The Changing Landscape in Stroke Prevention in Atrial Fibrillation: cases on optimal oral anti-coagulate treatment

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순서

1. NOAC 사용 증례
2. NOAC 사용시 유의할 점

증례 1: Newly Diagnosed, Low-Risk Patient; Prefer NOAC, Planning RFA

- Park SB, M/45
- Newly diagnosed with NVAF
- Risk factor of stroke
  - **Hypertension for 1 year**
  - **$CHADS_2$=1 (Hypertension)**
  - **CHA_2DS_2-VASc=1 (Hypertension)**
- Medication: CCB
- When discussing VKAs as an option, patient expresses strong desire to avoid INR monitoring

Stroke Risk in AF: CHA_2DS_2-VASc

CHA_2DS_2-VASc criteria	Score
Congestive heart failure/ left ventricular dysfunction	1
Hypertension	1
Age ≥75 yrs	2
Diabetes mellitus	1
Stroke/transient ischaemic attack/TE	2
Vascular disease (prior myocardial infarction, peripheral artery disease or aortic plaque)	1
Age 65–74 yrs	1
Sex category (i.e. female gender)	1

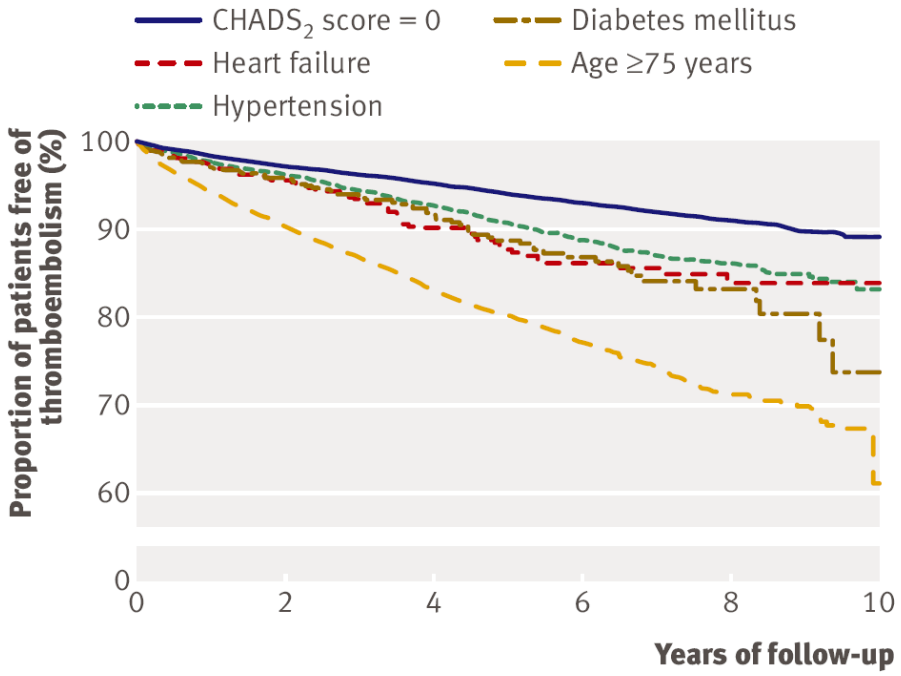
CHA_2DS_2-VASc	Adjusted stroke rate (%/year)
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

EHJ 2010;31:2369-2429

ESC guideline, 2010

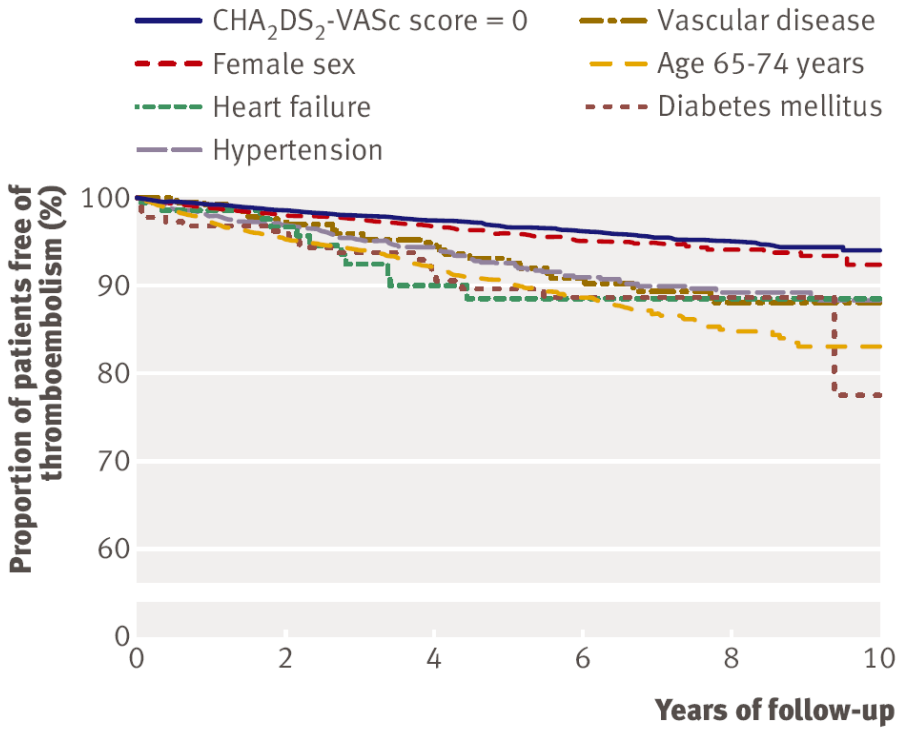
$CHADS_2$ vs CHA_2DS_2-VASc

All patients with AF not treated with VKA in Denmark 1997-2006



Kaplan-Meier estimate of probability of remaining free of thromboembolism with CHADS2 score 0 and 1. Only patients with CHADS2 scores 0 and 1 were included, and patients were censored at death for causes other than thromboembolism

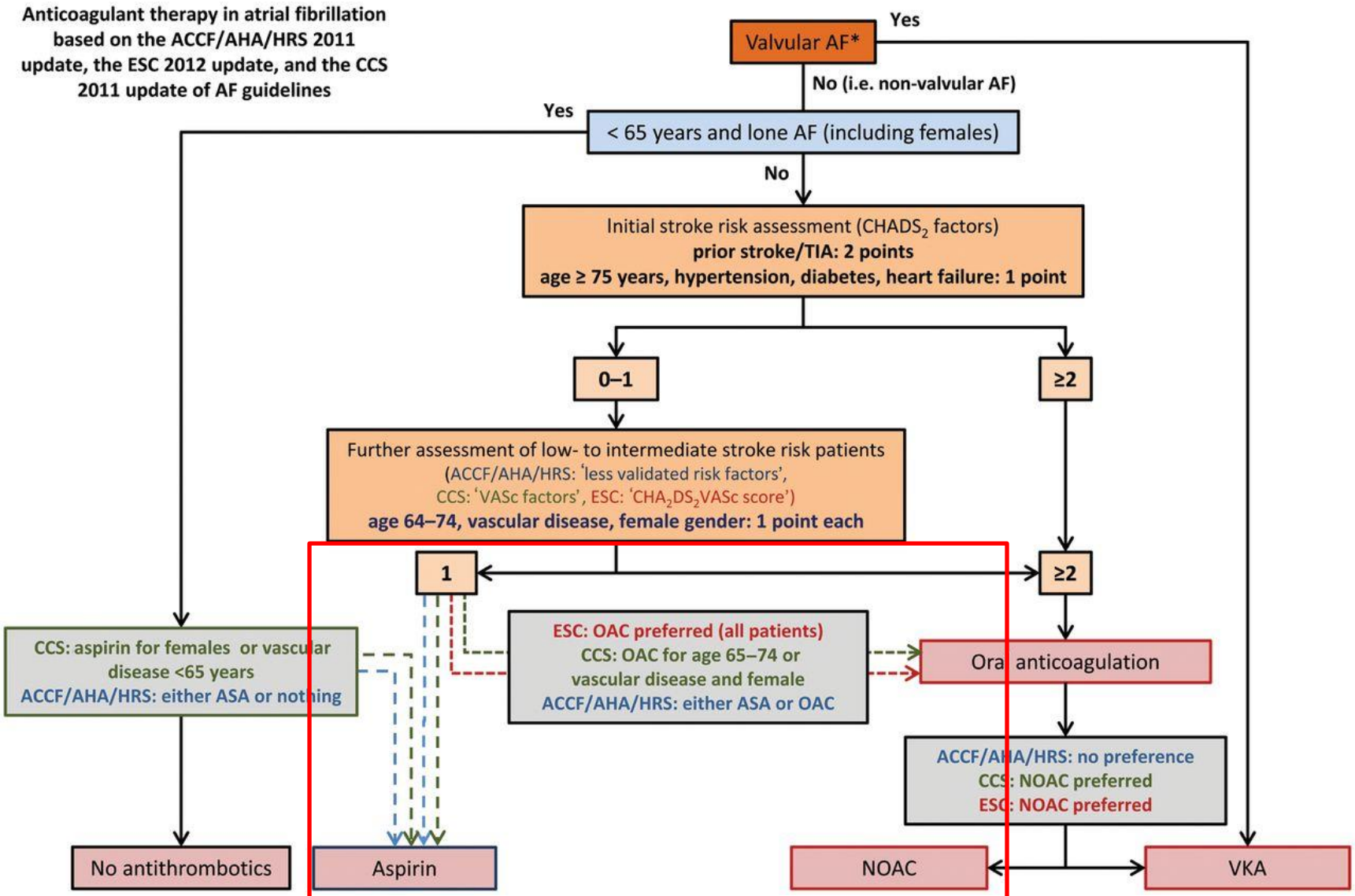
73.538 fulfilled the study inclusion criteria



Kaplan-Meier estimate of probability of remaining free of thromboembolism with CHA2DS2-VASc score 0 and 1. Only patients with CHA2DS2-VASc scores 0 and 1 were included, and patients were censored at death for causes other than thromboembolism

Olesen JB, et al. BMJ 2011;342:d124

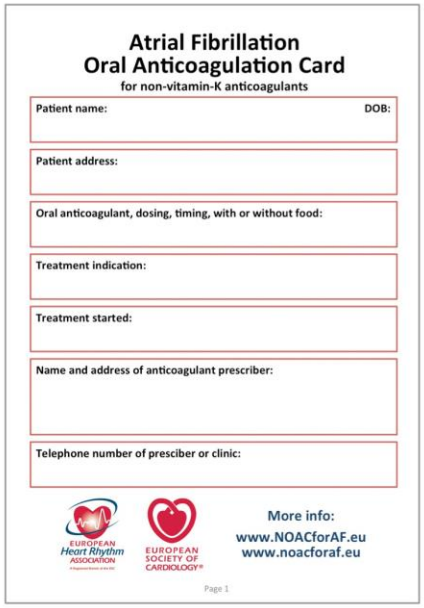
Anticoagulation in non-valvular AF



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

EHRA proposal for a universal NOAC anticoagulation card

Card can be downloaded in a printer-ready form or in a ppt format that can be configured to the local language from www.NOACforAF.eu



