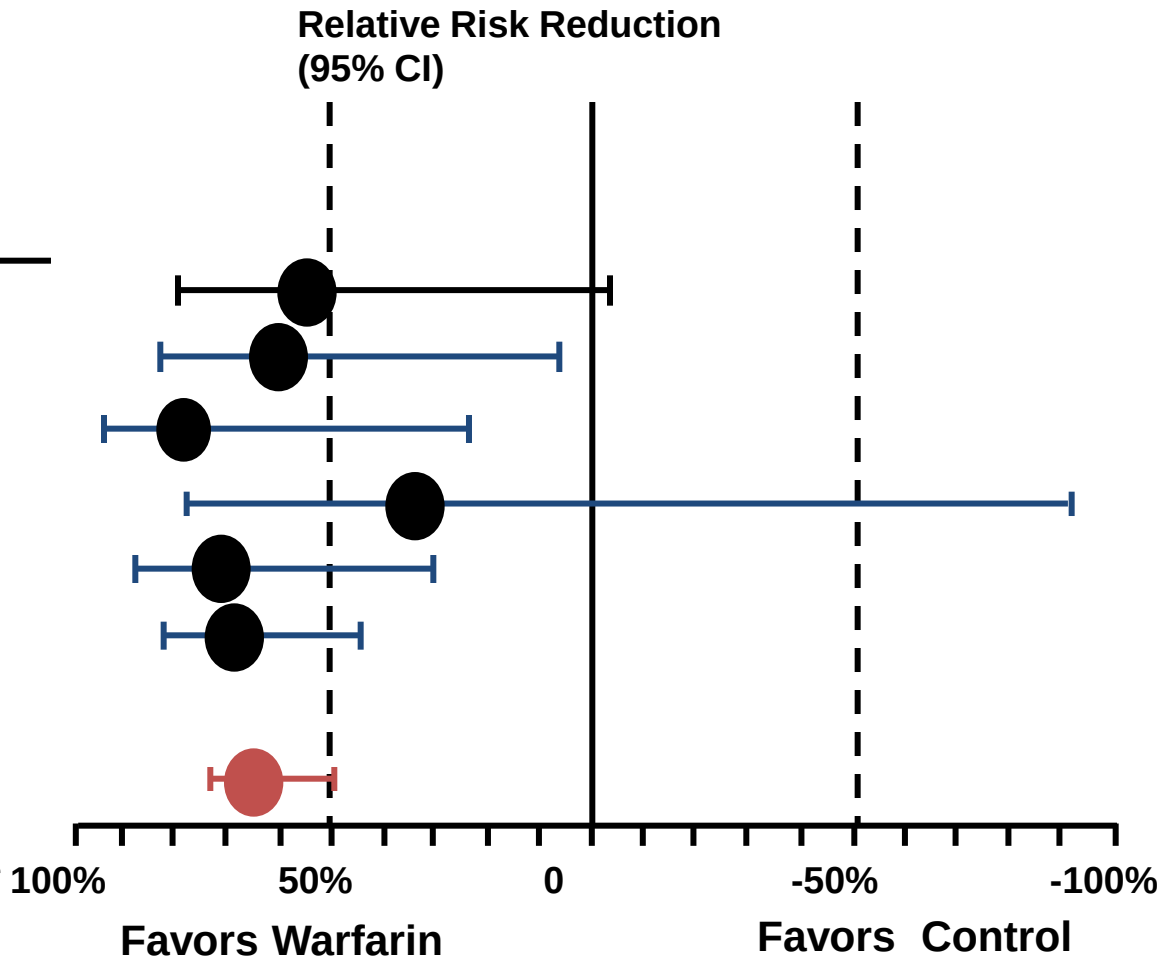
N Engl J Med 2002; 347: 1825-33.

Warfarin은 효과적인가?

Adjusted-dose warfarin compared with placebo or control

Study	Year
AFASAK I	1989; 1990
SPAF I	1991
BAATAF	1990
CAFA	1991
SPINAF	1992
EAFT	1993

All trials *(n=6)*
N=2,900

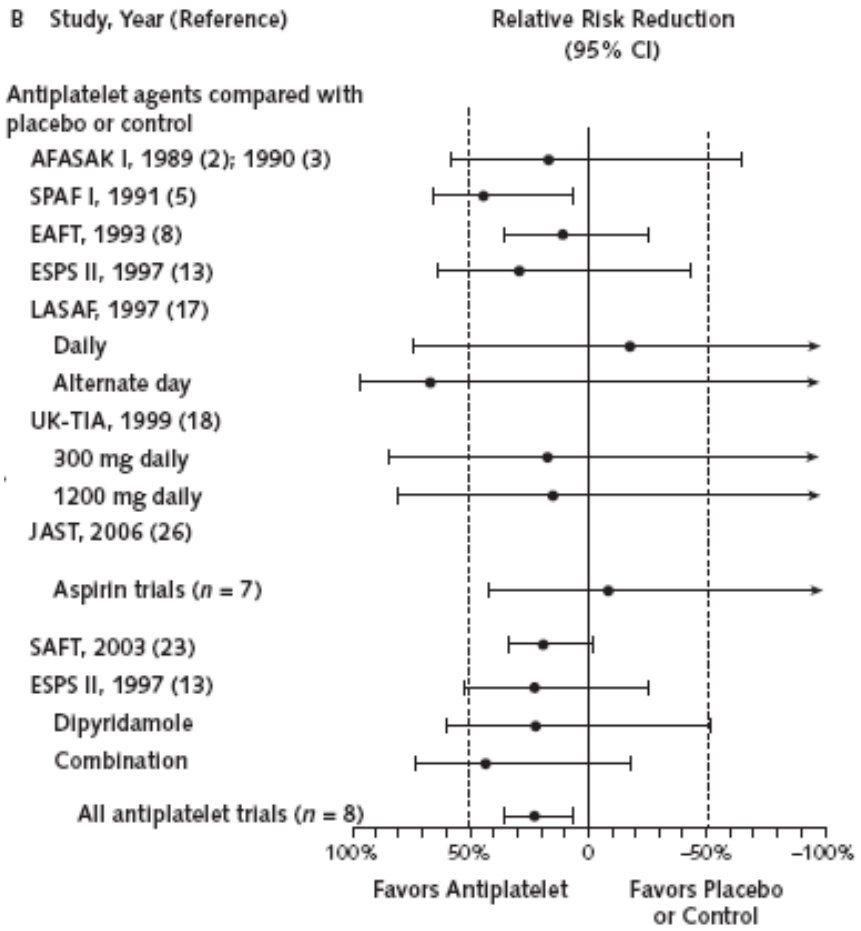


Warfarin reduce incidence of stroke by about 64%

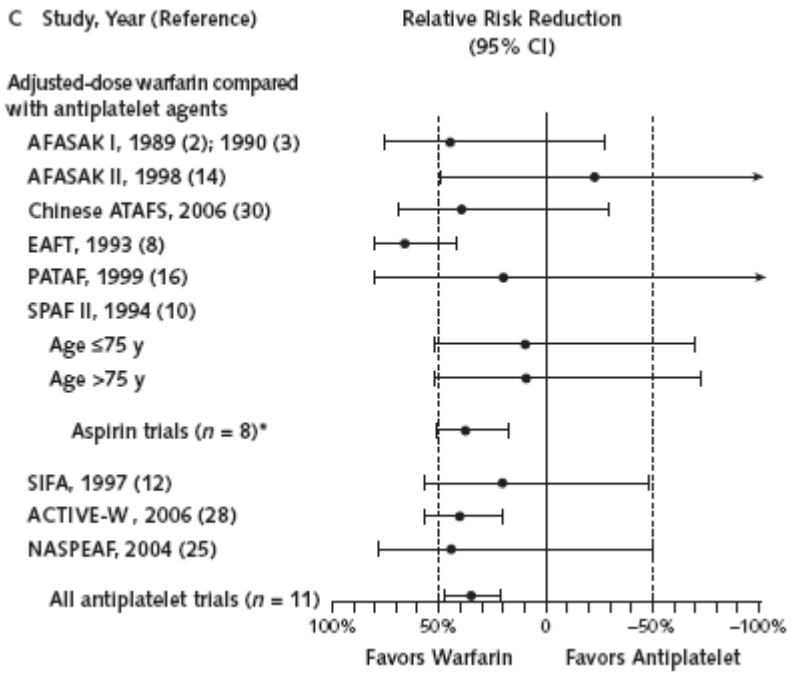
Ann Intern Med. 2007;146:857-867.

항혈소판제를 대신 사용하면 어떨까?

Antiplatelet agent vs placebo



Antiplatelet agent vs VKA



RR 38%

Ann Intern Med. 2007;146:857-867.

Dual antiplatelet agent vs aspirin

Absolute risk reduction

Endpoint	Events rate		Absolute risk reduction (ARR)
	Studied treat.	Control treat.	
thrombo-embolic event (cerebral or systemic)	22,06%	24,43%	-23,7‰
stroke (fatal and non fatal)	7,85%	10,79%	-29,4‰
ischemic stroke	6,23%	9,07%	-28,4‰
myocardial infarction (fatal and non fatal)	2,39%	3,04%	-6,5‰
All cause death	21,87%	22,24%	-3,7‰
Bleeding	26,88%	17,21%	9,7%
Major bleeding	6,65%	4,28%	2,4%
Minor bleeding	10,82%	4,63%	6,2%
Haemmorhagic stroke	7,95‰	5,82‰	2,1‰
Fatal bleeding	1,11%	7,14‰	4,0‰
Cardiovascular death	15,91%	15,84%	0,7‰
Fatal stroke	1,86%	2,46%	-6,0‰
TE event or ischemic stroke or systemic embolism	22,06%	24,43%	-23,7‰
intracranial hemorrhage	1,43%	7,67‰	6,6‰

Dual antiplt. Tx : safe and effective?

Table VI. Any fatal or nonfatal ischemic stroke.

	Comparator						
Intervention	Apixaban	Aspirin	Aspirin and Clopidogrel	Dabigatran	Placebo	Rivaroxaban	Warfarin
Apixaban	1						
Aspirin	2.42 (1.50–3.71)	1					
Aspirin and clopidogrel	1.83 (1.04–3.44)	**0.75 (0.52–1.26)**	1				
Dabigatran	0.97 (0.49–2.03)	0.40 (0.22–0.80)	0.53 (0.25–1.09)	1			
Placebo	3.45 (1.97–6.28)	**1.43 (0.97–2.26)**	1.87 (1.05–3.26)	3.52 (1.75–7.23)	1		
Rivaroxaban	0.95 (0.47–1.97)	0.39 (0.21–0.78)	0.52 (0.25–1.02)	0.97 (0.43–2.14)	0.27 (0.13–0.55)	1	
Warfarin	**1.04 (0.67–1.62)**	**0.43 (0.32–0.60)**	**0.56 (0.35–0.87)**	**1.06 (0.60–1.86)**	**0.30 (0.20–0.47)**	**1.09 (0.62–1.95)**	1

Table XI. Intracranial hemorrhage.

	Comparator				
Intervention	Apixaban	Aspirin	Aspirin and Clopidogrel	Dabigatran	Warfarin
Apixaban	1				
Aspirin	**1.22 (0.34–4.75)**	1			
Aspirin and clopidogrel	2.29 (0.39–13.57)	**1.90 (0.54–6.81)**	1		
Dabigatran	0.86 (0.15–4.72)	0.69 (0.10–5.16)	0.36 (0.04–3.98)	1	
Warfarin	**2.39 (0.79–7.84)**	**1.95 (0.45–9.29)**	1.03 (0.15–7.59)	**2.78 (0.83–9.91)**	1

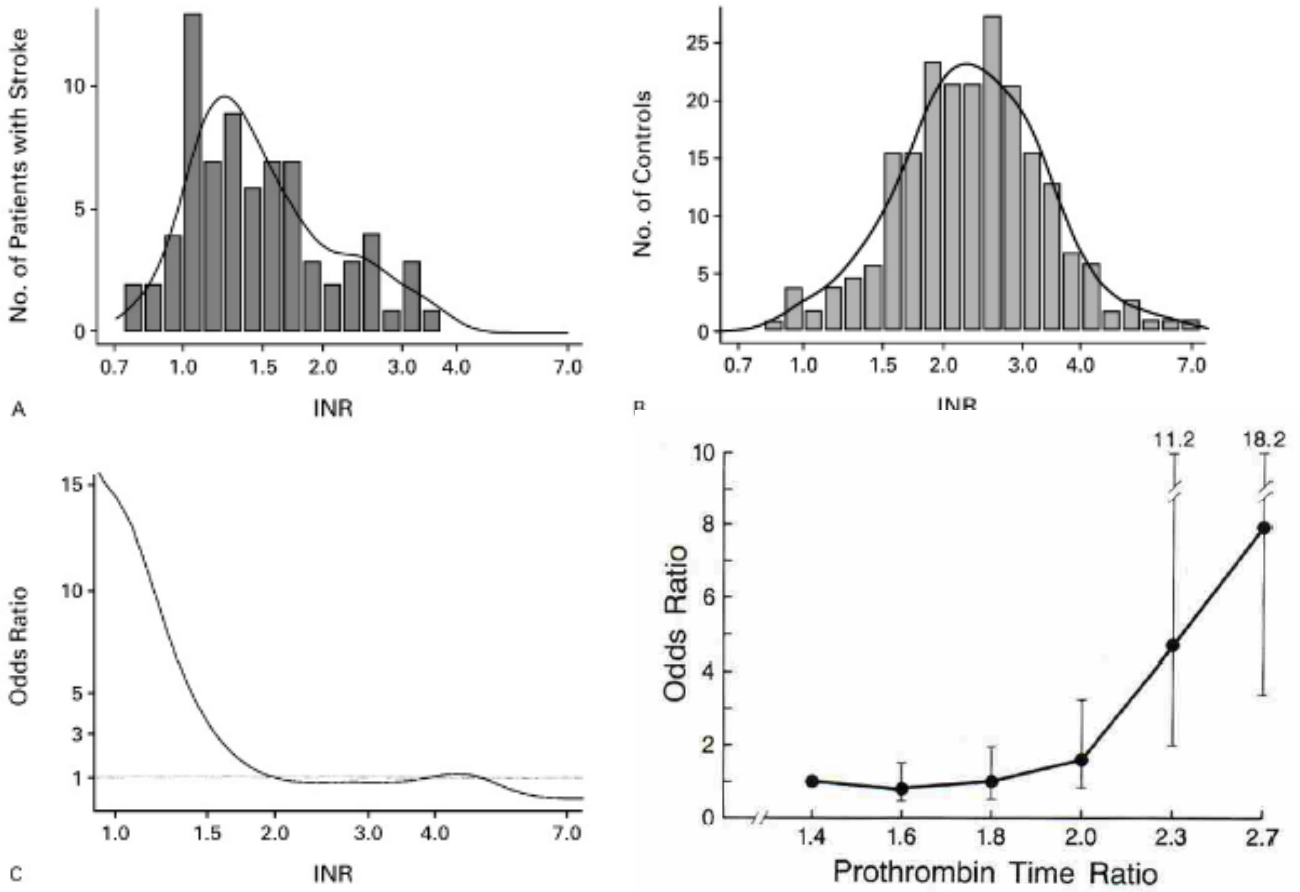
Clin Ther. 2013;35:967–984

Warfarin사용의 장애물들

- **Patients factor**
  - Perceived risk>benefit
  - Patients unreliable
  - Difficulty of maintaining therapeutic INR
- **Physician factor**
  - Underestimated risk of stroke and overestimate risk of bleeding
  - Physicians believe patients will refuse therapy
  - Monitoring was inconvenient

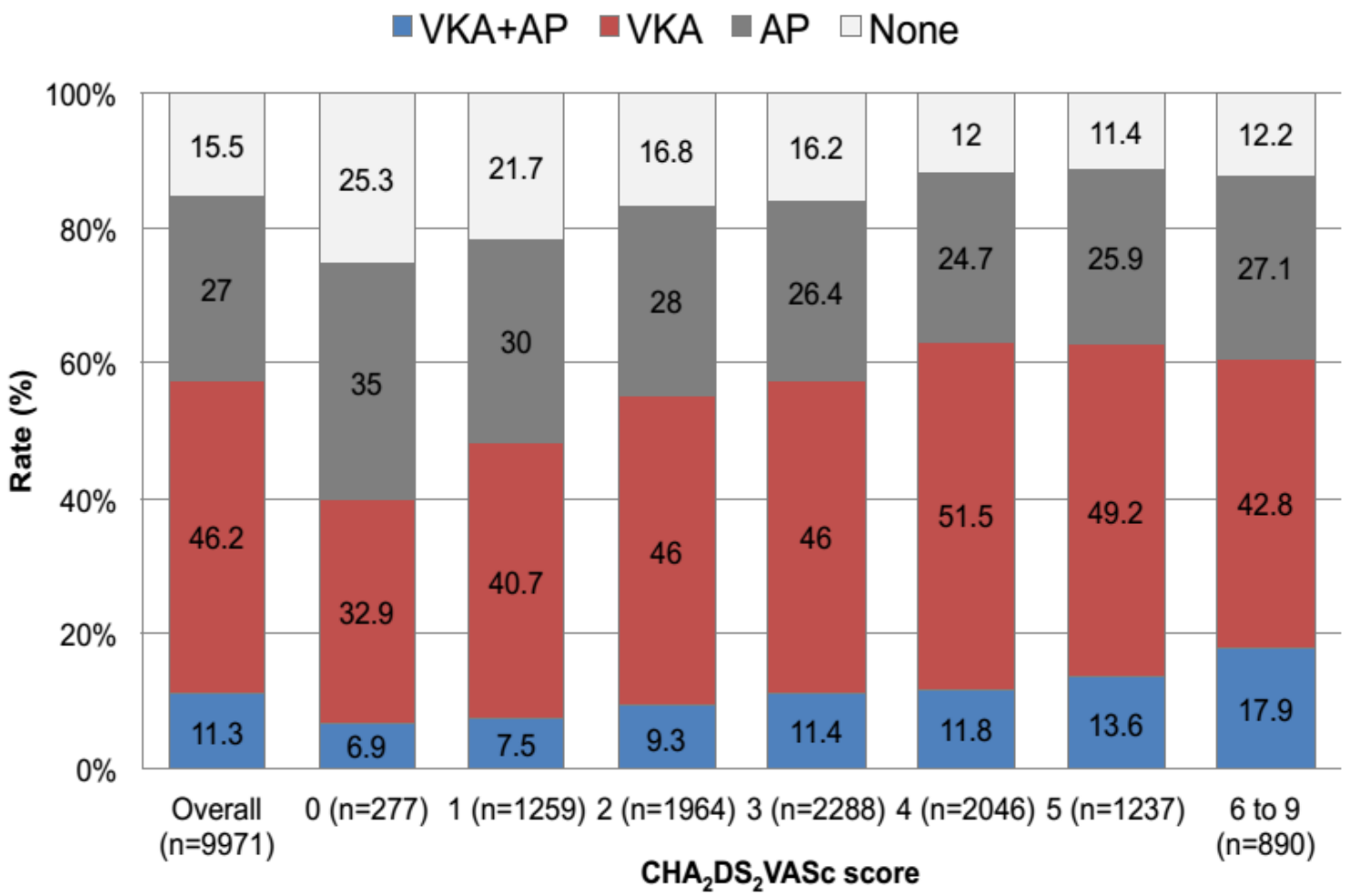
Arch Intern med 2000;160:41-46

Narrow therapeutic range



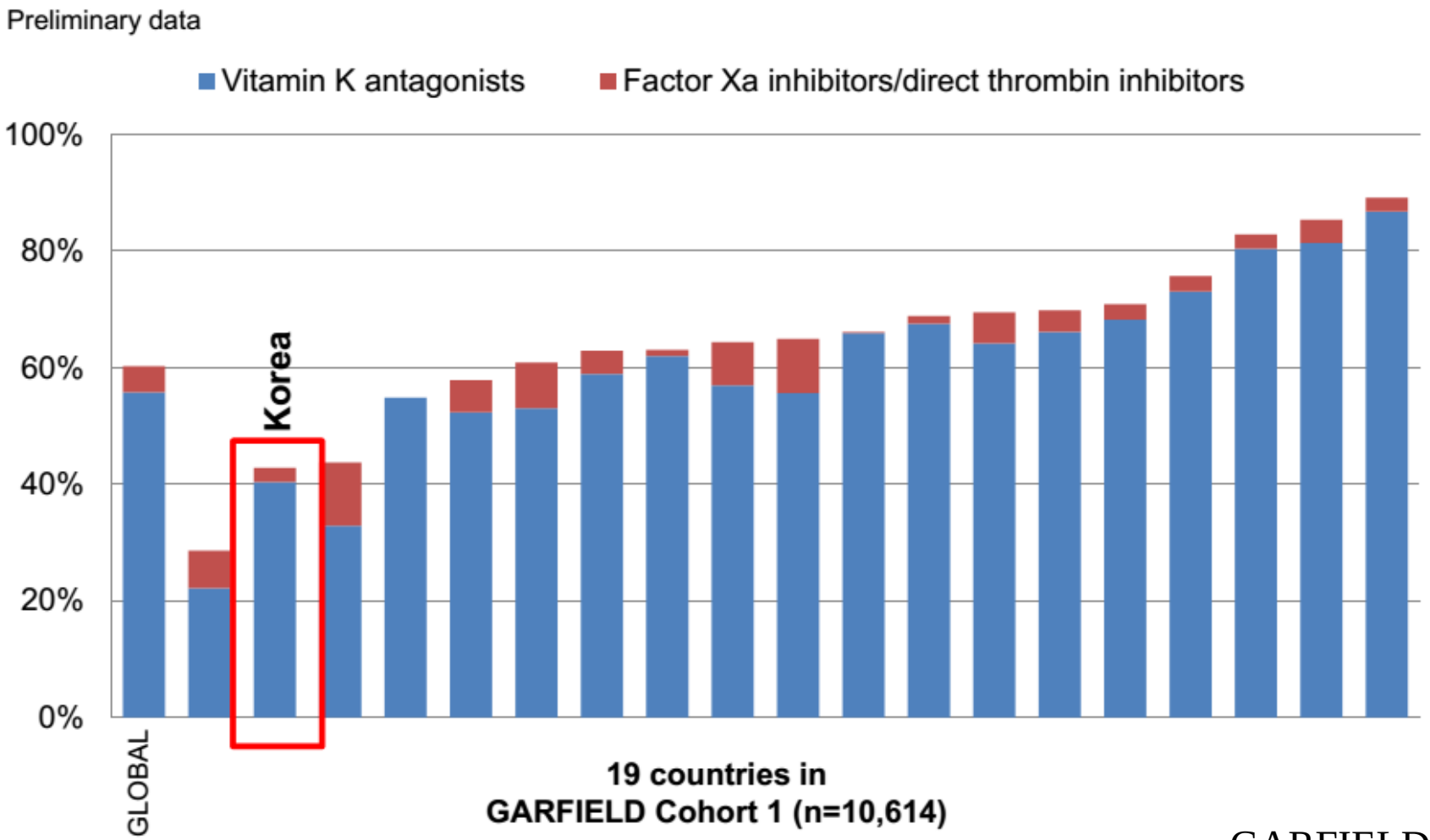
N Engl J Med 1996; 335:540-546
Ann of int med 1994;120:897-902

실제로는.....



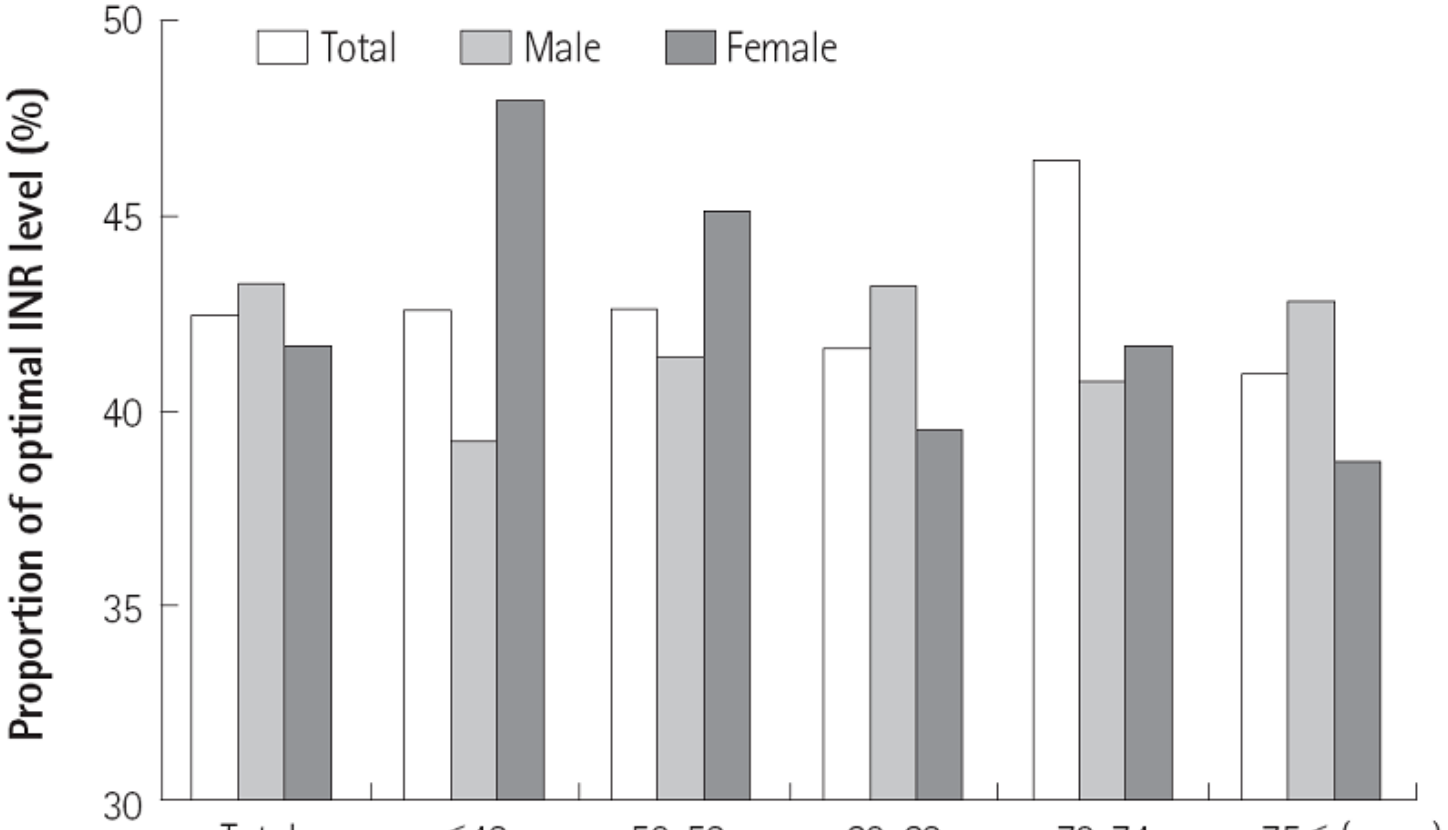
GARFIELD data

VKA use in real world



GARFIELD data

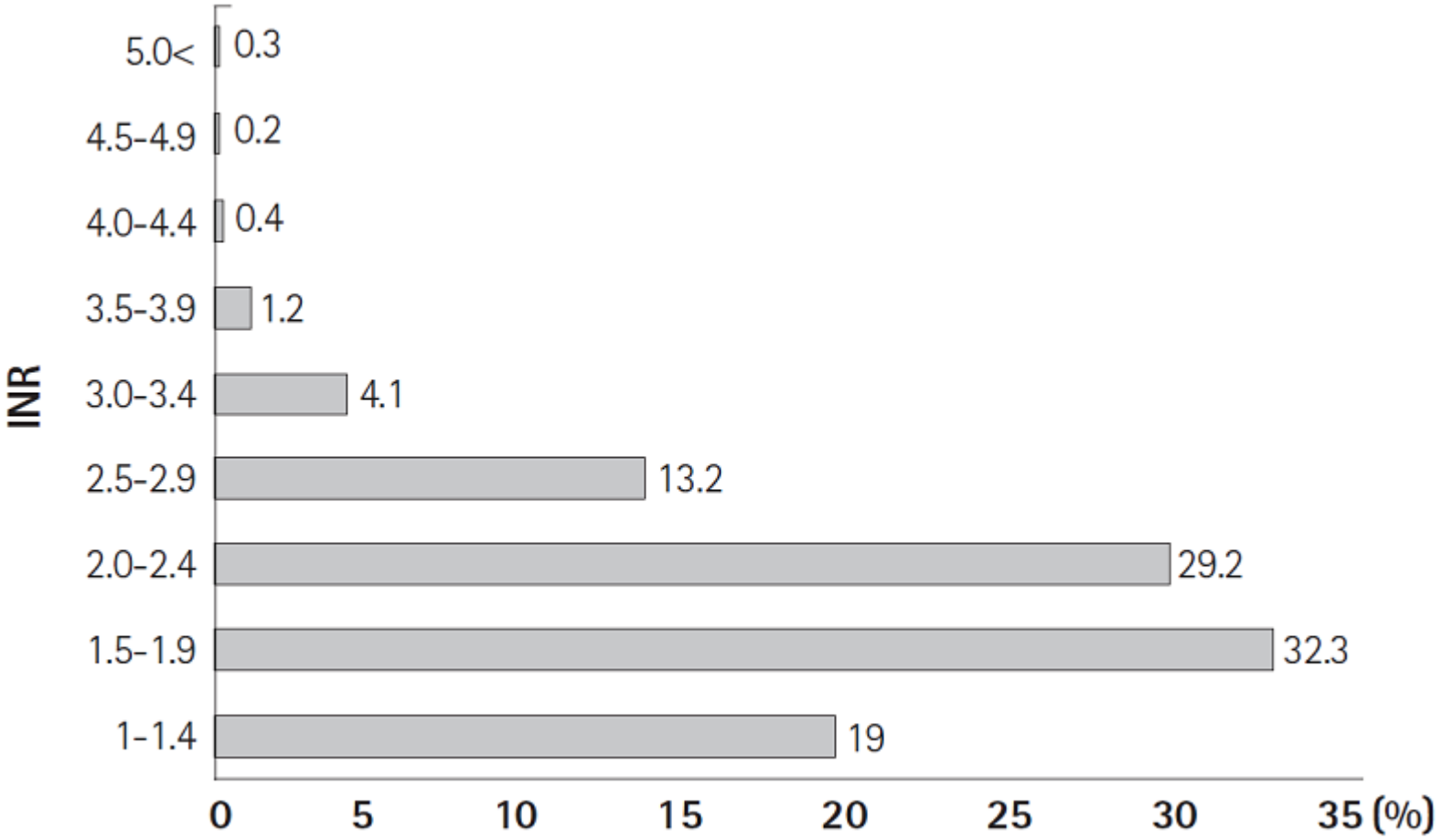
Optimal INR(2-3) : easy to achieve?