Atrial Fibrillation
Oral Anticoagulation Card
for non-vitamin-K anticoagulants

Patient name: DOB:

Patient address:

Oral anticoagulant, dosing, timing, with or without food:

Treatment indication:

Treatment started:

Name and address of anticoagulant prescriber:

Telephone number of presciber or clinic:

EUROPEAN Heart Rhythm ASSOCIATION

EUROPEAN SOCIETY OF CARDIOLOGY®

More info:
www.NOACforAF.eu
www.noacforaf.eu

Page 1

Planned or unplanned visits

Date (or date range):	Site (GP; clinic; cardiologist; ...):	To do / findings:

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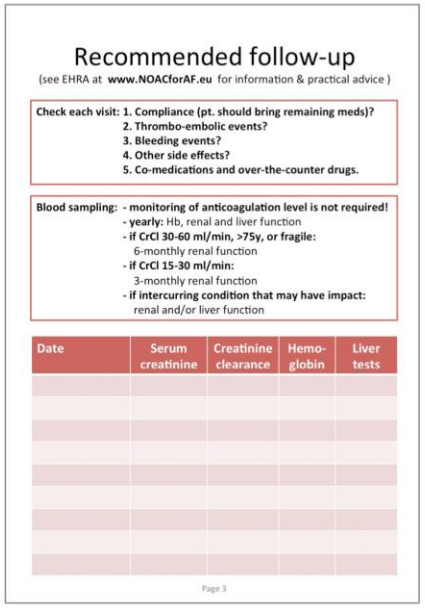

Recommended follow-up

(see EHRA at **www.NOACforAF.eu** for information & practical advice)

Check each visit: 1. Compliance (pt. should bring remaining meds)?
2. Thrombo-embolic events?
3. Bleeding events?
4. Other side effects?
5. Co-medications and over-the-counter drugs.

Blood sampling: - monitoring of anticoagulation level is not required!
- **yearly:** Hb, renal and liver function
- **if CrCl 30-60 ml/min, >75y, or fragile:**
6-monthly renal function
- **if CrCl 15-30 ml/min:**
3-monthly renal function
- **if intercurring condition that may have impact:**
renal and/or liver function

Date	Serum creatinine	Creatinine clearance	Hemo-globin	Liver tests

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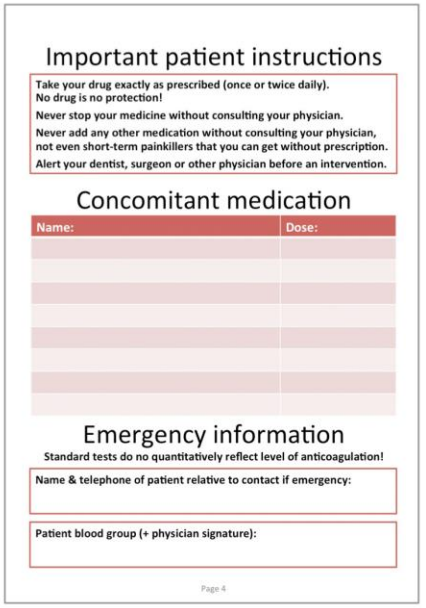

Important patient instructions

Take your drug exactly as prescribed (once or twice daily).
No drug is no protection!
Never stop your medicine without consulting your physician.
Never add any other medication without consulting your physician, not even short-term painkillers that you can get without prescription.
Alert your dentist, surgeon or other physician before an intervention.

Concomitant medication

Name:	Dose:

Emergency information

Standard tests do no quantitatively reflect level of anticoagulation!

Name & telephone of patient relative to contact if emergency:

Patient blood group (+ physician signature):

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Checklist during follow-up contacts of AF patients on anticoagulation

	Interval	Comments
1. Compliance	Each visit	• Instruct patient to bring remaining medication: note and calculate average adherence • Re-educate on importance of strict intake schedule • Inform about compliance aids (special boxes; smartphone applications; . . .)
2. Thrombo-embolism	Each visit	• Systemic circulation (TIA, stroke, peripheral) • Pulmonary circulation
3. Bleeding	Each visit	• 'Nuisance' bleeding: preventive measures possible? (PPI; haemorrhoidectomy; . . .). Motivate patient to diligently continue anticoagulation • Bleeding with impact on quality-of-life or with risk: prevention possible? Need for revision of anticoagulation indication or dose?
4. Other side effects	Each visit	• Carefully assess relation with NOAC: decide for continuation (and motivate), temporary cessation (with bridging), or change of anticoagulant drug.
5. Co-medications	Each visit	• Prescription drugs; over-the-counter drugs (see Section 4) • Careful interval history: also temporary use can be risk!
6. Blood sampling	Yearly 6 monthly 3 monthly On indication	• Haemoglobin, renal and liver function • Renal function if CrCl 30–60 ml/min, or if on dabigatran and >75 years or fragile • If CrCl 15–30 ml/min • If intercurring condition that may impact renal or hepatic function

Heidbuchel H et al. *Europace*. 2013;15:625-651.

Progress

- NOAC, CCB, AAD for 4 weeks
- → DC cardioversion

Standard use of a vitamin-K antagonist (VKA) for 3-4 weeks prior to cardioversion (or shorter periods if preceded by a negative TEE) will result in thromboembolic rates of <1% within 30 days.

Klein AL, et al. NEJM 2001;344:1411-1420.
Botkin SB, et al. Am Heart J 2003;145:233-8

- YUMC outpatient elective DC cardioversion
  - **Jan 2005 ~ Aug 2013**

Events	No. DC shock = 1,582
Stroke	**2 (0.13%)**
Bradyarrhythmia	**7 (0.44%)**
Bleeding	**3 (0.18%)**

조익성, unpublished

DC cardioversion on NOAC

- Outcomes After Cardioversion and Atrial Fibrillation Ablation in Patients Treated With Rivaroxaban and Warfarin in the ROCKET AF Trial

Endpoint Following ECV, PCV, or Ablation	Rivaroxaban (N = 160)	Warfarin (N = 161)	All (N = 321)
Stroke or systemic embolism	3 (1.88)	3 (1.86)	6 (1.87)
CV death	2 (1.25)	4 (2.48)	6 (1.87)
All-cause death	3 (1.88)	6 (3.73)	9 (2.80)
Hospitalization	50 (31.25)	48 (29.81)	98 (30.53)
Stroke or systemic embolism or CV death	5 (3.13)	7 (4.35)	12 (3.74)
Stroke or systemic embolism or death from any cause	6 (3.75)	9 (5.59)	15 (4.67)
Major or NMCR bleeding	30 (18.75)	21 (13.04)	51 (15.89)

Dabigatran: Nagarakanti R, et al. Circulation 2011;123:131-6.
Apixaban: Greg F, et al. J Am Coll Cardiol 2014

Piccini JP, et al. J Am Coll Cardiol 2013;61:1998-2006.

Recurrence of AF → RFA

Dabigatran vs warfarin for radiofrequency catheter ablation of atrial fibrillation

Jin-Seok Kim, MD, Fei She, MD, Krit Jongnarangsin, MD, Aman Chugh, MD, Rakesh Latchamsetty, MD, Hamid Ghanbari, MD, Thomas Crawford, MD, Arisara Suwanagool, MD, Mohammed Sinno, MD, Thomas Carrigan, MD, Robert Kennedy, MD, Wouter Saint-Phard, MD, Miki Yokokawa, MD, Eric Good, DO,

CONCLUSIONS When held for approximately 24 hours before the procedure and resumed 4 hours after vascular hemostasis, dabigatran appears to be as safe and effective as uninterrupted warfarin for periprocedural anticoagulation in patients undergoing RFA of AF.

coagulation with warfarin for periprocedural anticoagulation in patients undergoing RFA of AF.

METHODS In this case-control analysis, 763 consecutive patients (mean age 61 ± 10 years) underwent RFA of AF using dabigatran (N = 191) or uninterrupted warfarin (N = 572) for periprocedural anticoagulation. In all patients, anticoagulation was started ≥4 weeks before RFA. Dabigatran was held after the morning dose on the day before the procedure and resumed 4 hours after vascular hemostasis was achieved.

RESULTS A transesophageal echocardiogram performed in all patients receiving dabigatran did not demonstrate an intracardiac thrombus. There were no thromboembolic complications in either group. The prevalence of major (4 of 191, 2.1%) and minor (5 of 191, 2.6%) bleeding complications in the dabigatran group were similar to those in the warfarin group (12 of 572, 2.1%; $P = 1.0$ and 19 of 572, 3.3%; $P = .8$, respectively). Pericardial tamponade occurred in 2 of 191 (1%) patients in the dabigatran group and in 7 of 572 1.1–1.8; $P = .01$) were the independent risk factors of bleeding complications only in the warfarin group.

CONCLUSIONS When held for approximately 24 hours before the procedure and resumed 4 hours after vascular hemostasis, dabigatran appears to be as safe and effective as uninterrupted warfarin for periprocedural anticoagulation in patients undergoing RFA of AF.

KEYWORDS Atrial fibrillation; Catheter ablation; Warfarin; Dabigatran; Bleeding

ABBREVIATIONS **ACT** = activated clotting time; **AF** = atrial fibrillation; **CI** = confidence interval; **INR** = international normalized ratio; **LMWH** = low molecular weight heparin; **OR** = odds ratio; **PV** = pulmonary vein; **RFA** = radiofrequency catheter ablation; **TEE** = transesophageal echocardiogram

Major Complications in the Overall Population

Type of Complication	No. of Patients	Rate, %
Death	25	0.15
Tamponade	213	1.31
Pneumothorax	15	0.09
Stroke	37	0.23
Transient ischemic attack	115	0.71
Total artero-venous fistulae	88	0.54
Valve damage/requiring surgery	11/7	0.07
Atrium-esophageal fistulae	6	0.04
Stroke	37	0.23
Transient ischemic attack	115	0.71
PV stenoses requiring intervention	48	0.29
Total	741	4.54

Cappato et al. Circ Arrhythm Electrophysiol. 2010;3:32-38.