	Total	≤49	50-59	60-69	70-74	75≤ (years)
Total	2370	334	468	757	393	418
Male	1371	192	288	447	230	214
Female	999	142	180	310	163	204

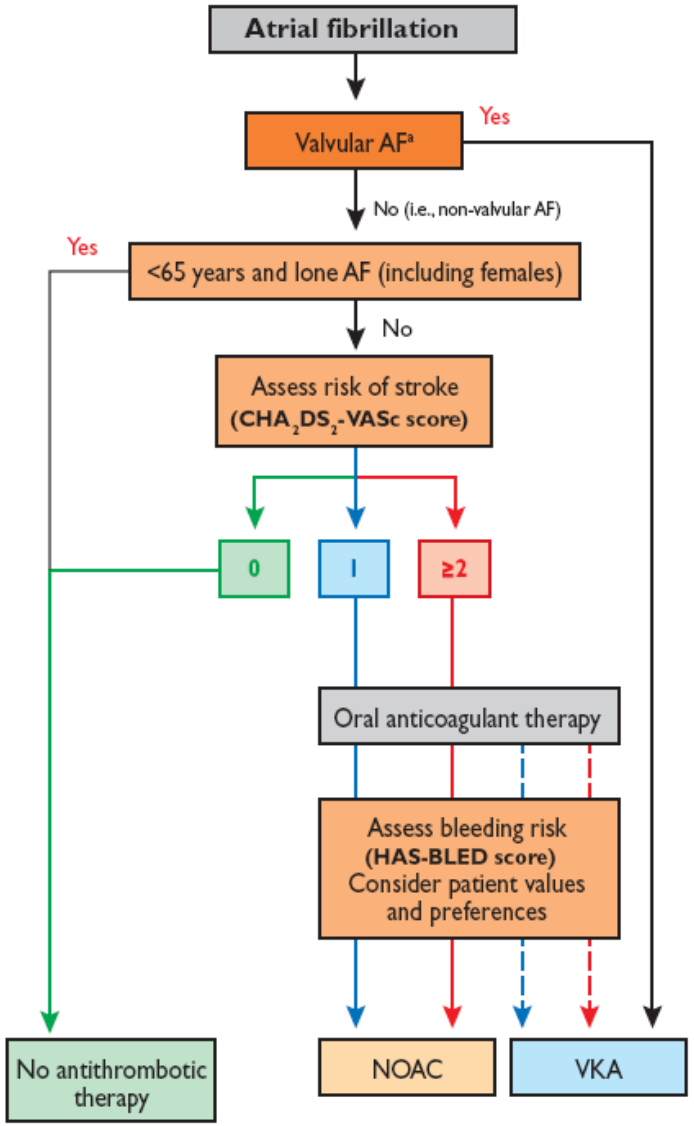
KORAF data

Optimal INR(2-3) : easy to achieve?



KORAF data

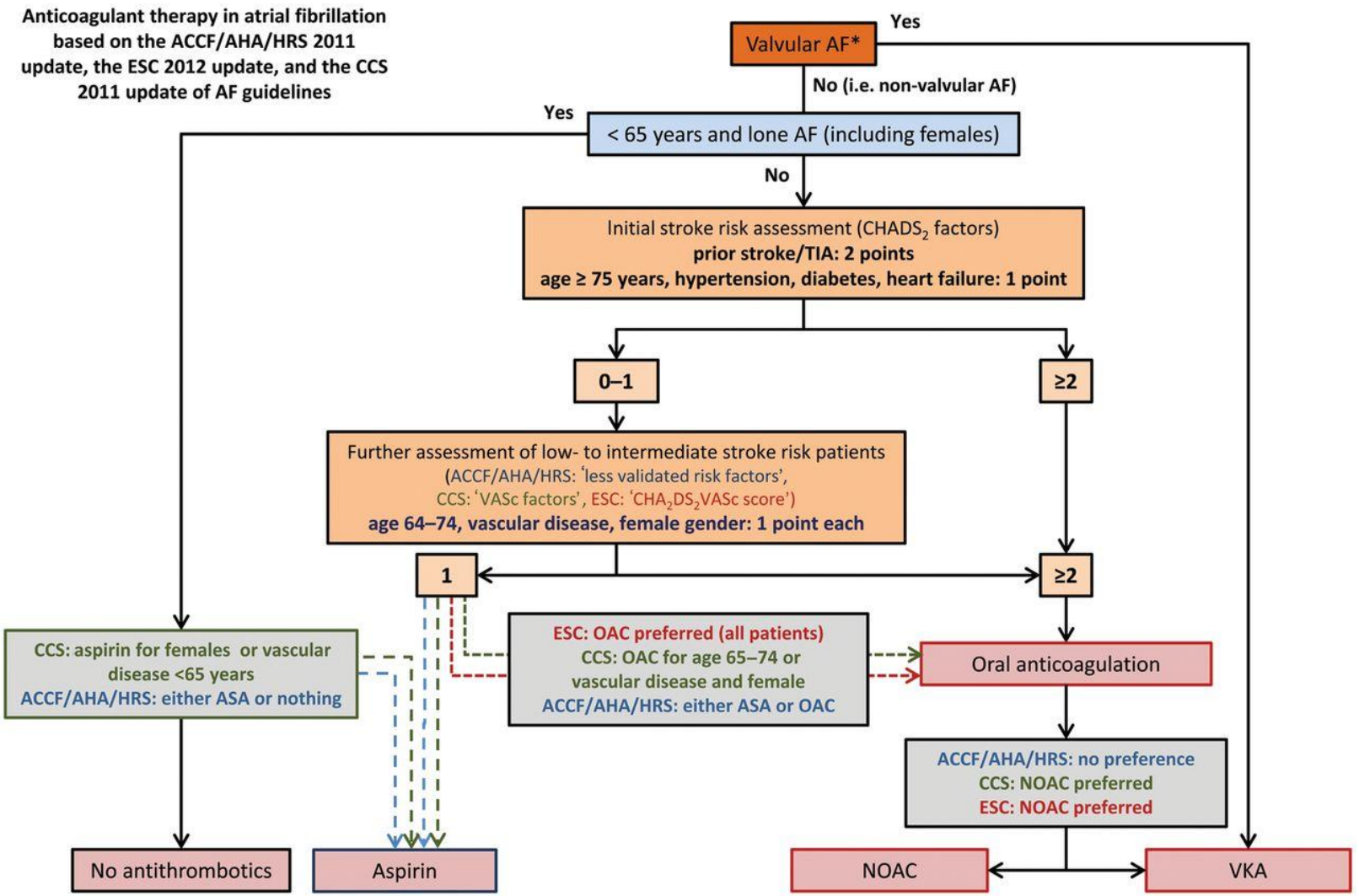
Guideline for anticoagulation in AF 2012 ESC focused update



	Multivariate hazard ratios (95% CI)
Age (years) <65 65–74 ≥75	 1.0 (Reference) 2.97 (2.54–3.48) 5.28 (4.57–6.09)
Female sex	1.17 (1.11–1.22)
Previous ischaemic stroke	2.81 (2.68–2.95)
Intracranial bleeding	1.49 (1.33–1.67)
Vascular disease (any) • Myocardial infarction • Previous CABG • Peripheral artery disease	1.14 (1.06–1.23) 1.09 (1.03–1.15) 1.19 (1.06–1.33) 1.22 (1.12–1.32)
Hypertension	1.17 (1.11–1.22)
Heart failure (history)	0.98 (0.93–1.03)
Diabetes mellitus	1.19 (1.13–1.26)
Thyroid disease Thyrotoxicosis	1.00 (0.92–1.09) 1.03 (0.83–1.28)

ESC/CCS/AHA guideline

Kirchhof P, et al. European Heart Journal (2013) 34, 1471–1474

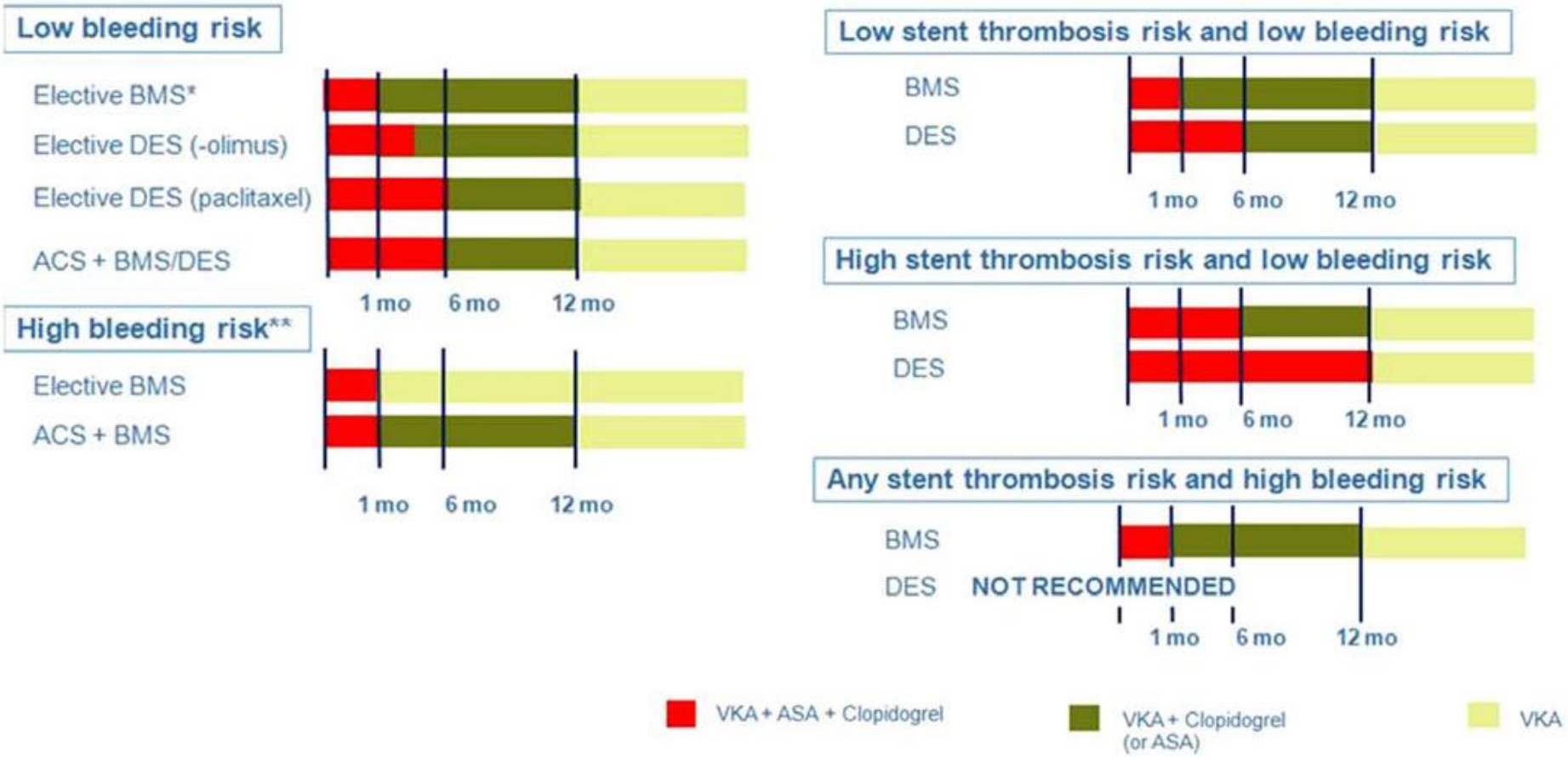


In this patient…

$CHAS_2$ score	2
CHA_2DS_2-VASC score	4
- CHF	0
- HTN	1
- Age≥75	0
- DM	1
- Stroke or TIA	0
- Vascular disease	1
- Age≥65	1
- female	0

Indication for warfarin Tx

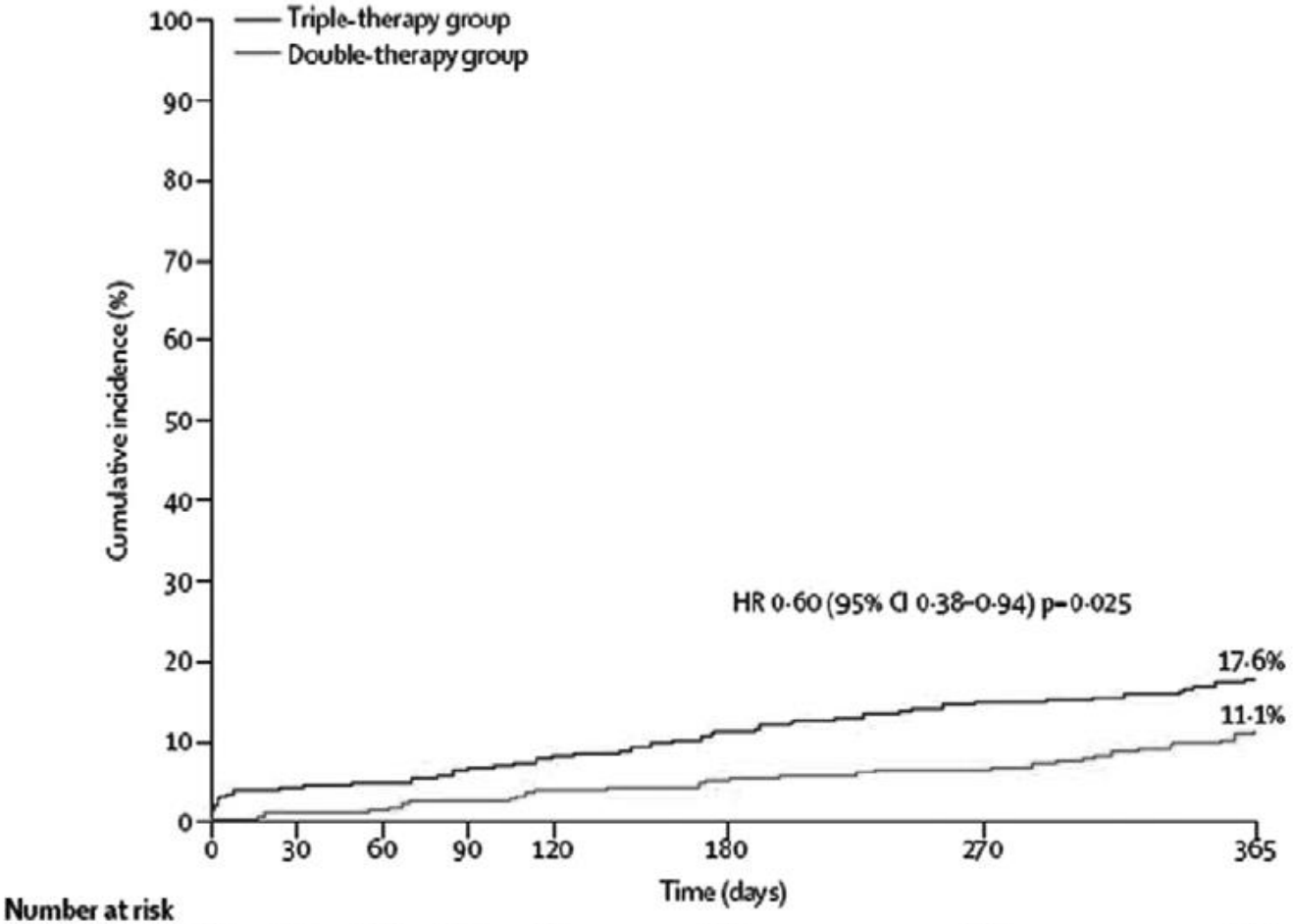
ESC guideline for antithrombotic Tx in PCI Pt.



WOEST trial

- **Dual(clopid+VKA) vs Triple(Clopid+asp+VKA)**
- **573 patients, 1yr**
- **MI (3.2% vs 4.6%), stroke (1.1% vs 2.8%), target vessel revascularization (7.2% vs 6.7%), stent thrombosis (1.4% vs 3.2%)**
  - ▶ did not differ significantly between the groups
- **All-cause mortality : 2.5% vs 6.3%; *P=0.027***
- **The combination of the ischemic end points occurred : 11.1% vs17.6% (hazard ratio, 0.56; 95% confidence interval, 0.35–0.91)**

WOEST trial


Triple-therapy group
Double-therapy group
Cumulative incidence (%)
100
90
80
70
60
50
40
30
20
10
0
HR 0·60 (95% CI 0·38–0·94) p=0·025
17·6%
11·1%
0
30
60
90
120
180
270
365
Time (days)
Number at risk
Triple therapy 284 272 270 266 261 252 242 223
Double therapy 279 276 273 270 266 263 258 234

In this patient…

$CHAS_2$ score	2
CHA_2DS_2-VASC score	4
- CHF	0
- HTN	1
- Age≥75	0
- DM	1
- Stroke or TIA	0
- Vascular disease	1
- Age≥65	1
- female	0

Date	INR	warfarin
OPD1	4.5	4
OPD2	1.6	3
OPD3	4.0	3.5
OPD4	2.8	3/3.5
OPD5	4.2	3/3.5
OPD6	1.8	3
OPD7		NOAC

PCI(DES) d/t AMI

Novel oral anticoagulant (NOAC) 급여인정조건

와파린 초기치료(2개월 혹은 INR 2 이상 도달)

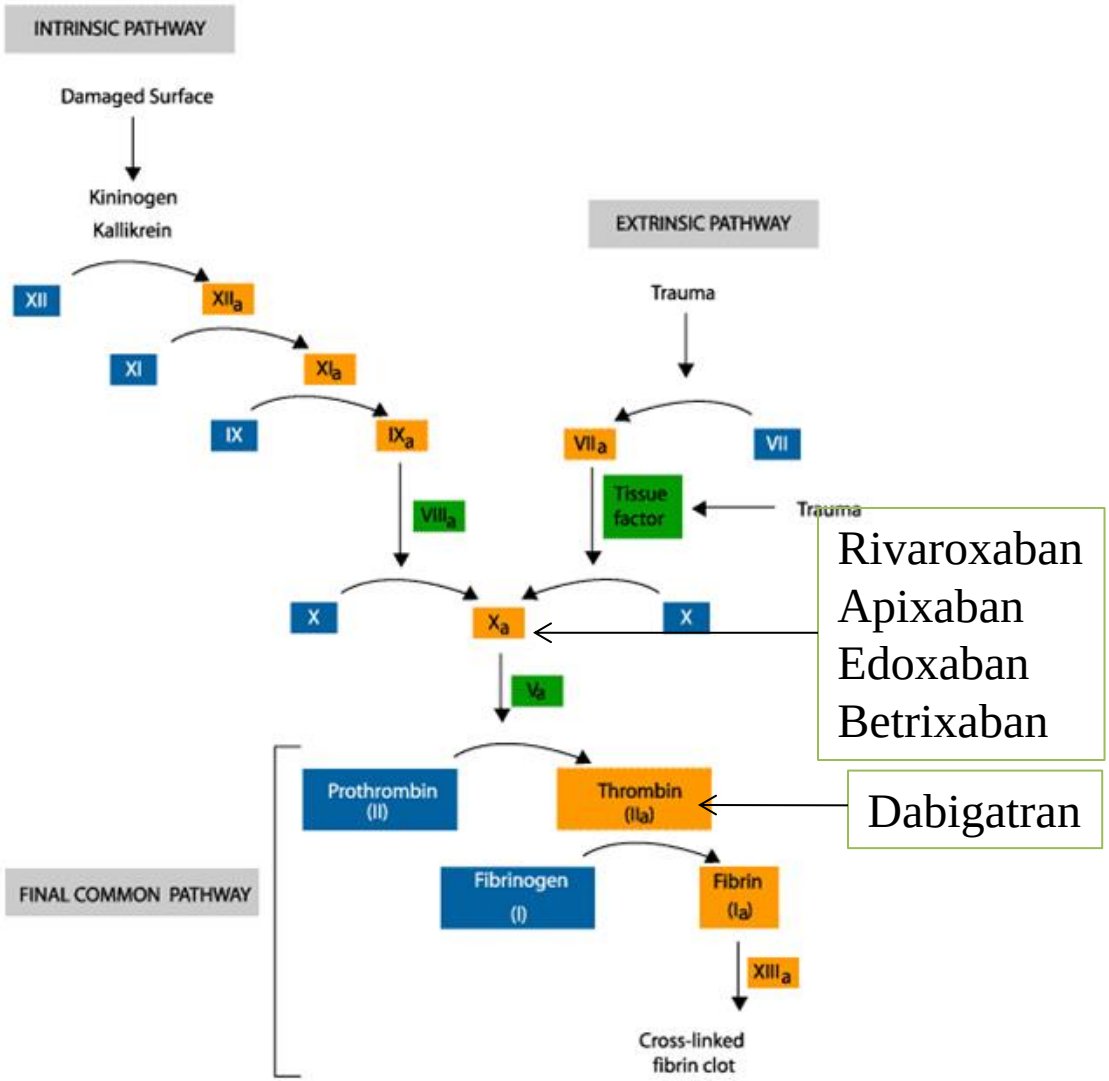
1. **1mg**으로 **5**일 이상 투여 후 **INR 3.0** 이상
2. **10mg** 이상으로 **5**일 이상 투여 후 **INR 2.0**미만
3. 최초 **2**개월 와파린 용량 조절 기간 동안 **INR**검사 **7**일 간격으로 측정시 **3**회 이상 **3.5** 초과한 경우

와파린 유지 기간

유지 용량 결정 후 최근 **6**개월간 측정한 **INR** 검사치가 **target INR(2.0-3.0)**을 **40%** 이상 벗어난 경우, 단 최근 **6**개월간 **INR**검사가 **5**회 미만인 경우 이전 검사를 포함하여 **5**회 **INR**검사 중 **2**번 이상 벗어난 경우

- **기타 급여 인정 : 와파린 복용 중 중요 장기 출혈이나 2unit 이상의 심한 bleeding을 경험한 환자**

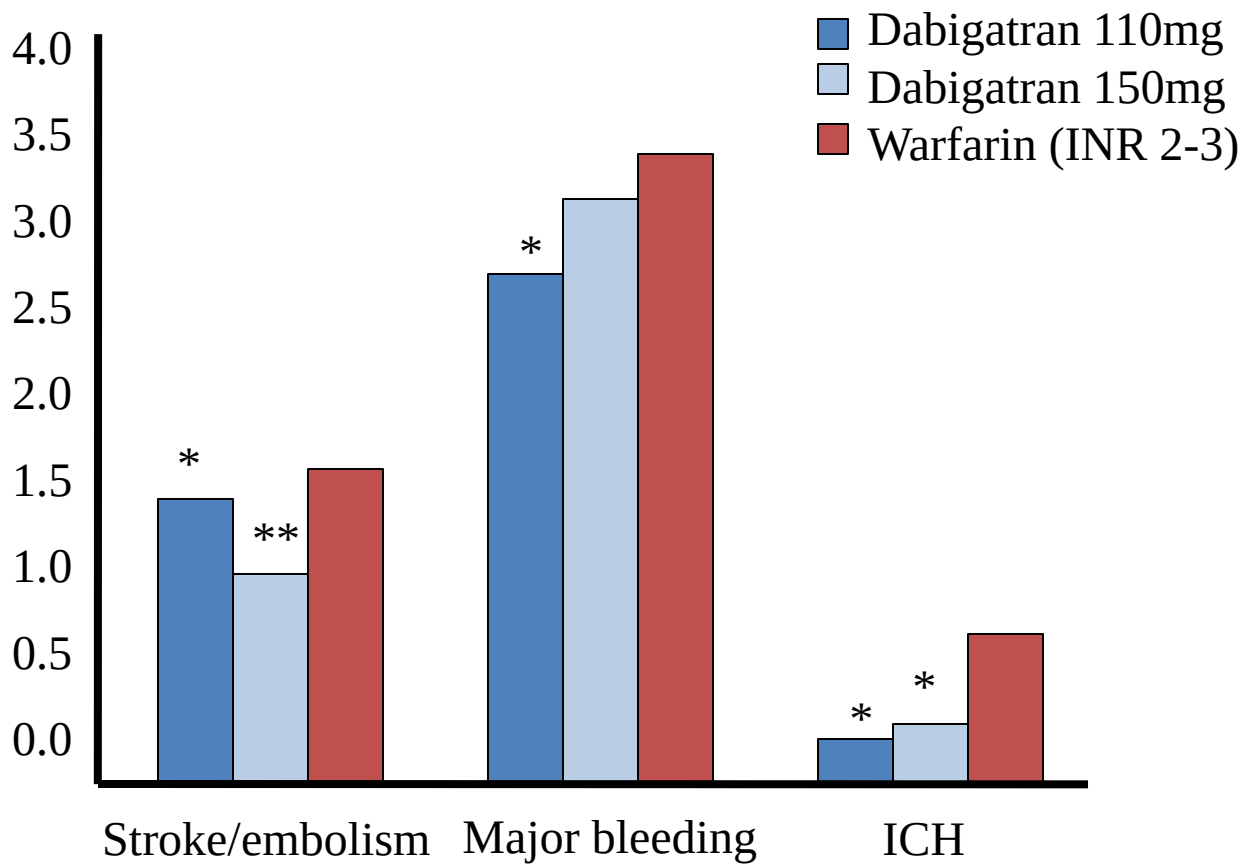
Novel oral anticoagulant (NOAC)



Novel oral anticoagulant (NOAC)

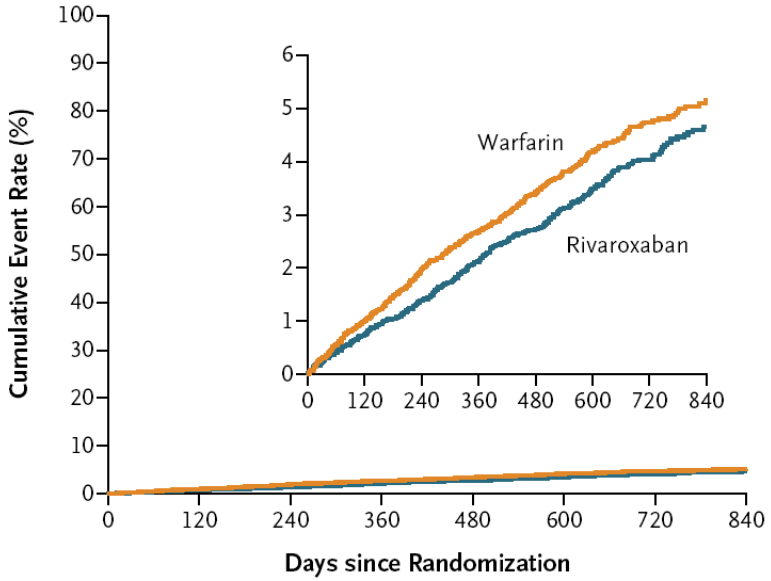
	Dabigatran (RE-LY)[70, 71]	Rivaroxaban (ROCKET-AF)[3]	Apixaban (ARISTOTLE)[4]
Drug characteristics			
Mechanism	Oral direct thrombin inhibitor	Oral direct factor Xa inhibitor	Oral direct factor Xa inhibitor
Bioavailability, %	6	60–80	50
Time to peak levels, h	3	3	3
Half-life, h	12–17	5–13	9–14
Excretion	80% renal	2/3 liver, 1/3 renal	25% renal, 75% faecal
Dose	150 mg b.i.d.	20 mg o.d.	5 mg b.i.d.
Dose in renal impairment	110 mg b.i.d.	15 mg o.d. (if CrCl 30-49 mL/min)	2.5 mg b.i.d.
Special considerations	Intestinal absorption is pH-dependent and is reduced in patients taking proton pump inhibitors	Higher levels expected in patients with renal or hepatic failure	
	Increased risk of bleeding in patients taking verapamil/amiodarone/quinidine/ketoconazole	Activity lower in fasted patients so should be taken after food	

Dabigatran : RE-LY trial



N Engl J Med 2009; 361 : 1139-51.

Rivaroxaban : ROCKET AF



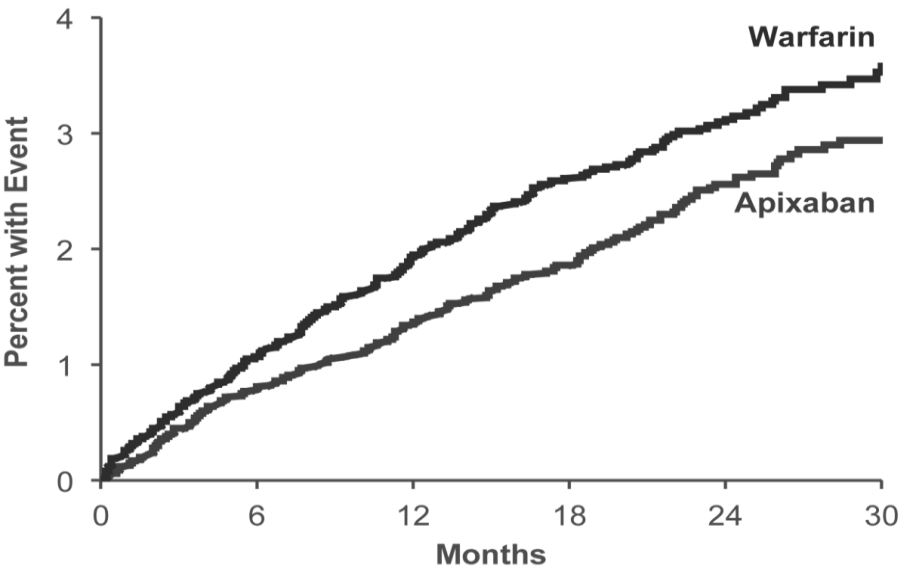
No. at Risk

Rivaroxaban	7081	6879	6683	6470	5264	4105
Warfarin	7090	6871	6656	6440	5225	4087

Variable	Rivaroxaban (N=7111) Events *no. (%)*	Rivaroxaban (N=7111) Event Rate *no./100 patient-yr*	Warfarin (N=7125) Events *no. (%)*	Warfarin (N=7125) Event Rate *no./100 patient-yr*	Hazard Ratio (95% CI)†	P Value‡
Principal safety end point: major and nonmajor clinically relevant bleeding§	1475 (20.7)	14.9	1449 (20.3)	14.5	1.03 (0.96–1.11)	0.44
Major bleeding						
Any	395 (5.6)	3.6	386 (5.4)	3.4	1.04 (0.90–1.20)	0.58
Decrease in hemoglobin ≥2 g/dl	305 (4.3)	2.8	254 (3.6)	2.3	1.22 (1.03–1.44)	0.02
Transfusion	183 (2.6)	1.6	149 (2.1)	1.3	1.25 (1.01–1.55)	0.04
Critical bleeding¶	91 (1.3)	0.8	133 (1.9)	1.2	0.69 (0.53–0.91)	0.007
Fatal bleeding	27 (0.4)	0.2	55 (0.8)	0.5	0.50 (0.31–0.79)	0.003
Intracranial hemorrhage	55 (0.8)	0.5	84 (1.2)	0.7	0.67 (0.47–0.93)	0.02
Nonmajor clinically relevant bleeding	1185 (16.7)	11.8	1151 (16.2)	11.4	1.04 (0.96–1.13)	0.35