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journal homepage: www.elsevier.com/locate/ijcard

Routine preprocedural transesophageal echocardiography might not be necessary for stroke prevention evaluation in AF patients on anticoagulation therapy ☆

Jae-Hyun Han [a], Dong-Ho Shin [a], Hye-Jeong Lee [b], Young Jin Kim [b], Seung-Hyun Lee [a], Jaemin Shim [a], Jae-Sun Uhm [a], Jong-Youn Kim [a], Hyuk-Jae Chang [a], Hui-Nam Pak [a], Moon-Hyoung Lee [a], Boyoung Joung [a,*]

[a] Cardiology Division, Department of Internal Medicine, Yonsei University Medical College, Seoul, Republic of Korea
[b] Department of Radiology, Research Institute of Radiological Science, Yonsei University Medical College, Seoul, Republic of Korea

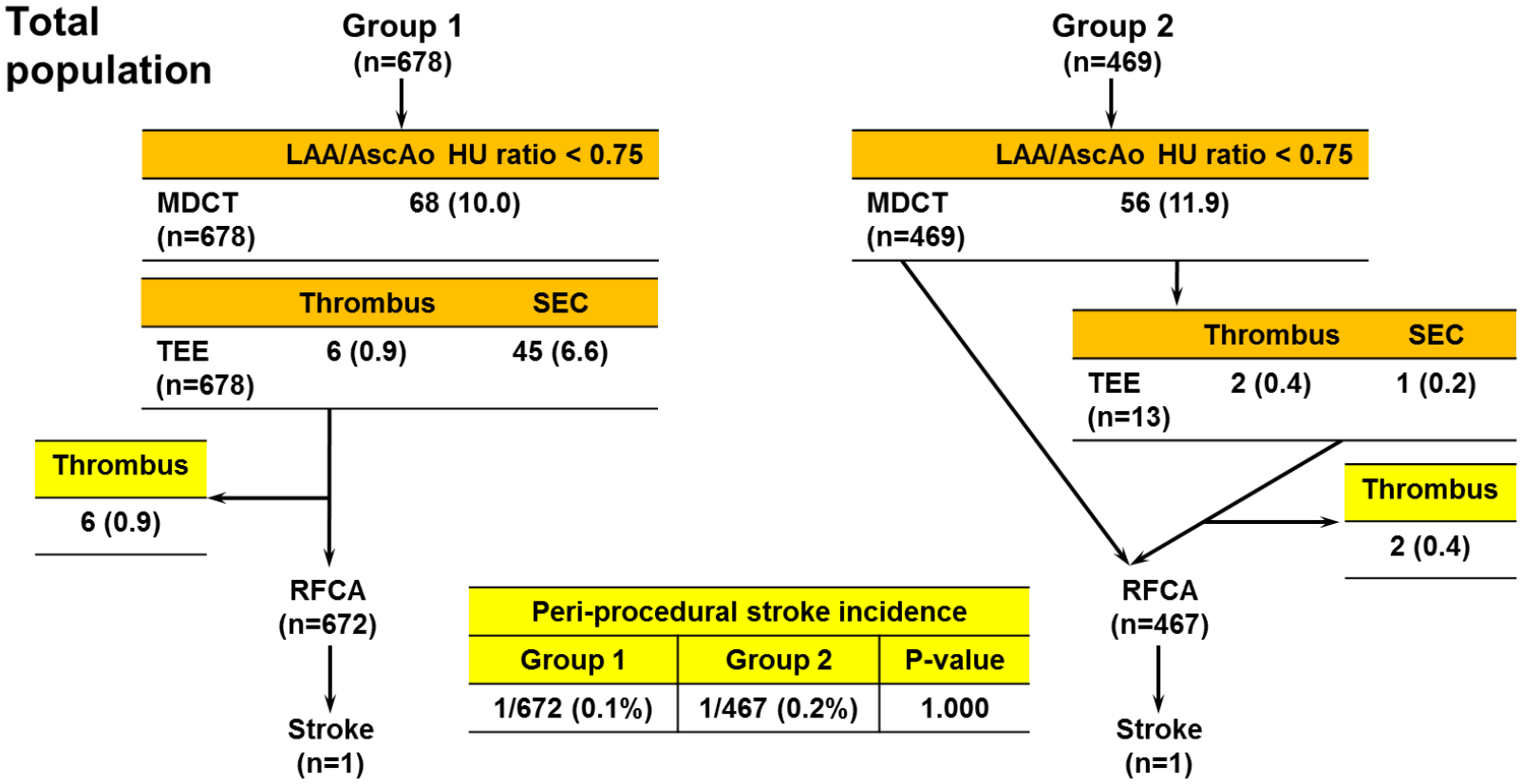
Background: Preprocedural transesophageal echocardiography (TEE) is used to reduce the stroke during atrial fibrillation (AF) ablation. This study evaluated whether routine preprocedural TEE in addition to multidetector computed tomography (MDCT) is necessary to prevent periprocedural stroke in AF ablation.

Methods: Each patient underwent MDCT and TEE (group 1, n = 247) or MDCT alone (group 2, n = 103) for the initial evaluation before AF ablation. In group 2, TEE was performed only in patients who had left atrial (LA) thrombus or blood stasis in MDCT.

Results: There was no difference in sex, $CHADS_2$ score, or LA dimension between the two groups. In group 1, a thrombus was detected in 12 (5%) and 6 (2%) patients by the MDCT and TEE, respectively. All (100%) patients, who were revealed to have thrombus in TEE, also had a thrombus in MDCT. In group 2, 3 (3%) patients exhibited LA thrombus in MDCT, among whom thrombus was observed in only one patient (1%) in TEE. AF ablation was not performed in patients with thrombus. While one patient had a periprocedural stroke in group 1, no patient had in group 2 (P = 0.52).

Conclusion: The overall periprocedural stroke rate was low (0.3%) in AF patients on anticoagulation therapy. The preprocedural MDCT detected all patients with the LA thrombus. In AF patients with low CHADS2 score, optimal anticoagulation and relatively preserved left ventricular ejection fraction, routine preprocedural TEE in addition to the MDCT might not be necessary to decrease the periprocedural stroke rate.

Multidetector Computed Tomography Might be an Enough Screening Test to Prevent Periprocedural Stroke in Atrial Fibrillation Ablation; a Multicenter Propensity Matched Analysis



Peri-procedural stroke incidence		
Group 1	Group 2	P-value
1/672 (0.1%)	1/467 (0.2%)	1.000

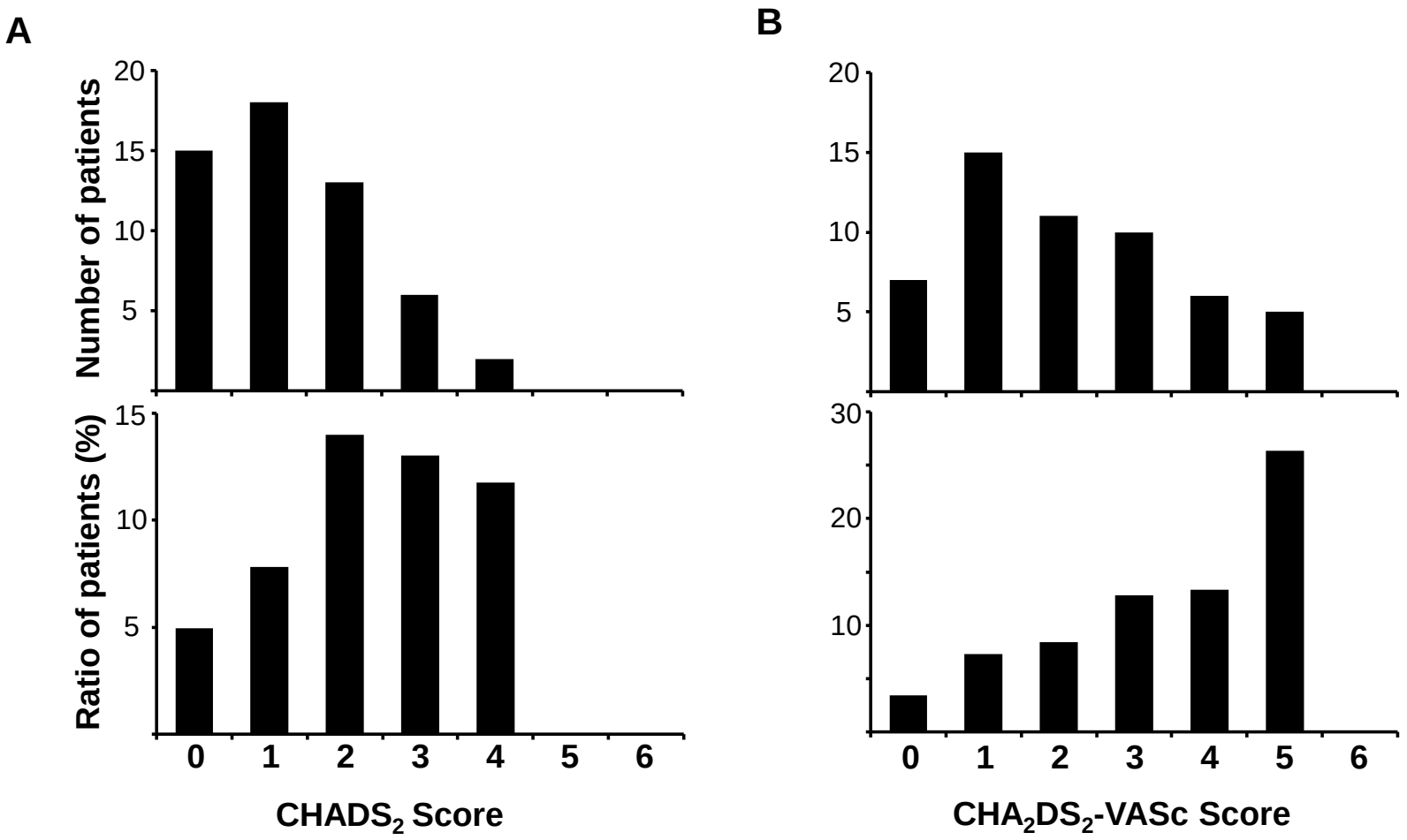
TEE \ MDCT	Thrombus (n=12)	Blood stasis (n=56)	Negative (n=610)
Thrombus (n=6)	4	2	0
SEC (n=45)	0	13	32
Negative (n=627)	8	41	578

TEE \ MDCT	Thrombus (n=7)	Blood stasis (n=49)*
Thrombus (n=2)	2	0
SEC (n=1)	1	0
Negative (n=10)	4	6

* TEE was not performed in 43 patients.