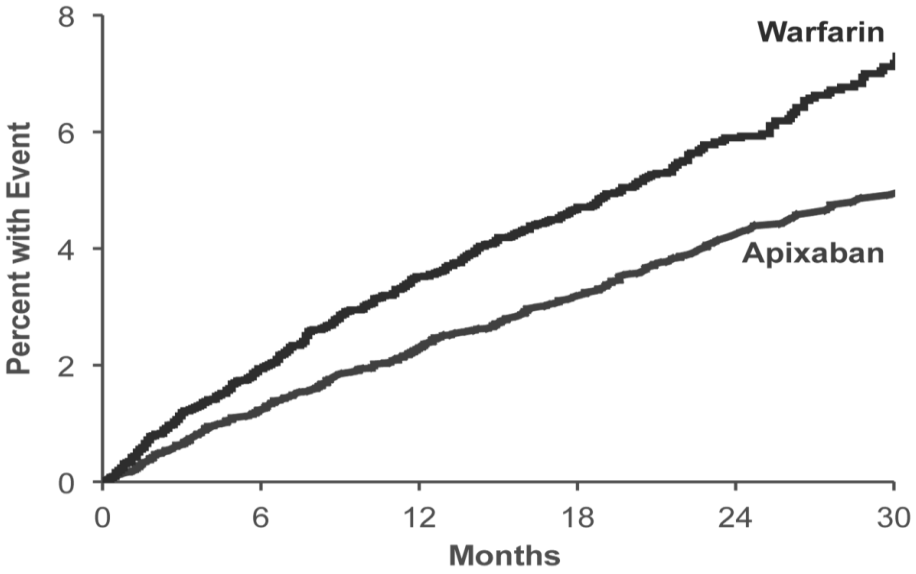
Apixaban : ARISTOTLE

Risk of Stroke



Apixaban 212 patients, 1.27% per year
Warfarin 265 patients, 1.60% per year
HR 0.79 (95% CI, 0.66–0.95); P (superiority)=0.011

Risk of major bleeding



Apixaban 327 patients, 2.13% per year
Warfarin 462 patients, 3.09% per year
HR 0.69 (95% CI, 0.60–0.80); P<0.001

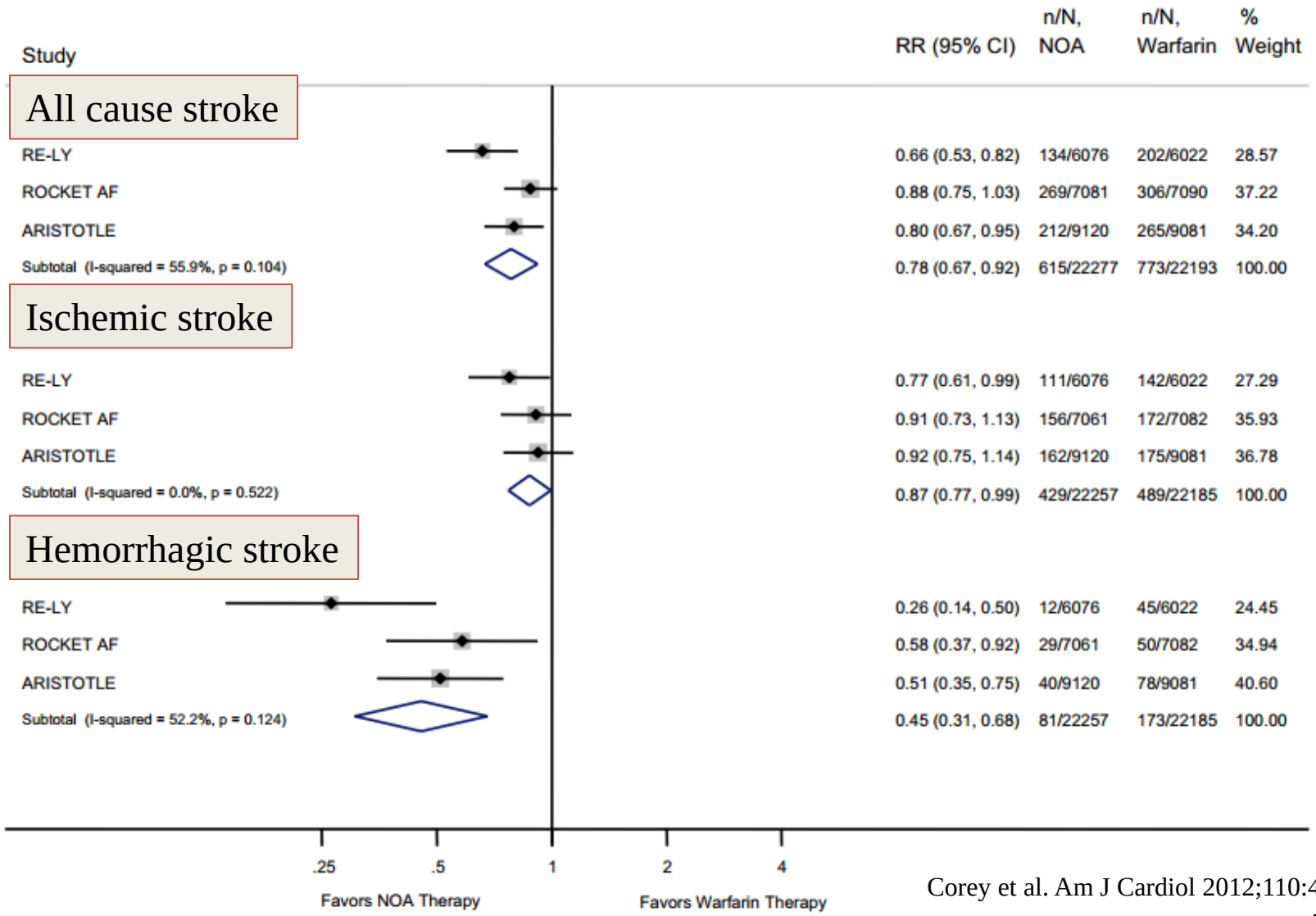
Novel oral anticoagulant (NOAC)

Baseline patient characteristics							
Age, years	71.5 ± 8.7 (mean ± SD)			73 (65–78) [median (interquartile range)]		70 (63–76) [median (interquartile range)]	
Male sex, %	63.6			61.3		64.5	
$CHADS_2$ (mean)	2.1			3.5		2.1	
Outcomes (% per year)							
	Warfarin	Dabigatran 150	Dabigatran 110	Warfarin	Rivaroxaban	Warfarin	Apixaban
	(*n* = 6022)	(*n* = 6076)	(*n* = 6015)	(*n* = 7133)	(*n* = 7131)	(*n* = 9081)	(*n* = 9120)
		(RR, 95% CI; *P* value)	(RR, 95% CI; *P* value)		(HR, 95% CI; *P* value)		(HR, 95% CI; *P* value)
Stroke/systemic embolism	1.69	1.11 (0.66, 0.53–0.82; *P* for superiority <0.001)	1.53 (0.91, 0.74–1.11; *P* for non-inferiority <0.001)	2.4	2.1 (0.88, 0.75–1.03; *P* for non-inferiority <0.001, *P* for superiority = 0.12) (ITT)	1.6	1.27 (0.79, 0.66–0.95; *P* <0.001 for non-inferiority, *P* = 0.01 for superiority)
Ischaemic stroke	1.2	0.92 (0.76, 0.60–0.98; *P* = 0.03)	1.34 (1.11, 0.89–1.40; *P* = 0.35)	1.42	1.34 (0.94; 0.75–1.17; *P* = 0.581)	1.05	0.97 (0.92, 0.74–1.13; *P* = 0.42)
Haemorrhagic stroke	0.38	0.10 (0.26, 0.14–0.49; *P* <0.001)	0.12 (0.31, 0.17–0.56; *P* <0.001)	0.44	0.26 (0.59; 0.37–0.93; *P* =0.024)	0.47	0.24 (0.51, 0.35–0.75; *P* <0.001)
Major bleeding	3.36	3.11 (0.93, 0.81–1.07; *P* = 0.31)	2.71 (0.80, 0.69–0.93; *P* = 0.003)	3.4	3.6 (*P* = 0.58)	3.09	2.13 (0.69, 0.60–0.80; *P* <0.001)
Intracranial bleeding	0.74	0.30 (0.40, 0.27–0.60; *P* <0.001)	0.23 (0.31, 0.20–0.47; *P* <0.001)	0.7	0.5 (0.67; 0.47–0.93; *P* = 0.02)	0.80	0.33 (0.42, 0.30–0.58; *P* <0.001)

Novel oral anticoagulant (NOAC)

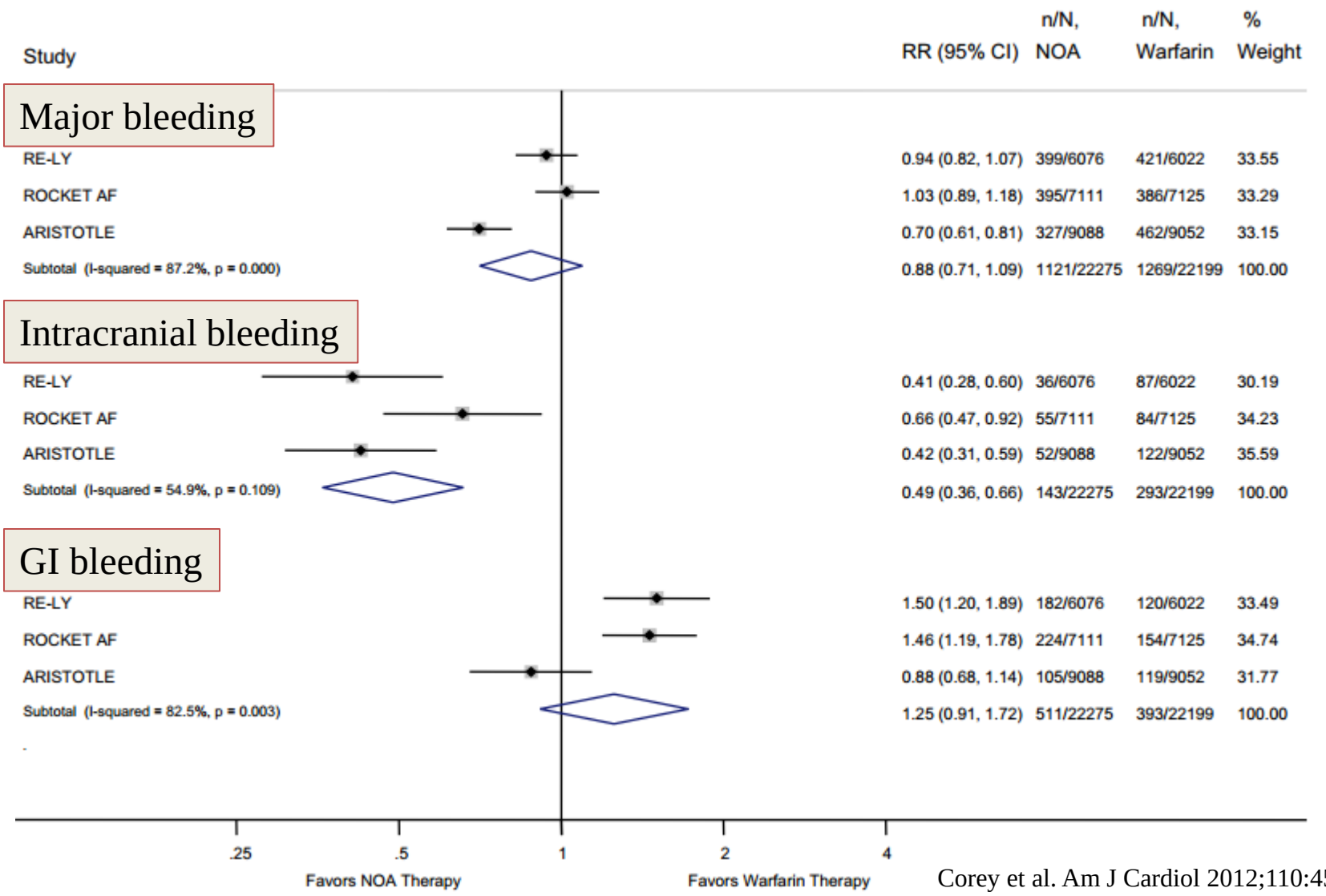
	Dabigatran (RE-LY)[70,71]			Rivaroxaban (ROCKET-AF)[3]		Apixaban (ARISTOTLE)[4]	
Outcomes (% per year)							
Gastrointestinal bleeding	1.02	1.51 (1.50, 1.19–1.89; *P* <0.001)	1.12 (1.10, 0.86–1.41; *P* = 0.43)	2.2	3.2 (*P* <0.001)	0.86	0.76 (0.89, 0.70–1.15; *P* = 0.37)
Myocardial infarction	0.64	0.81 (1.27, 0.94-1.71; *P* = 0.12)	0.82 (1.29, 096-1.75; *P* = 0.09)	1.1	0.9 (0.81; 0.63–1.06; *P* = 0.12)	0.61	0.53 (0.88, 0.66–1.17; *P* = 0.37)
Death from any cause	4.13	3.64 (0.88, 0.77–1.00; *P* = 0.051)	3.75 (0.91, 0.80–1.03; *P* = 0.13)	2.2	1.9 (0.85; 0.70–1.02; *P* = 0.07)	3.94	3.52 (0.89, 0.80–0.99; *P* = 0.047)
% Discontinuation at the end of follow-up	10.2	15.5	14.5	22.2	23.7	27.5	25.3
% Discontinuation/year	5.1	7.8	7.3	11.7	12.5	15.3	14.1

Novel oral anticoagulant (NOAC)



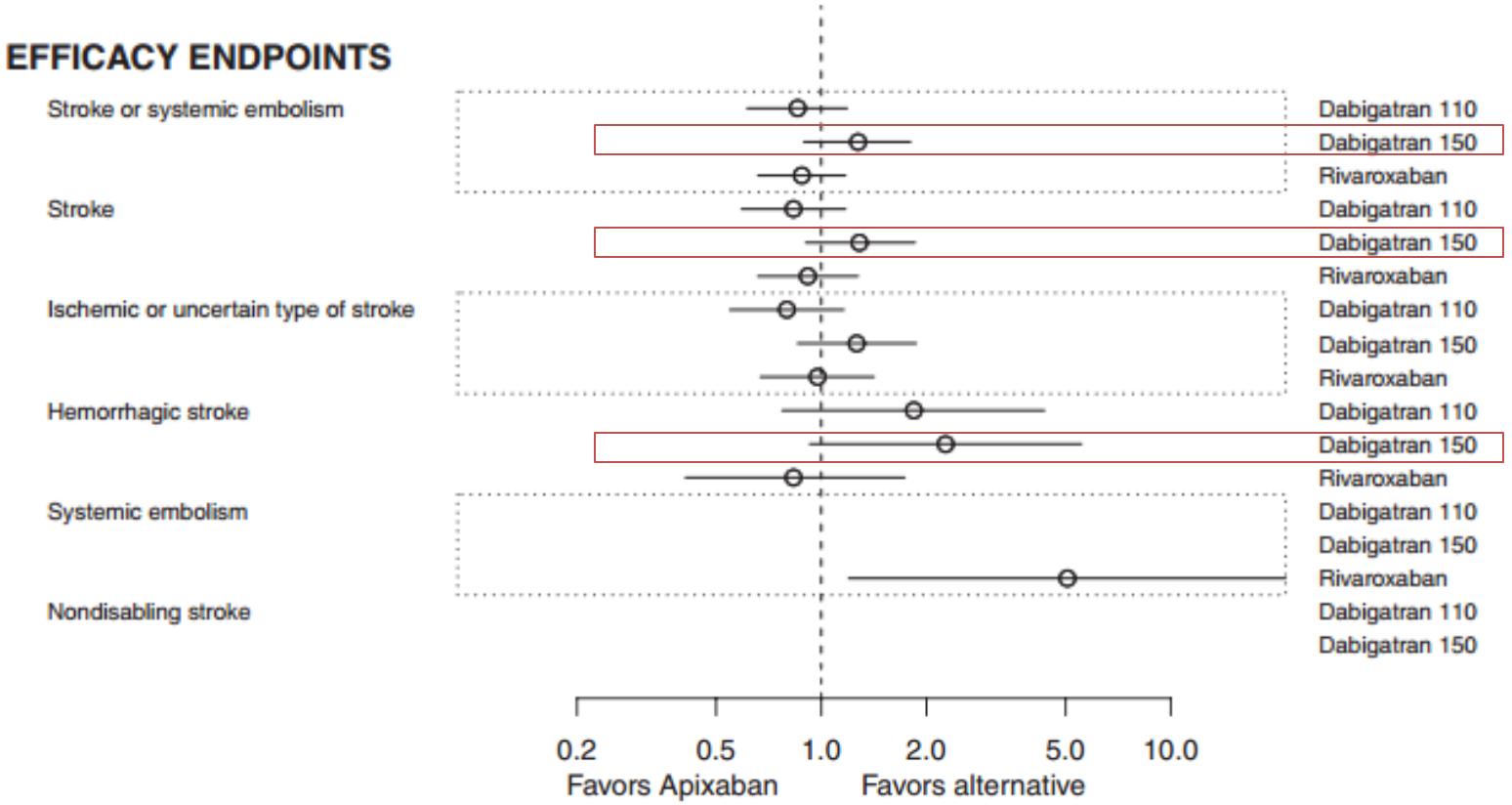
Corey et al. Am J Cardiol 2012;110:453– 460)