Hong SJ, et al, Heart rhythm 2014, in press

Thrombi or SEC according to stroke risk



Hong SJ, et al, Heart rhythm 2014, in press

증례 2: High-Risk Warfarin Patient With INRs Frequently Out of Range

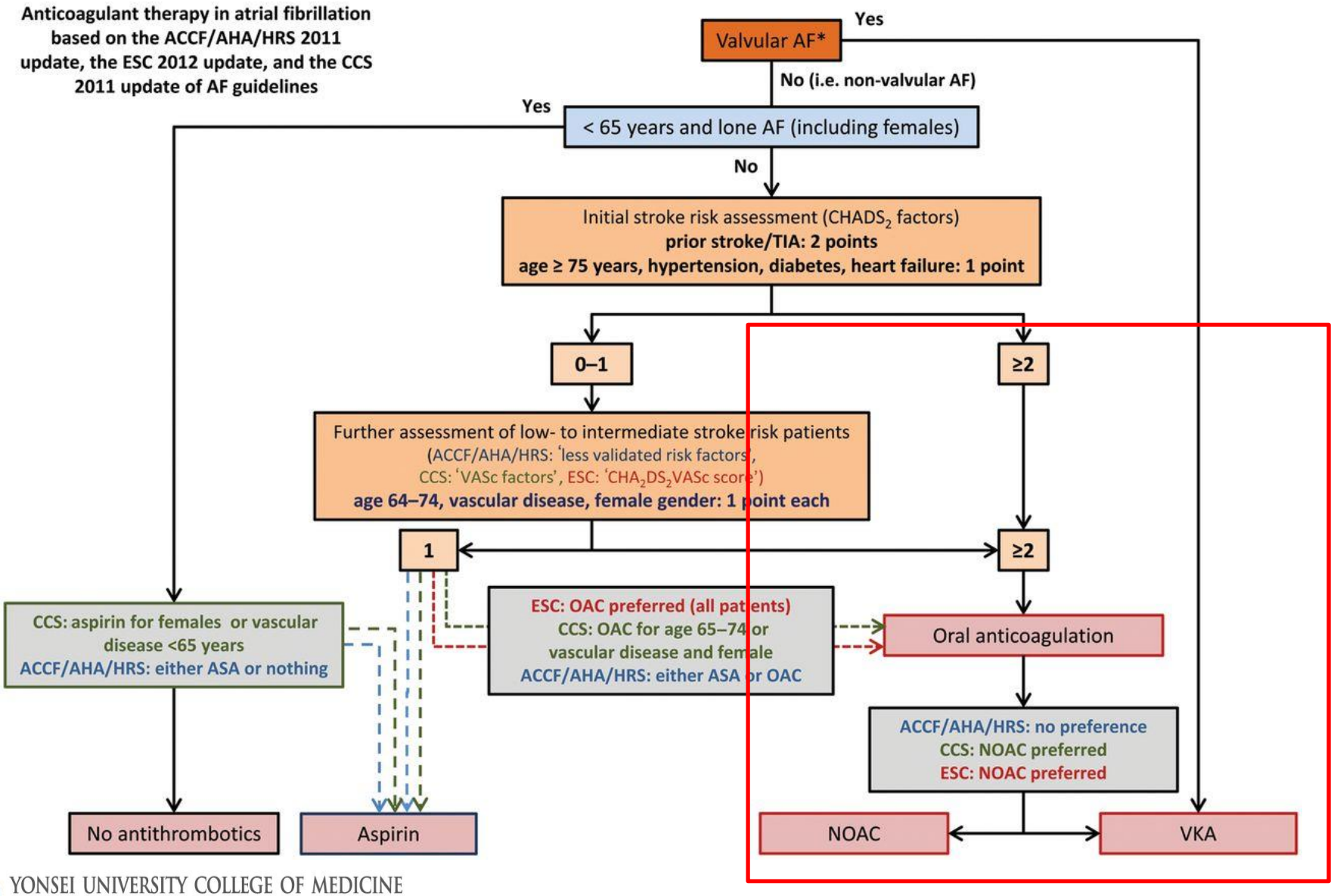
- Ko SK, M/70

- Diagnosed with NVAF 9 years ago
- Hypertension (controlled) 20 years
- Diagnosed with a stroke 3 years ago

- Stroke risk
  - **$CHADS_2$=3, CHA_2DS_2-VASc=4**

- Ko's INRs have been in range only from 3 out of 5 of his follow-ups.

Anticoagulation in non-valvular AF



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

INR 조절실패 및 기타 급여인정 사유

- **와파린 초기치료(2개월 혹은 INR 2 이상 도달)**

1. 1mg으로 5일 이상 투여 후 INR 3.0 이상
2. 10mg 이상으로 5일 이상 투여 후 INR 2.0 미만
3. 최초 2개월 와파린 용량 조절 기간 동안 INR검사 7일 간격으로 측정 시 3회 이상 3.5 초과한 경우

- **와파린 유지 기간**

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

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

Labile INR

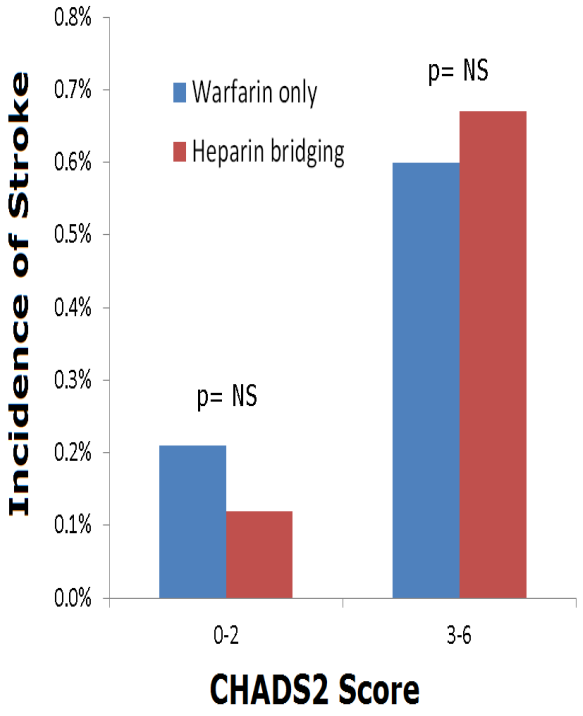
Age	**72**
CHADS2 score	**2**
- Congestive HF	**X**
- Hypertension	**O**
- Age ≥ 75	**X**
- Diabetes Mellitus	**O**
- Stroke or TIA	**X**

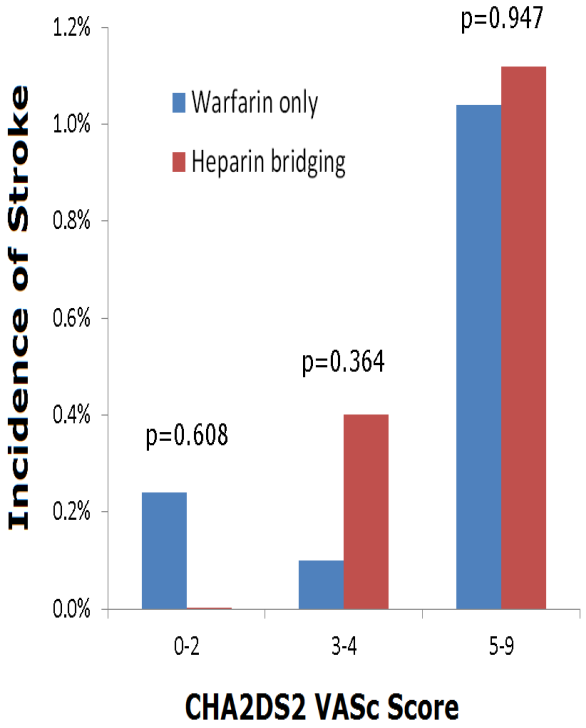
INR 조절 실패 사유일 경우		
Date	**와파린 용량**	**INR**
2013-09-10	**NOAC**	**1.66**
2013-05-14	**3 mg - 4 mg 격일**	**2.06**
2013-01-15	**3 mg - 4 mg 격일**	**2.33**
2012-09-18	**3 mg - 4 mg 격일 증량**	**1.65**
2012-06-12	**3 mg 감량**	**3.68**
2012-02-28	**4 mg**	**3.09**

항응고제 종류 변경시

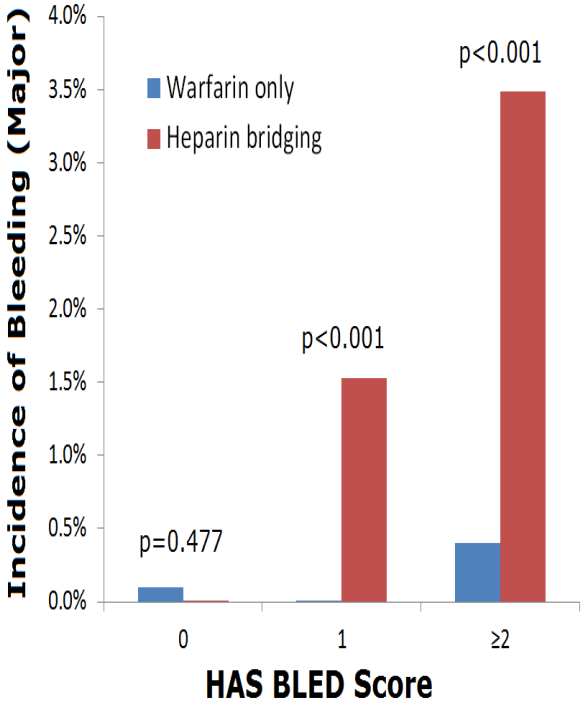
VKA to NOAC	**INR <2.0: immediate** INR 2.0–2.5: immediate or next day INR >2.5: use INR and VKA half-life to estimate time to INR <2.5
Parenteral anticoagulant to NOAC: IV unfractioned heparin (UFH) Low molecular weight heparin (LMWH)	**Start once UFH discontinued (t½=2h).** May be longer in patients with renal impairment Start when next dose would have been given
NOAC to VKA	**Administer concomitantly until INR in appropriate range** Measure INR just before next intake of NOAC Re-test 24h after last dose of NOAC Monitor INR in first month until stable values (2.0–3.0) achieved
NOAC to parenteral anticoagulant	Initiate when next dose of NOAC is due
NOAC to NOAC	Initiate when next dose is due except where higher plasma concentrations expected (e.g. renal impairment)
Aspirin or clodiprogel to NOAC	**Switch immediately**, unless combination therapy needed

Stroke according to CHA_2DS_2-VASc





Bleeding according to HAS BLED



Kim TH et al, HRS 2014

증례 3: High-Risk Warfarin Patient With INRs Frequently Out of Range

- Lee JB, F/76

- Diagnosed with NVAF 15 years ago
- Hypertension (controlled) 20 years
- The 1st stroke 3 years ago
- Warfarin use
- Upper GI bleeding 1 years ago, transfusion