Novel oral anticoagulant (NOAC)



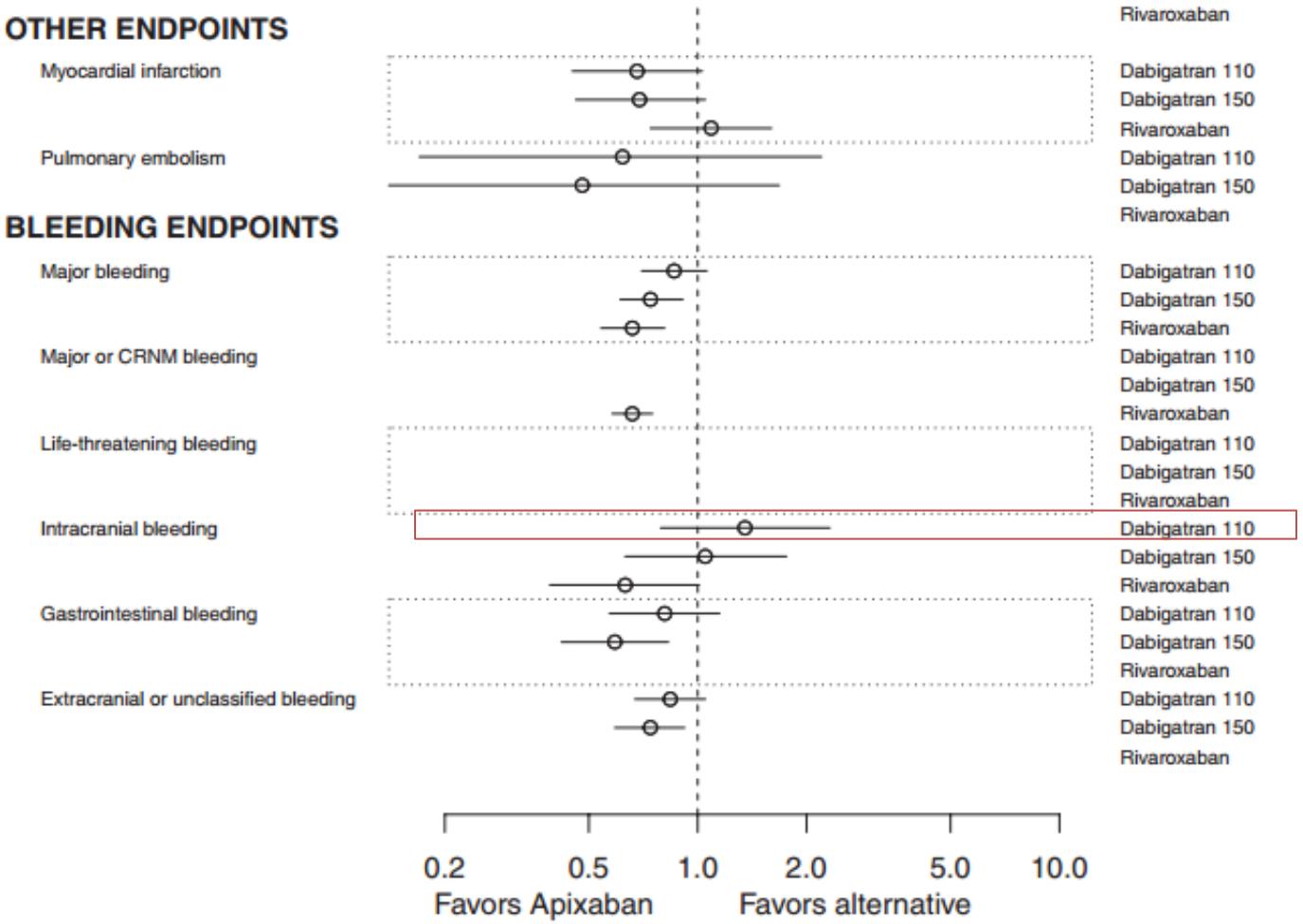
Corey et al. Am J Cardiol 2012;110:453– 460)

Indirect comparison btw NOACs



Lip et al. J Am Coll Cardiol 2012;60:738–46

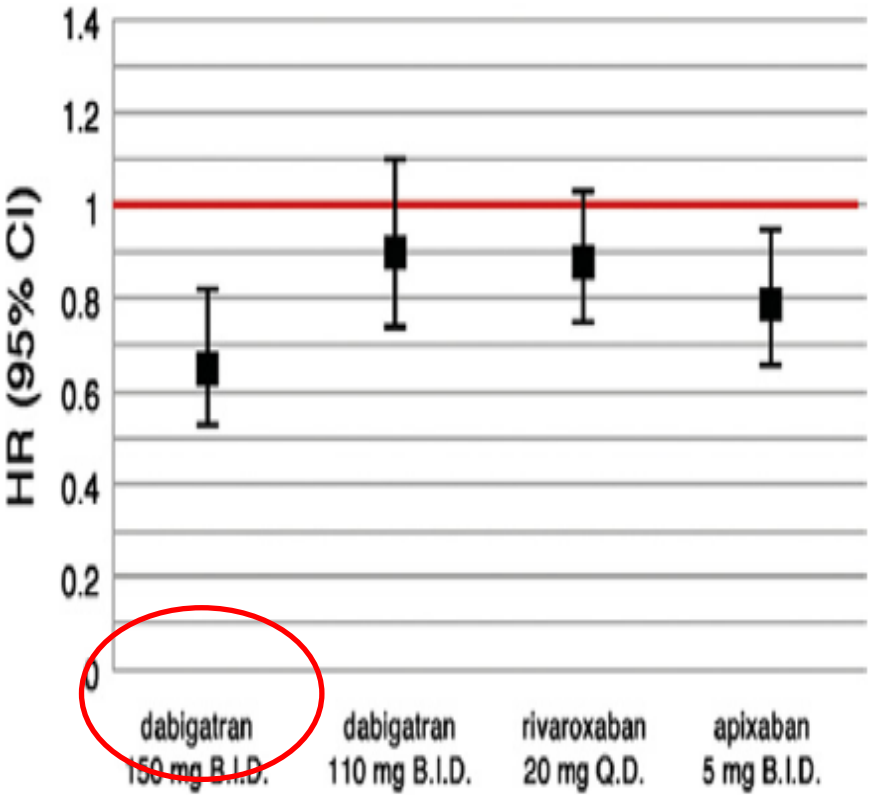
Indirect comparison btw NOACs



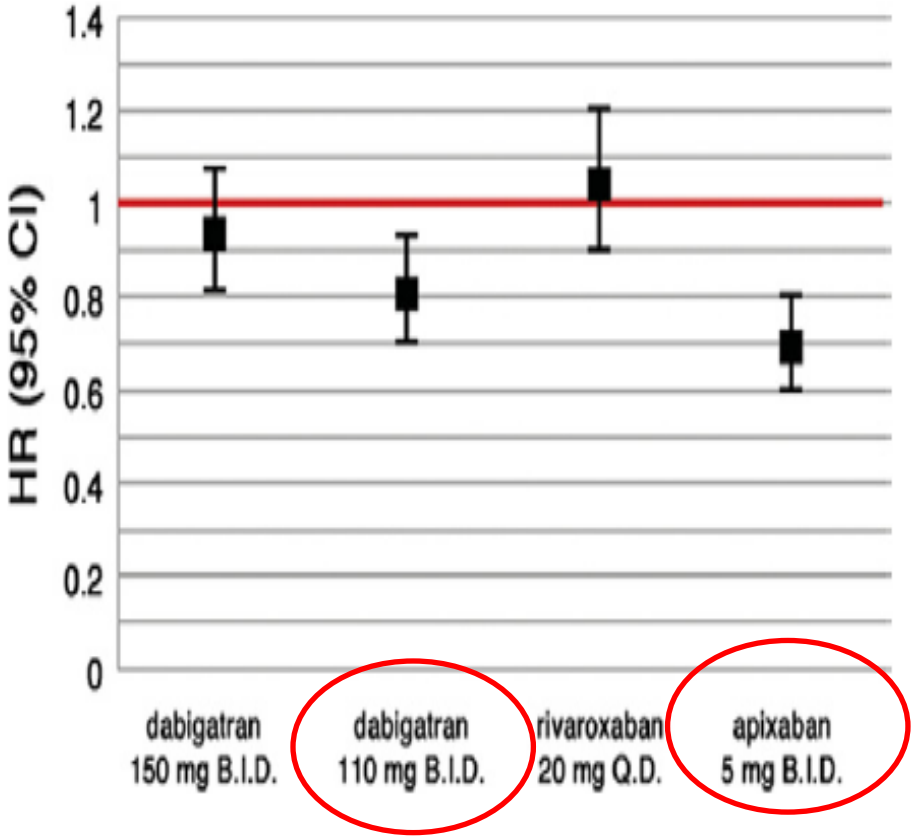
Lip et al. J Am Coll Cardiol 2012;60:738–46

Novel oral anticoagulant (NOAC)

Stroke or Systemic Embolism

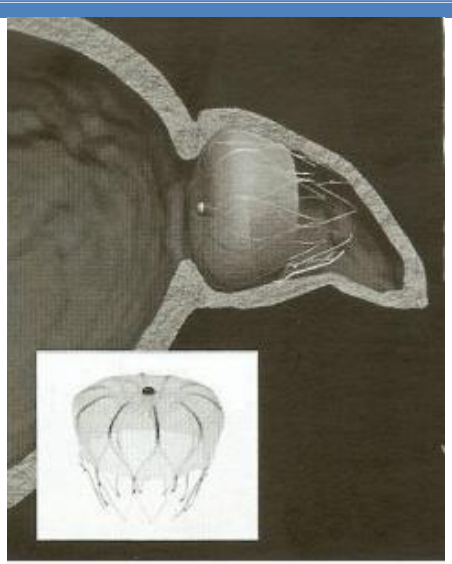


Major Bleeding



De Caterina R, et al. J Am Coll Cardiol 2012;59:1413–25

New option : LAA occlusion device

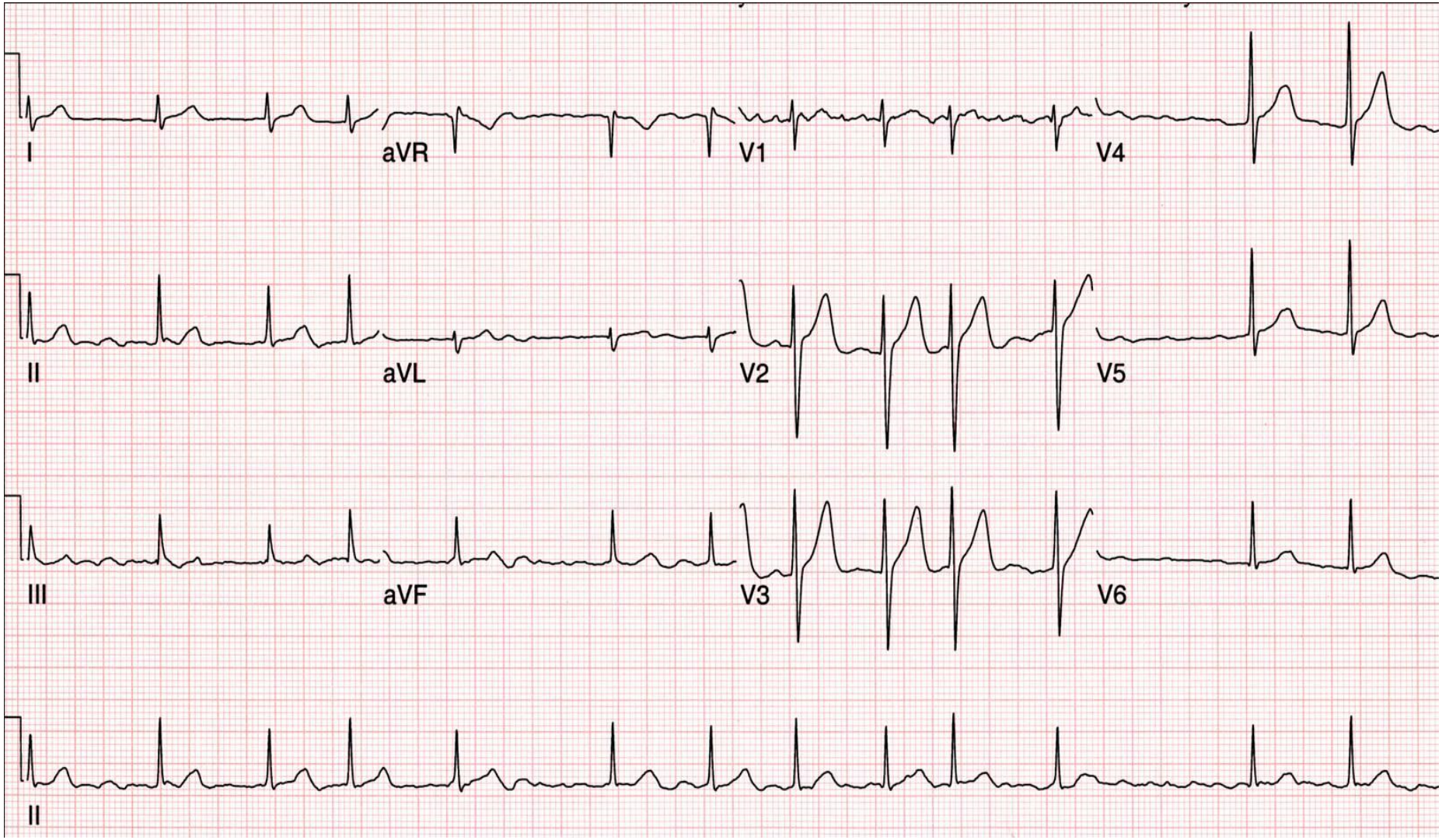


Watchman Device positioned in LAA

Protect-AF study : warfarin vs device

	Device		Control		Posterior Probabilities		
	Events/Pt-Yrs	OR/100 Pt-Yrs (95% CI)	Events/Pt-Yrs	OR/100 Pt-Yrs (95% CI)	RR* (95% CI)	Noninferior	Superior
Primary efficacy	31/1,025.7	3.0 (2.1–4.3)	24/562.7	4.3 (2.6–5.9)	0.71 (0.44–1.30)	>0.99	0.88
Ischemic stroke	19/1,026.3	1.9 (1.1–2.9)	8/564.9	1.4 (0.6–2.4)	1.30 (0.66–3.60)	0.76	0.18
CV/unexplained death	11/1,050.4	1.0 (0.5–1.8)	16/573.2	2.8 (1.5–4.2)	0.38 (0.18–0.85)	>0.99	0.99
Hemorrhagic stroke	3/1,050.3	0.3 (0.1–0.7)	7/571.0	1.2 (0.5–2.3)	0.23 (0.04–0.79)	>0.99	0.99
Systemic embolism	3/1,049.8	0.3 (0.1–0.7)	0/573.2	0	—	—	—
All stroke	21/1,026.3	2.0 (1.3–3.1)	15/562.7	2.7 (1.5–4.1)	0.77 (0.42–1.62)	>0.99	0.73
All-cause mortality	34/1,050.4	3.2 (2.3–4.5)	26/573.2	4.5 (2.8–6.2)	0.71 (0.46–1.28)	>0.99	0.85
Primary safety	54/979.9	5.5 (4.2–7.1)	2/554.6	3.6 (2.2–5.3)	0.53 (0.95–2.70)	—	—