- Stroke risk
  - **$CHADS_2$=4, CHA_2DS_2-VASc=7**

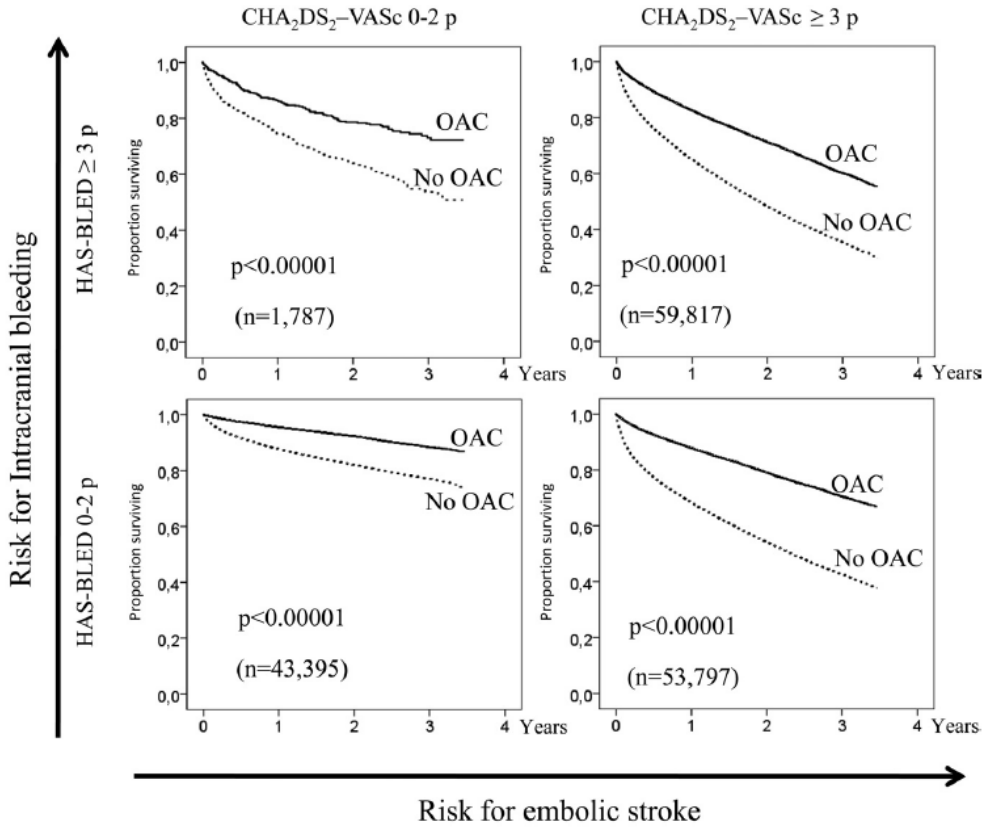
- Bleeding risk
  - **HAS-BLED = 101 1010 = 4**

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

* a score of ≥3 indicates 'high risk

Net clinical benefit of warfarin in patients with AF: a report from the Swedish AF cohort study.



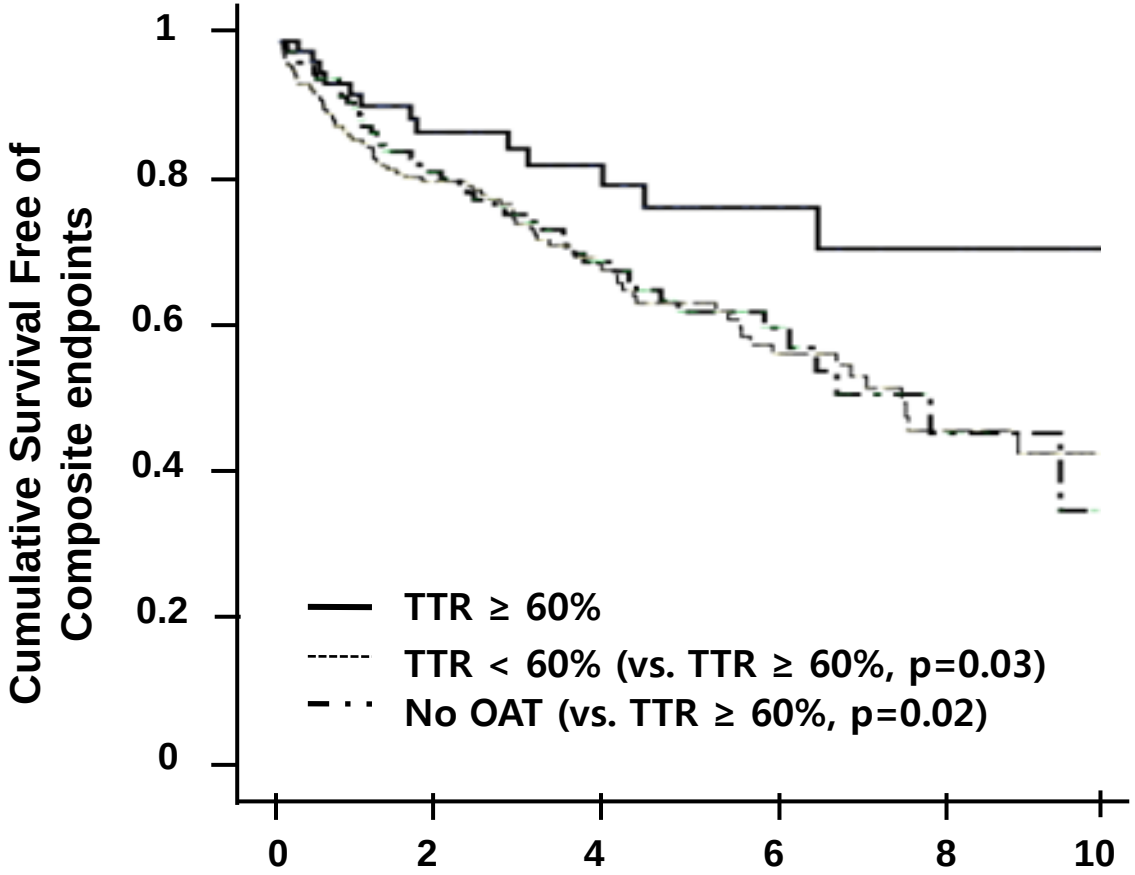
In almost all patients with AF, the risk of ischemic stroke without OAT is higher than the risk of intracranial bleeding with OAT.

Analysis of the net benefit indicates that more patients may benefit from OAT.

The CHA2DS2-VASc score was more sensitive than the CHADS2 score in identifying patients who were truly low risk in whom anticoagulation may be associated with a net disadvantage.

Friberg L, et al. Circulation 2012;125:2298-307

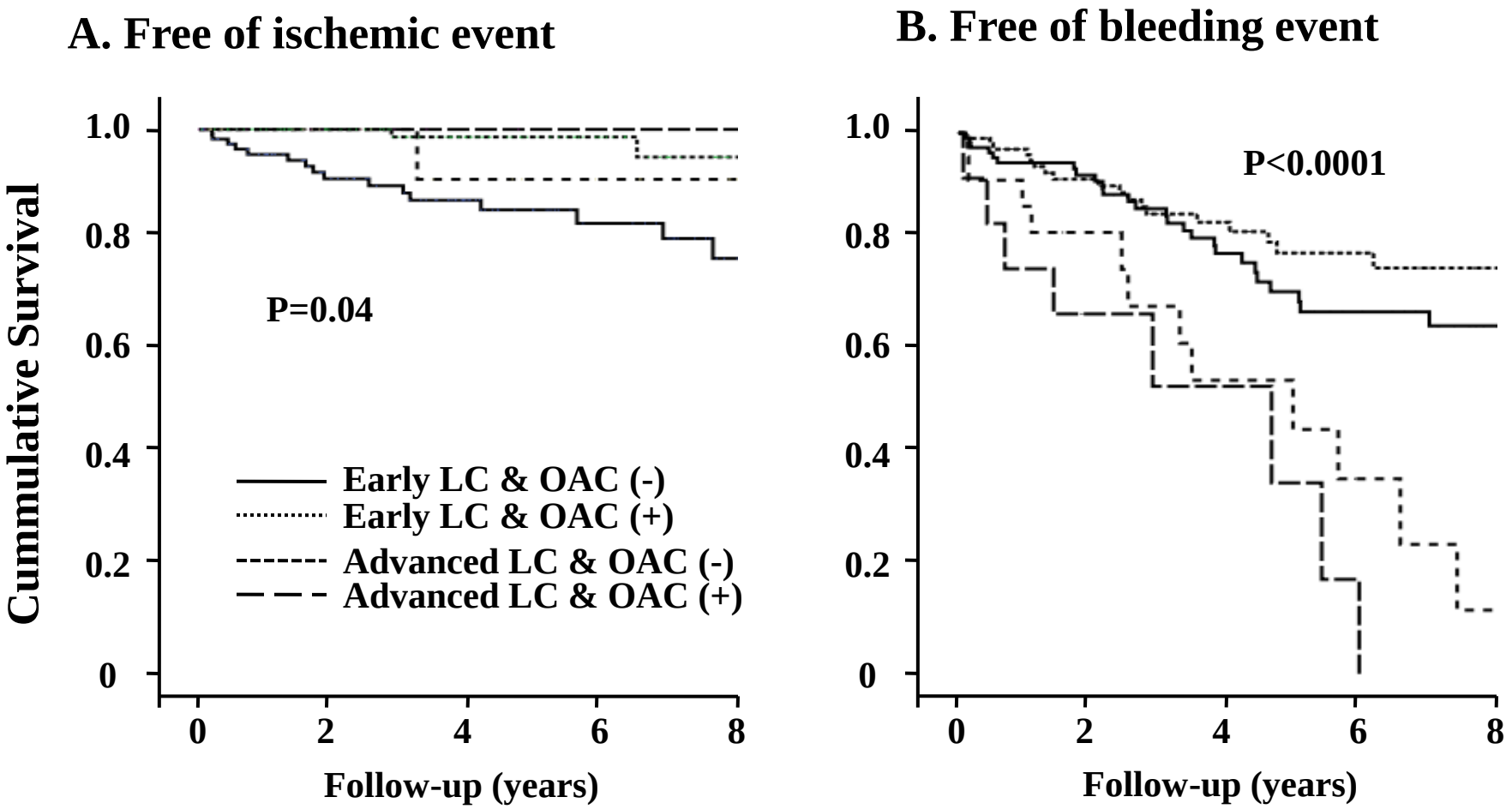
Bleeding Risk and Major Adverse Events in Patients With Previous Ulcer on Oral Anticoagulation Therapy



Number at risk						
TTR ≥ 60%	71	43	25	15	8	0
TTR < 60%	129	80	52	21	6	0
No OAC	230	129	71	41	17	1

Lee S, et al. Am J Cardiol 2012;110:373–377

The Safety and efficacy of oral anticoagulation in Patients with Liver Cirrhosis on Vitamin K Antagonist Treatment