항응고제 + 베타차단제 : 두근거림 지속



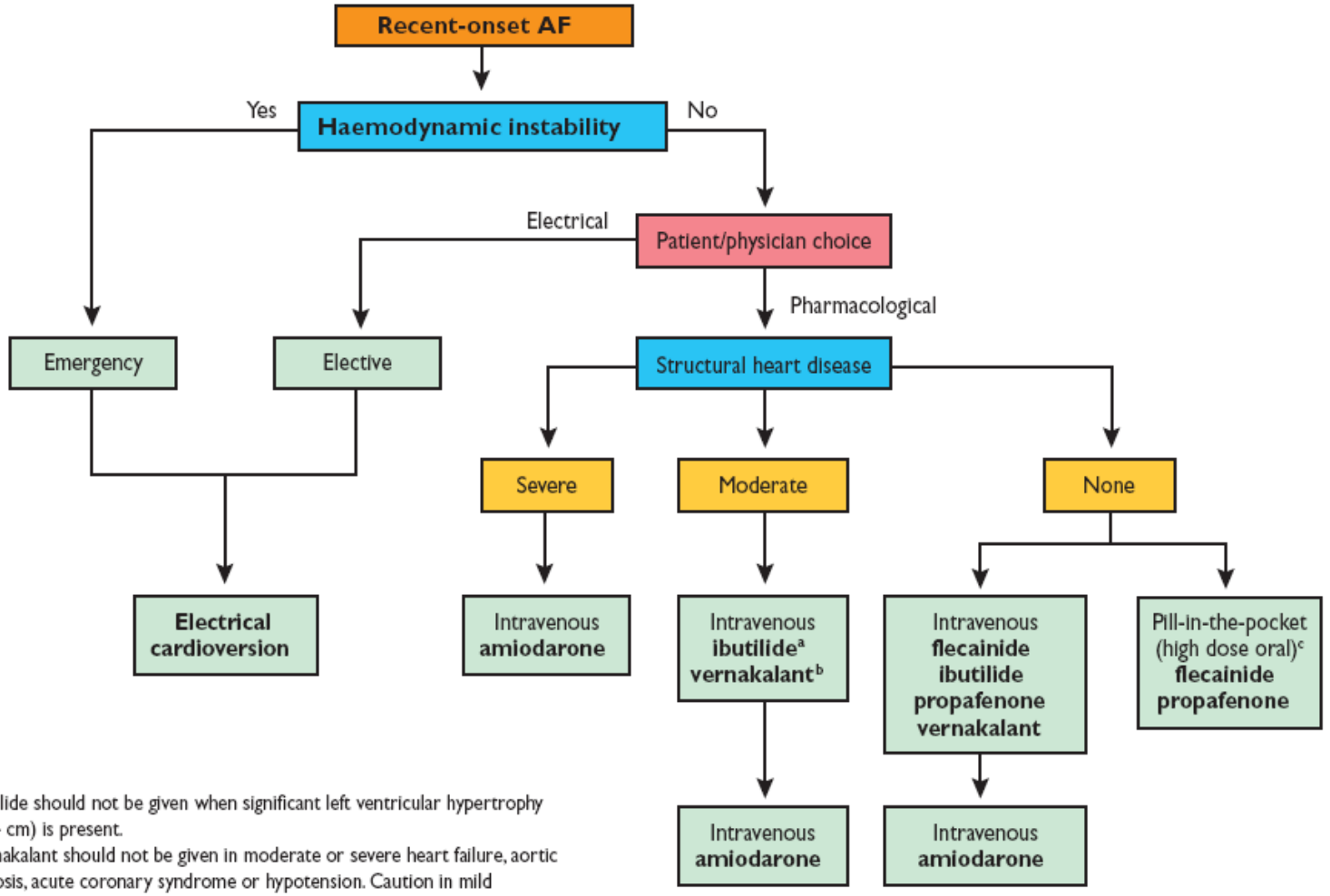
동율동 전환을 하는 것이 좋을까요?

- **Rate control only**
- **Sinus rhythm conversion : electrical/phamarcological**

ESC guideline

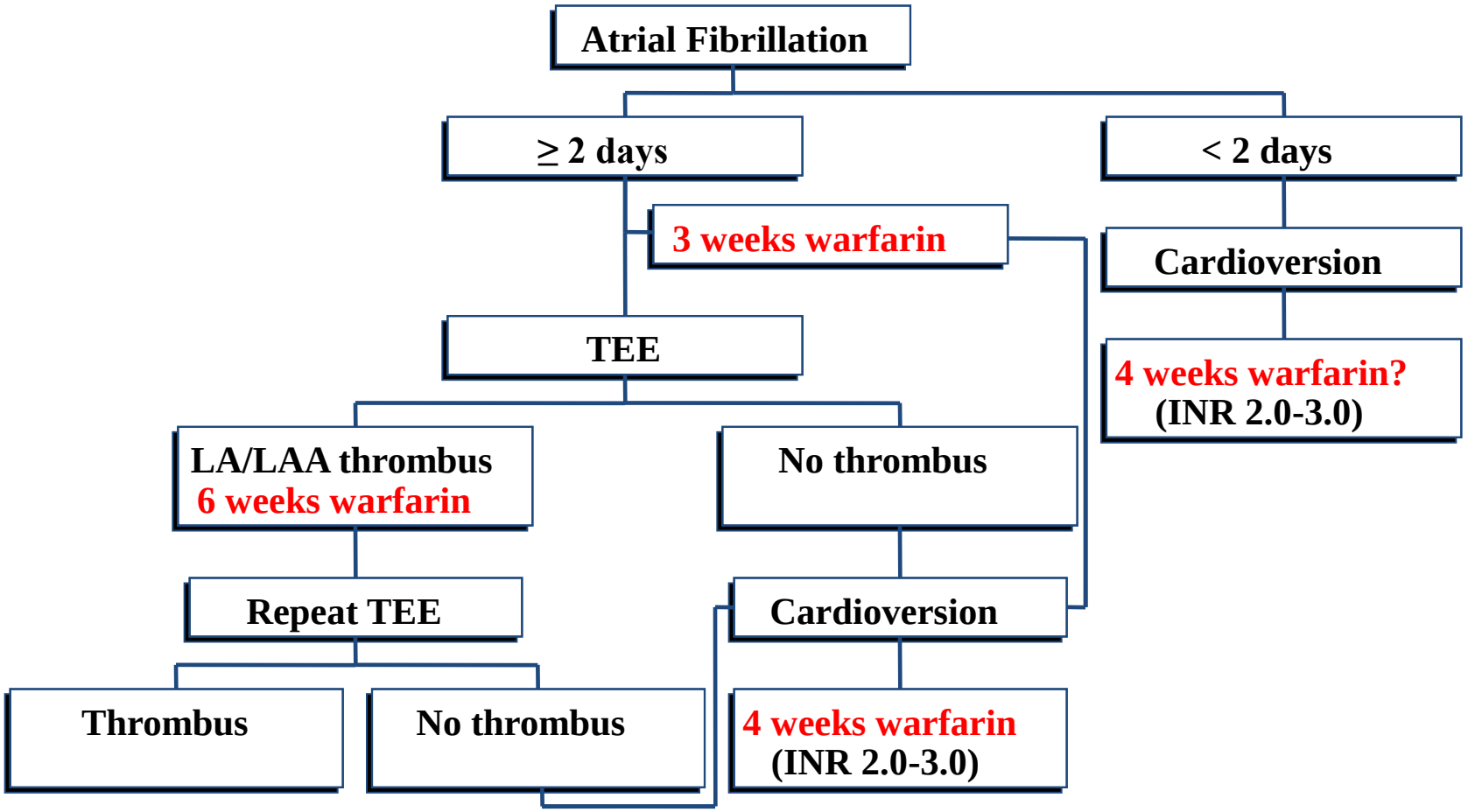
Recommendations	Class[a]	Level[b]
Rate control should be the initial approach in elderly patients with AF and minor symptoms (EHRA score 1).	I	A
Rhythm control is recommended in patients with symptomatic (EHRA score ≥ 2) AF despite adequate rate control.	I	B
Rate control should be continued throught a rhythm control approach to ensure adequate control of the ventricular rate during recurrences of AF.	I	A
Rhythm control as an initial approach should be considered in young symptomatic patients in whom catheter ablation treatment has not been ruled out.	IIa	C
Rhythm control should be considered in patients with AF secondary to a trigger or substrate that has been corrected (e.g. ischaemia, hyper-thyroidism).	IIa	C
Rhythm control in patients with AF and AF-related heart failure should be considered for improvement of symptoms.	IIa	B

동율동전환

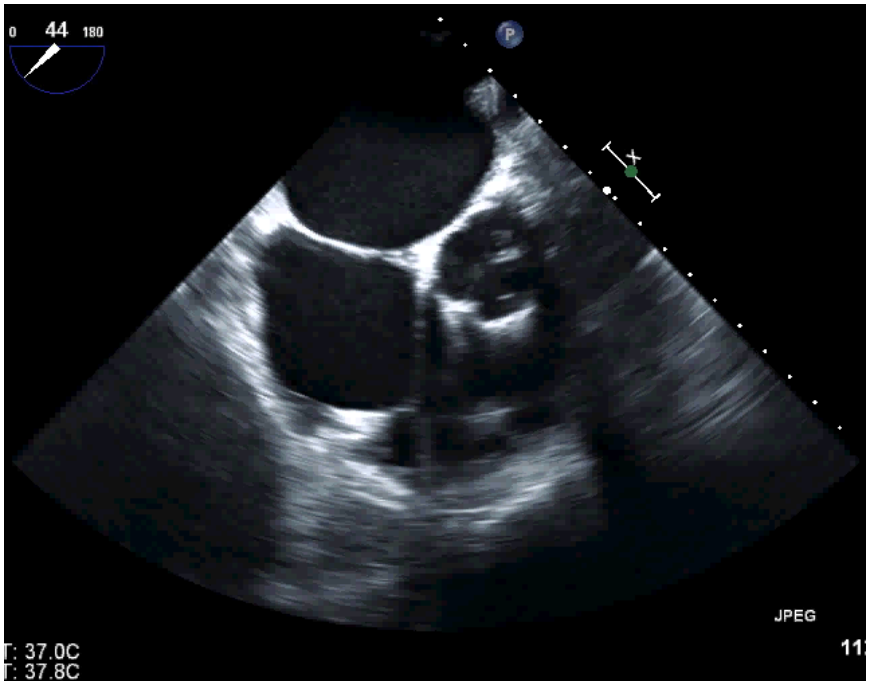


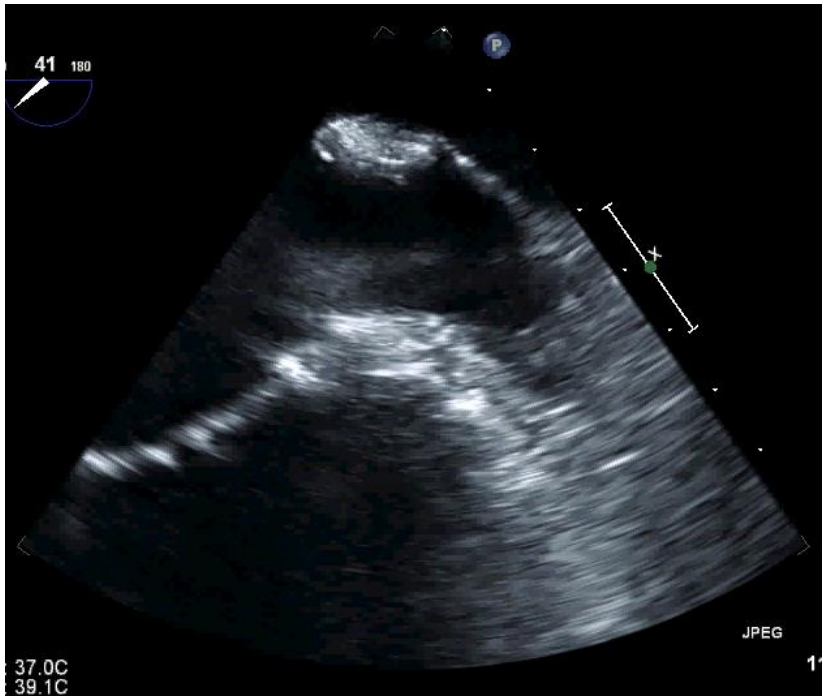
Ibutilide should not be given when significant left ventricular hypertrophy ≥1.4 cm) is present.
Vernakalant should not be given in moderate or severe heart failure, aortic stenosis, acute coronary syndrome or hypotension. Caution in mild heart failure.
'Pill-in-the-pocket' technique – preliminary assessment in a medically safe environment and then used by the patient in the ambulatory setting.

동율동 전환 바로 시행해도 될까요?