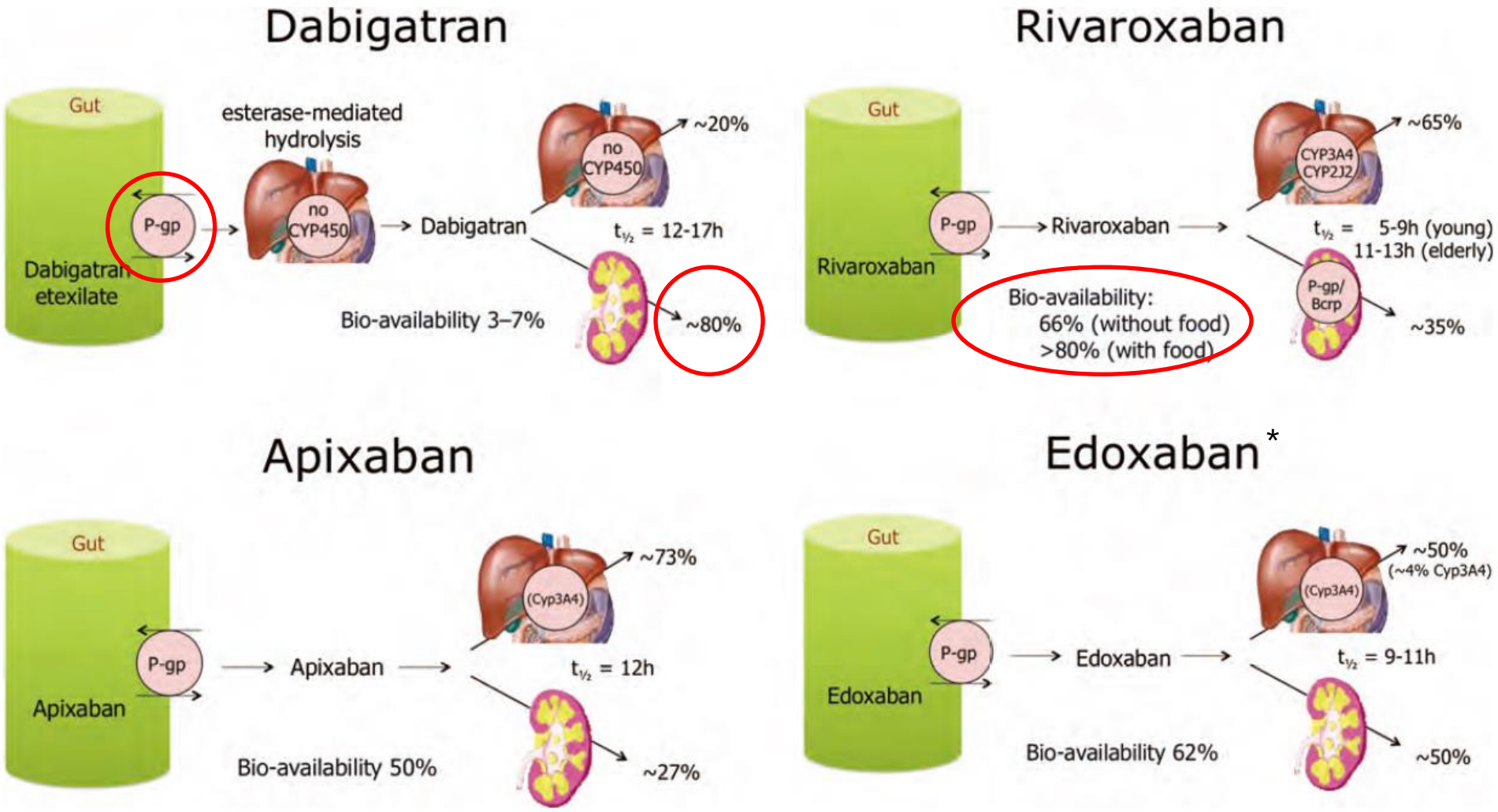


Lee S, et al. APHRS 2013

순서

1. NOAC 사용 증례
2. NOAC 사용시 유의할 점

Absorption and Metabolism of NOACs



***Edoxaban is not approved in Korea**

Heidbuchel H et al. *Europace*. 2013;15:625-651.

Absorption and metabolism of the different NOACs

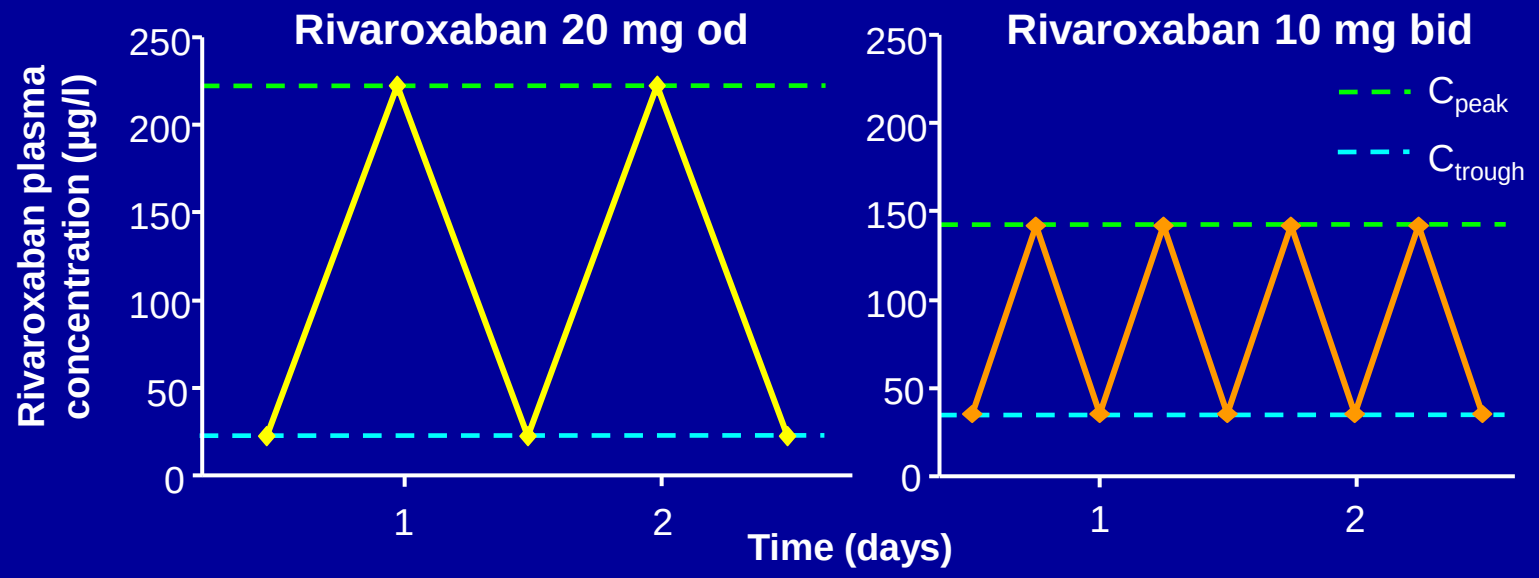
***Edoxaban is not approved in Korea**

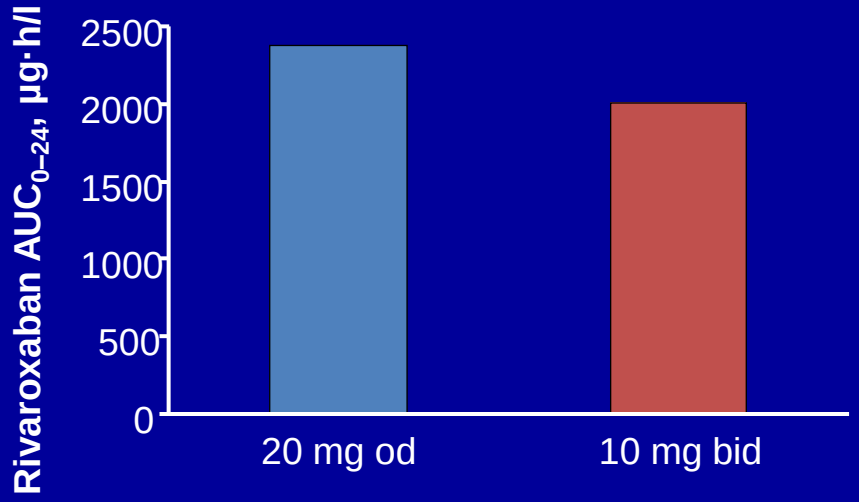
	Dabigatran	Apixaban	Edoxaban[a] *	Rivaroxaban
Bio-availability	3–7%	50%	62%[17]	66% without food Almost 100% with food
Prodrug	Yes	No	No	No
Clearance non-renal/renal of absorbed dose (if normal renal function; see also Section 8)	20%/80%	73%/27%[18]	50%/50%[9]	65%/35%
Liver metabolism: CYP3A4 involved	No	Yes (elimination; minor CYP3A4 contribution)[19]	Minimal (<4% of elimination)	Yes (elimination)
Absorption with food	No effect	No effect	6–22% more[20]	+39% more[21]
Intake with food recommended?	No	No	No official recommendation yet	Mandatory
Absorption with H2B/PPI	−12–30%[22–24]	No effect	No effect	No effect[21,25]
Asian ethnicity	+25%[24]	No effect	No effect[20]	No effect
GI tolerability	Dyspepsia 5–10%	No problem	No problem	No problem
Elimination half-life	12–17 h[23]	12 h	9–11 h[9]	5–9 h (young) 11–13 h (elderly)

Please note this information is from separate, independent studies and therefore should be carefully interpreted

Heidbuchel H et al. *Europace*. 2013;15:625-651.

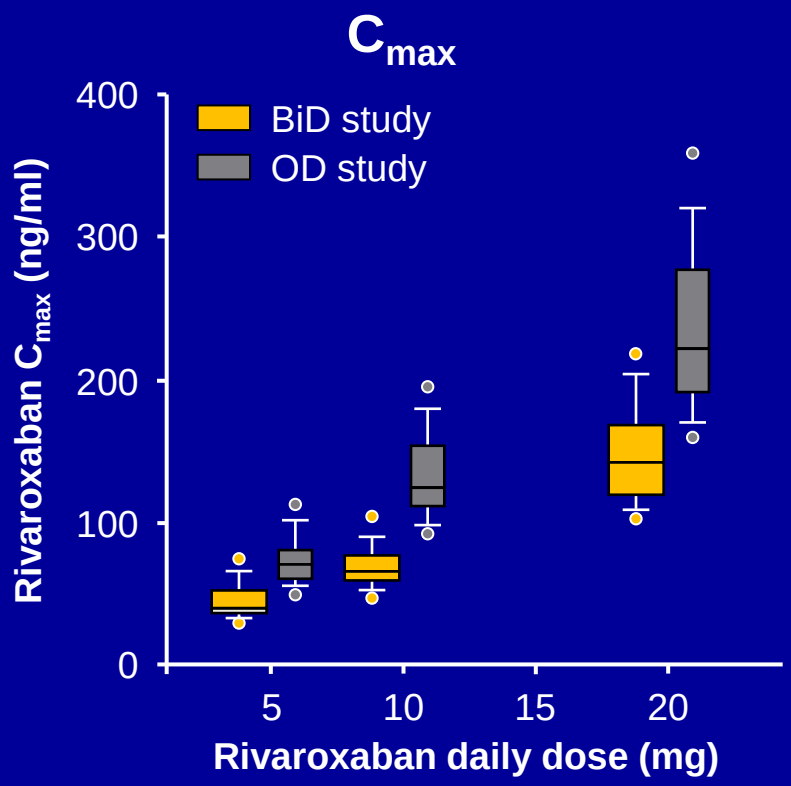
Rivaroxaban once daily versus twice daily dosing