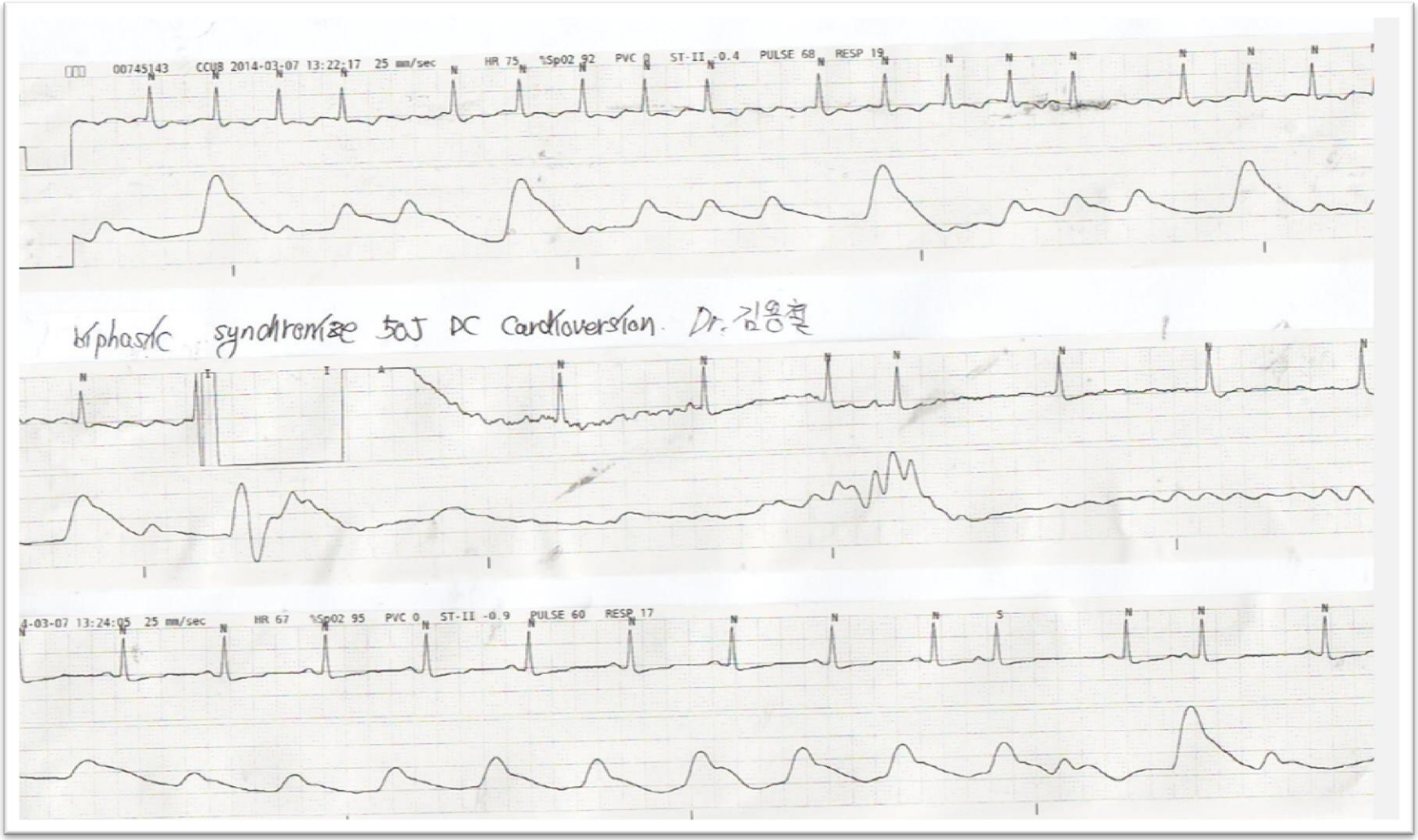


경식도 초음파 : transesophageal echo

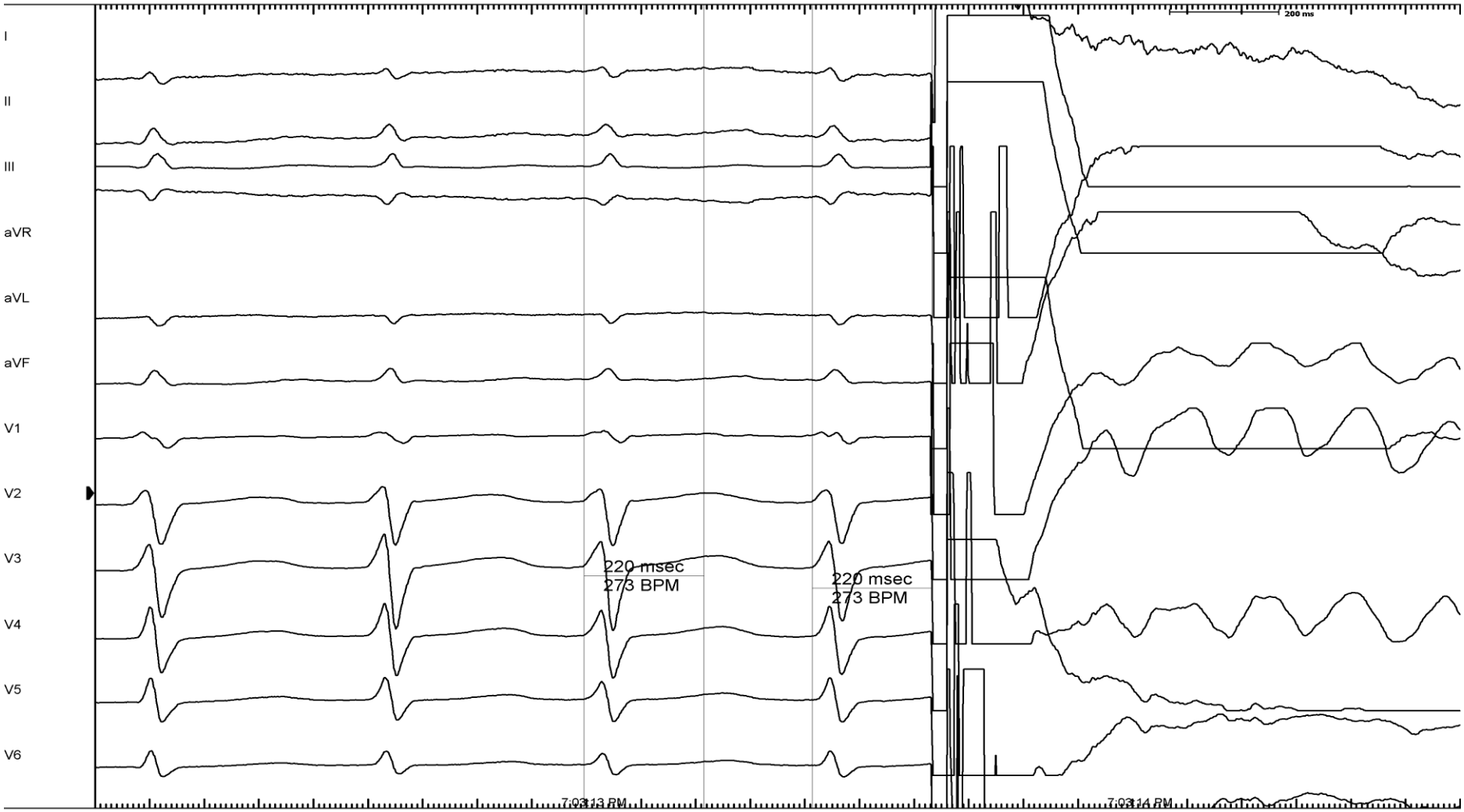




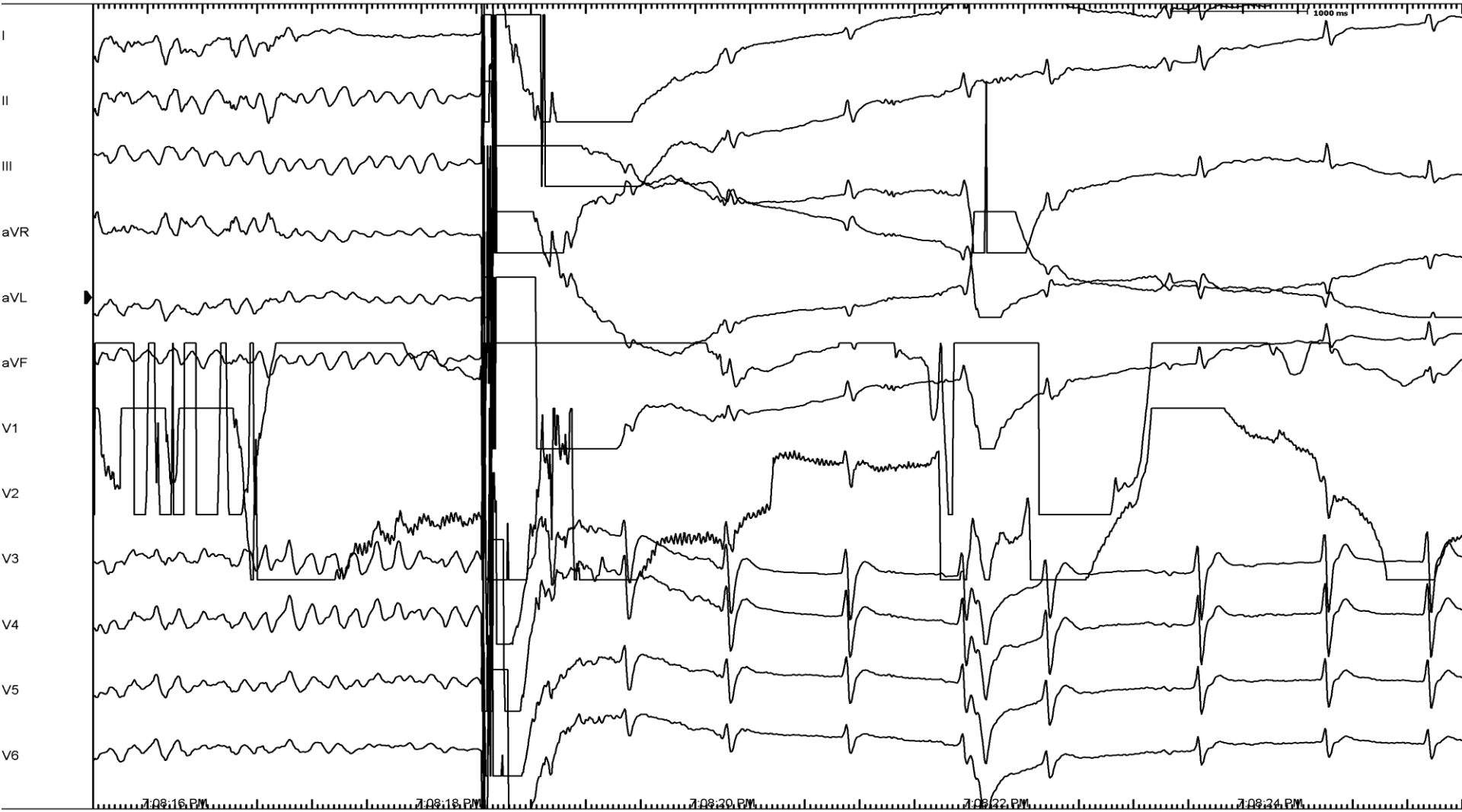
Electrical cardioversion



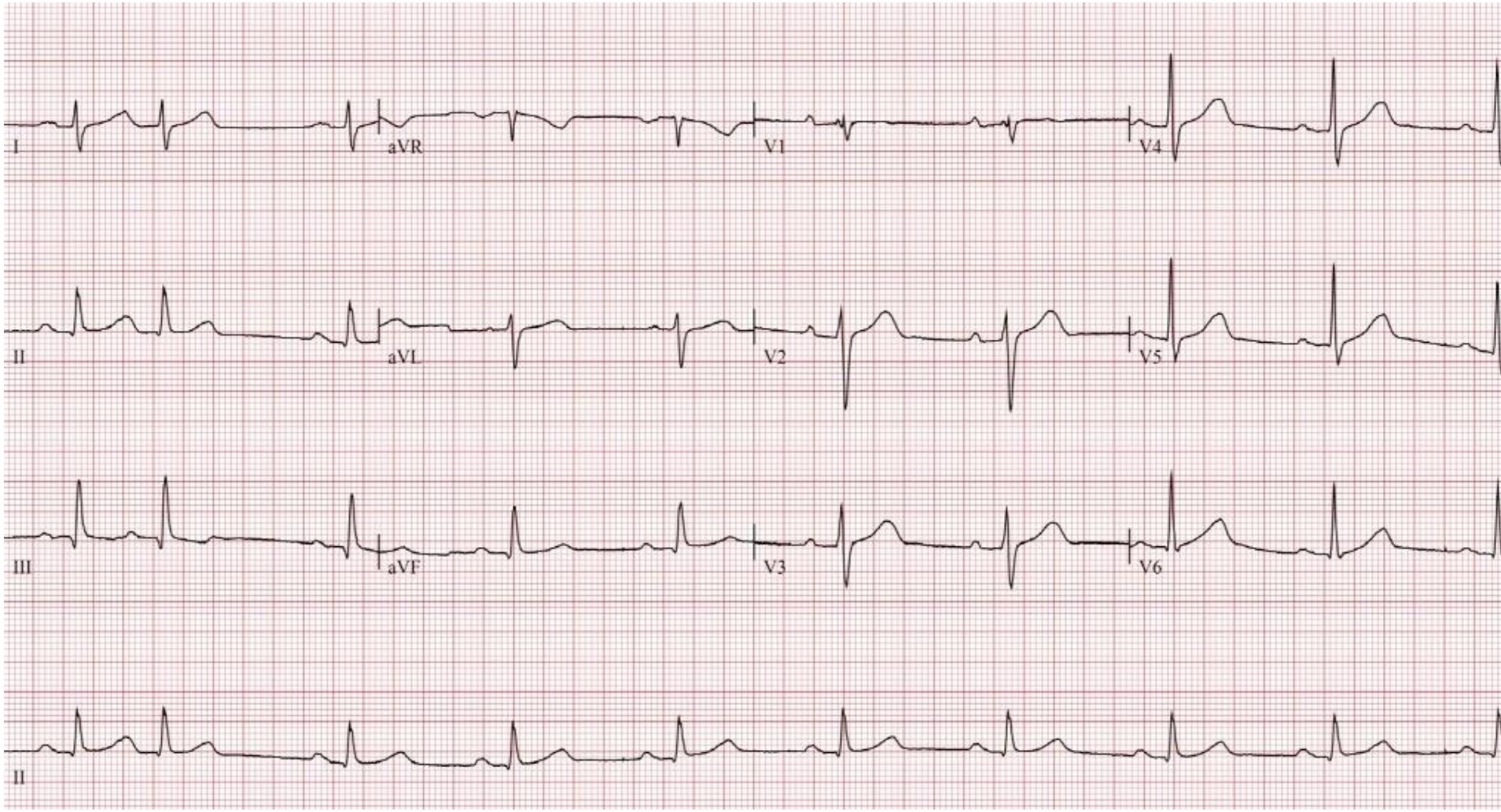
잘못된 **cardioversion**



잘못된 **cardioversion**



베타차단제+항응고제+항부정맥제



이 환자가 수술을 해야 한다면?

Thromboembolic risk가 높은 경우에는 wafarin중단에 의한 thromboembolic complication을 막기 위해 heparin을 투여한다. thromboembolic risk가 중등도 이거나 낮은 경우에는 heparin대체 요법은 반드시 시행할 필요는 없으며 상황에 따라 선택적으로 적용한다.(표 참조)

		High	*Moderate*	*Low*
Prosthetic valve	Localization	Mitral Aortic single-leaflet Two prosthetic heart valves	Aortic valve and ≥ 2 TE risk factors*	Aortic valve and < 2 TE risk factors*
	Type	First generation valve: caged-ball valve (e.g., Starr-Edwards) Single-leaflet tilting disc type (e.g., Bjork-Shiley, Medtronic-Hall)		Bi-leaflet tilting disc type (e.g., St. Jude, Carbomedics)
Chronic atrial fibrillation (AF)		Recent history of stroke or transient ischemic attack (TIA) Rheumatic mitral valvular heart disease	≥ 2 TE risk factors*	Lone AF, ≤ 65 yr old, and < 2 TE risk factors*
Venous thromboembolism (VTE)		Recent (≤ 1 month) episode of VTE Cancer Antiphospholipid antibody Chronic cardiac or pulmonary disease	VTE episode ≤ 6 months VTE recurrence associated with previous warfarin interruption	
Perioperative substitution anticoagulant therapy		Strongly recommended	Should be considered	Optional

*Thromboembolism (TE) risk factors include atrial fibrillation, atrial dilatation, left ventricular dysfunction, cardiomyopathy, history of a TE event (TIA or stroke), hypertension, diabetes mellitus, age > 75 yr.

Take home massage

- 심방세동 환자에서 뇌졸중 발생 위험성은 생각보다 높다.
- 뇌졸중 위험 발생 위험성이 높은 환자에서는 항응고제를 반드시 투여하여야 한다.
- 항응고제의 선택은 환자의 특성에 맞게 선택하여야 한다.