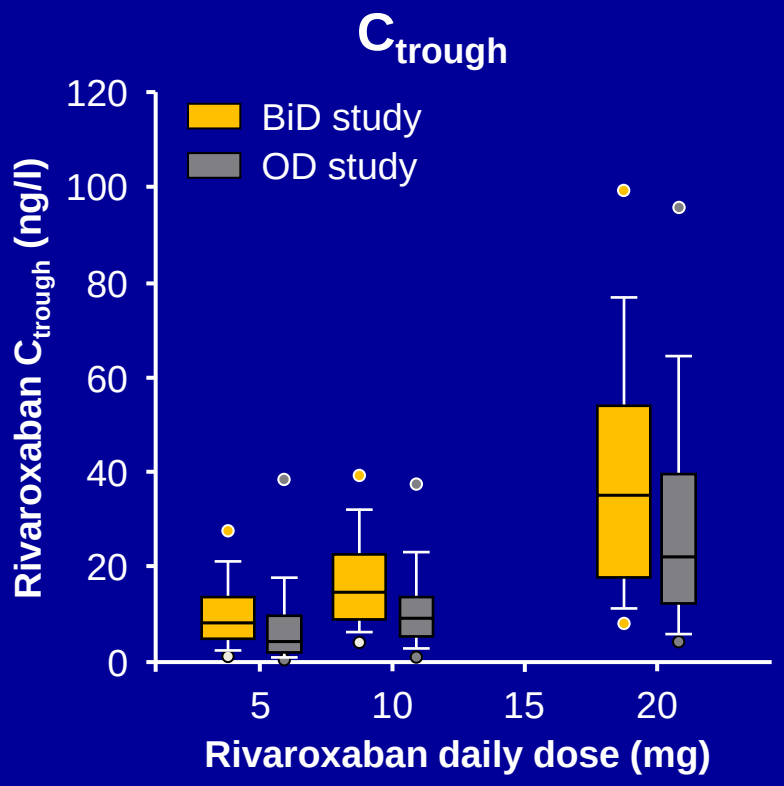




Mueck *et al*, Thromb Haemost 2008;100:453–461

Rivaroxaban: OD and BiD pharmacokinetics



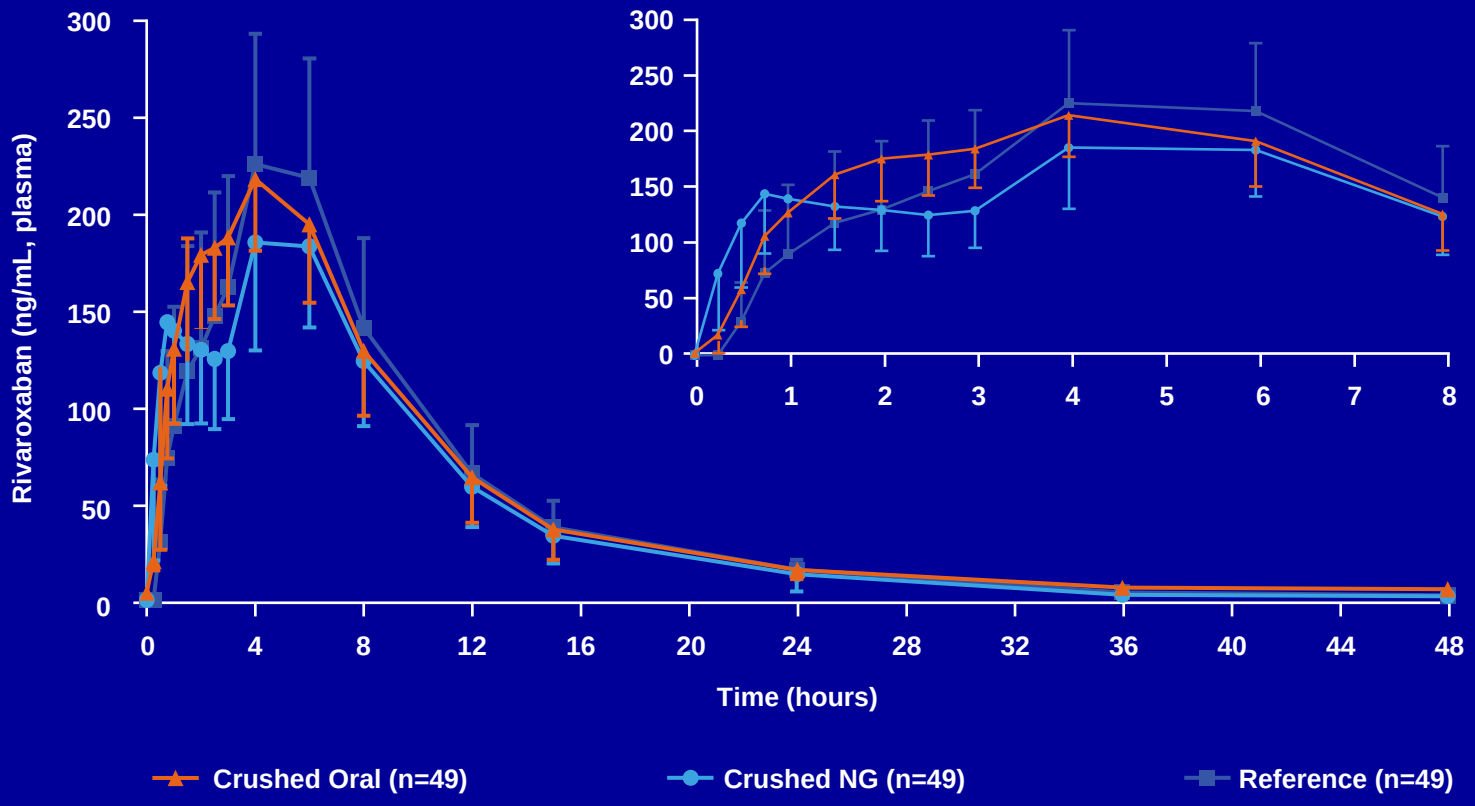


Maximum (C_{max}) and minimum (C_{trough}) rivaroxaban plasma concentrations in the BiD and OD studies, with 25th and 75th percentiles (horizontal lines) and 5th and 95th percentiles (circles)

Mueck *et al*, Thromb Haemost 2008;100:453–461

Rivaroxaban orally or via nasogastric tube – Results

Mean (±SD) plasma rivaroxaban concentration-time profiles following administration of rivaroxaban (linear-linear) (Overall PK Analysis Data Set)

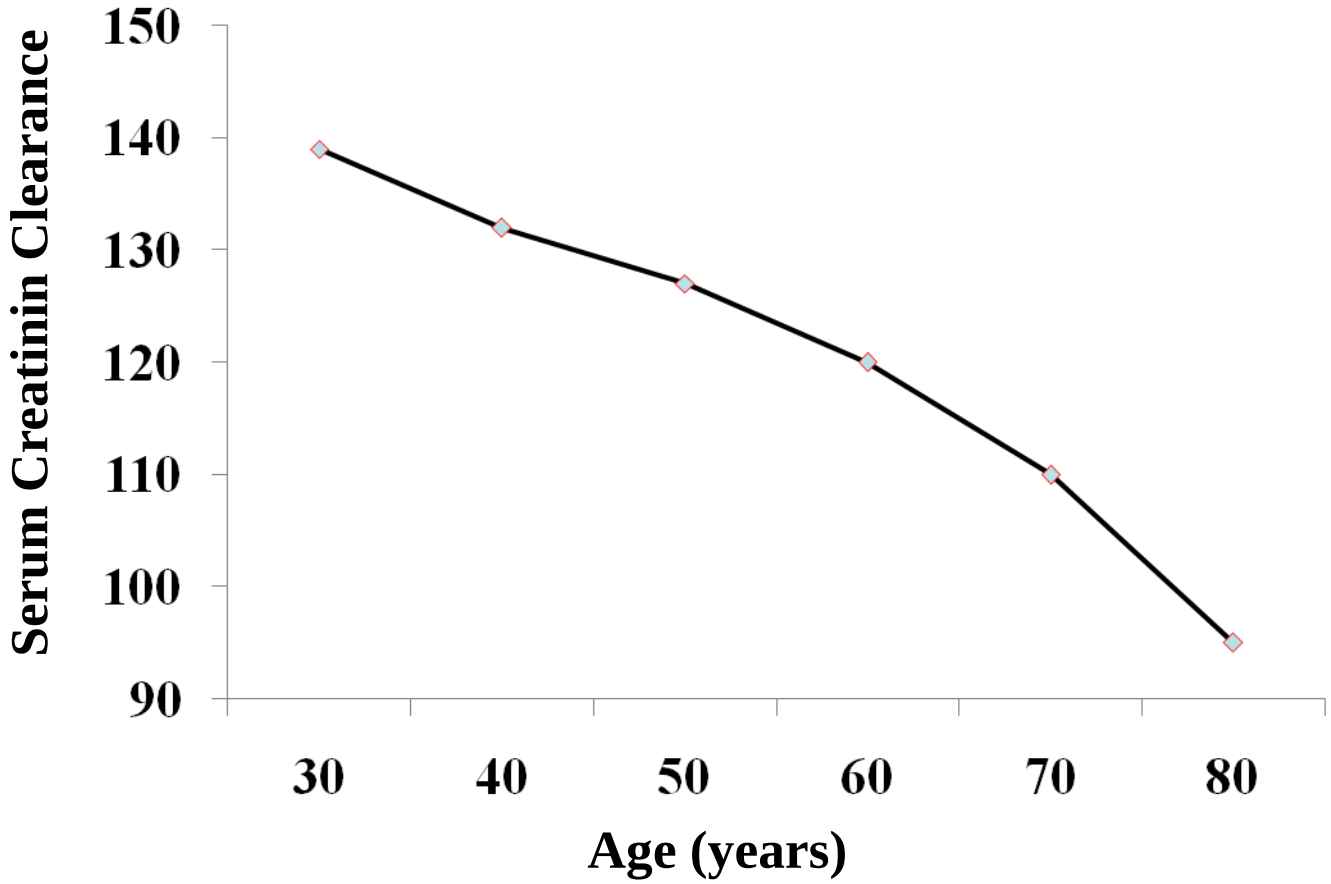


SD, standard deviation; PK, pharmacokinetic; NG, nasogastric.

Moore KT et al. presented at ACCP 2012; Pharmacotherapy 2012; 32 (10): e185-186

Kideny Function and Age

Bleeding problem in old age Pts with CKD



Decline of kidney function with age, as measured by the decline in creatine clearance (Andres and Tobin, 1976)

NOACs in renal dysfunction – Practical recommendations for dosing in chronic kidney disease

CrCl	Dabigatran	Apixaban	Rivaroxaban
≥ 50 ml/min	150 mg bid	5 mg bid	20 mg qd
30-49 ml/min	150 mg bid	5 mg bid	15 mg qd
15-30 ml/min	No (75 mg bid, USA)	2.5 mg bid	15 mg qd
< 15 ml/min	No	No	No

Apixaban: 혈중 creatinine ≥ 1.5 mg/dl, 연령≥80세 혹은 체중≤60kg: 2.5 mg bid

1. Camm et al, Eur Heart J 2012;33:2719-47

Please note this information is from separate, independent studies and therefore should be carefully interpreted

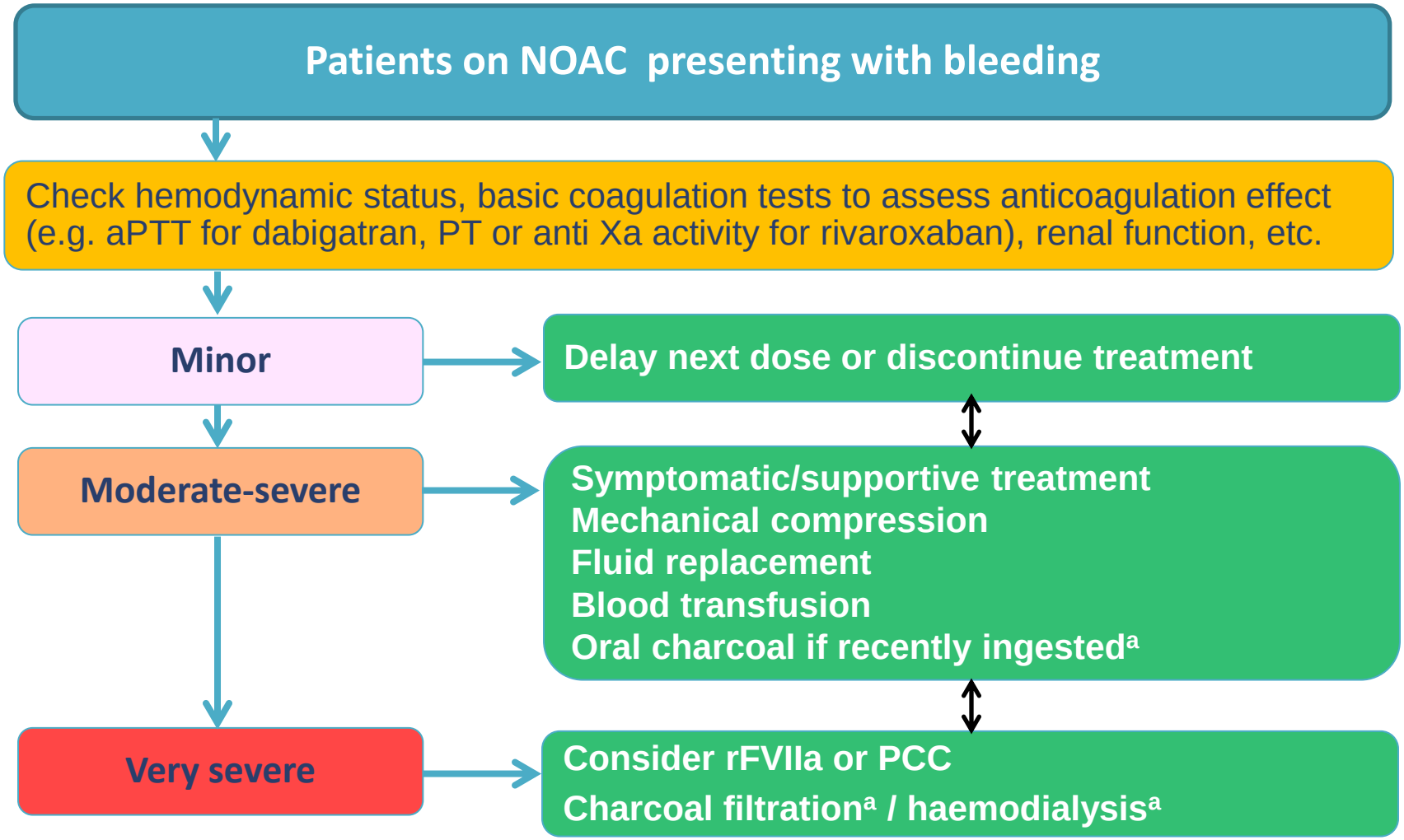
출혈 발생시 ?
:Measuring the anticoagulant effect of NOACs

*Edoxaban is not approved in Korea

	Dabigatran	Apixaban	Edoxaban*	Rivaroxaban
Plasma peak	2h after ingestion	1-4h post ingestion	1-2h after ingestion	2-4h after ingestion
Plasma trough	12-24h after ingestion	12-24h after ingestion	12-24h after ingestion	16-24h after ingestion
PT	cannot be used	cannot be used	prolonged but no known relation with bleeding risk	**prolonged: may indicate excess bleeding risk but local calibration required**
INR	cannot be used	cannot be used	cannot be used	cannot be used
aPTT	**at trough >2x ULN suggests excess bleeding risk**	cannot be used	prolonged but no known relation with bleeding risk	cannot be used
dTT	At trough >200ng/ml ≥ 65s: excess bleeding risk	cannot be used	cannot be used	cannot be used
Anti-FXa assays	n/a	no data yet	quantitative; no data on threshold values for bleeding or thrombosis	quantitative; no data on threshold values for bleeding or thrombosis
Ecarin clotting time	at trough >2x ULN: excess bleeding risk	not affected; cannot be used	not affected; cannot be used	not affected; cannot be used

Please note this information is from separate, independent studies and therefore should be carefully interpreted

ESC recommendations – Management of bleeding in patients taking NOAC



[a]*With dabigatran*

Adapted from Camm et al. Eur Heart J 2012;e-published August 2012, doi:10.1093/eurheartj/ehs253.

Dabigatran and Postmarketing Reports of Bleeding

Intracranial and Gastrointestinal Bleeding Events in New Users of Dabigatran and Warfarin from the Mini-Sentinel Distributed Database, October 2010 through December 2011.*

Analysis	Dabigatran			Warfarin		
	No. of Patients	No. of Events	Incidence *no. of events/ 100,000 days at risk*	No. of Patients	No. of Events	Incidence *no. of events/ 100,000 days at risk*
Gastrointestinal hemorrhage						
Analysis with required diagnosis of atrial fibrillation	10,599	16	1.6	43,541	160	3.5
Sensitivity analysis without required diagnosis of atrial fibrillation	12,195	19	1.6	119,940	338	3.1
Intracranial hemorrhage						
Analysis with required diagnosis of atrial fibrillation	10,587	8	0.8	43,594	109	2.4
Sensitivity analysis without required diagnosis of atrial fibrillation	12,182	10	0.9	120,020	204	1.9

New Engl J Med 2013

2013 ASH annual meeting

3636 A Phase 2 Randomized, Double-Blind, Placebo-Controlled Trial Demonstrating Reversal Of Rivaroxaban-Induced Anticoagulation In Healthy Subjects By Andexanet Alfa (PRT064445), An Antidote For Fxa Inhibitors

Program: Oral and Poster Abstracts
Session: 332. Antithrombotic Therapy: Poster III

Monday, December 9, 2013, 6:00 PM-8:00 PM
Hall E (Ernest N. Morial Convention Center)

Crowther Mark, MD[1*], *Mathur Vandana, MD*[2*], *Kitt Michael, MD*[3*], *Lu Genmin, PhD*[4*], *Pamela B. Conley, Ph.D.*[5], *Hollenbach Stanley, JD*[4*], *Janice Castillo*[6*], *Athiwat Hutchaleelaha, Ph.D.*[7*], *Mark Karbarz, Ph.D.*[6*], *Joyce P Lin*[8*], *Lee Barron, PhD*[6*], *Sandra Russell, R.N*[6*], *Gallia G. Levy, MD, PhD*[6], *Stuart Connolly, M.D.*[9*] *and John T. Curnutte, MD, PhD*[6]

[1]*McMaster University, Hamilton, ON, Canada*
[2]*MathurConsulting, Woodside, CA*
[3]*Clinical Development, Portola Pharmaceuticals, South San Francisco, CA*
[4]*Research, Portola Pharmaceuticals, South San Francisco, CA*
[5]*Biology, Portola Pharmaceuticals Inc, S San Francisco, CA*
[6]*Portola Pharmaceuticals, South San Francisco, CA*
[7]*Consultant, Portola Pharmaceuticals, South San Francisco, CA*
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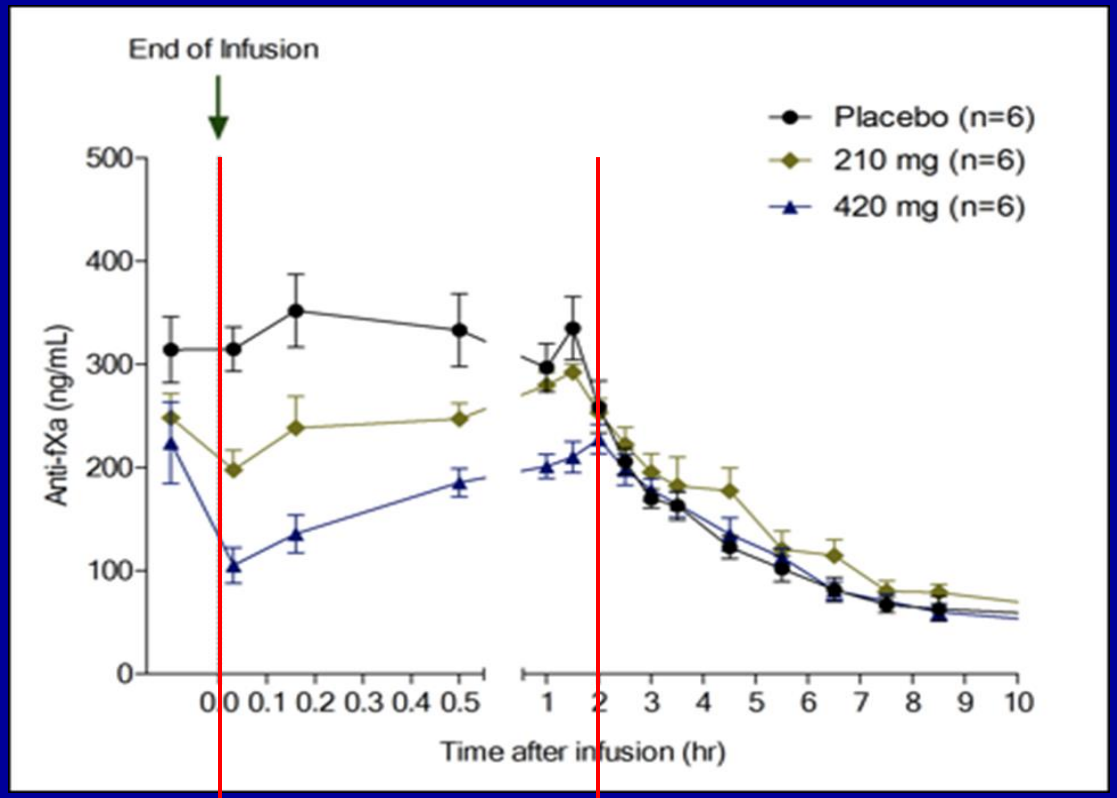
[9]*Population Health Research Institute / McMaster University, Hamilton, ON, Canada*

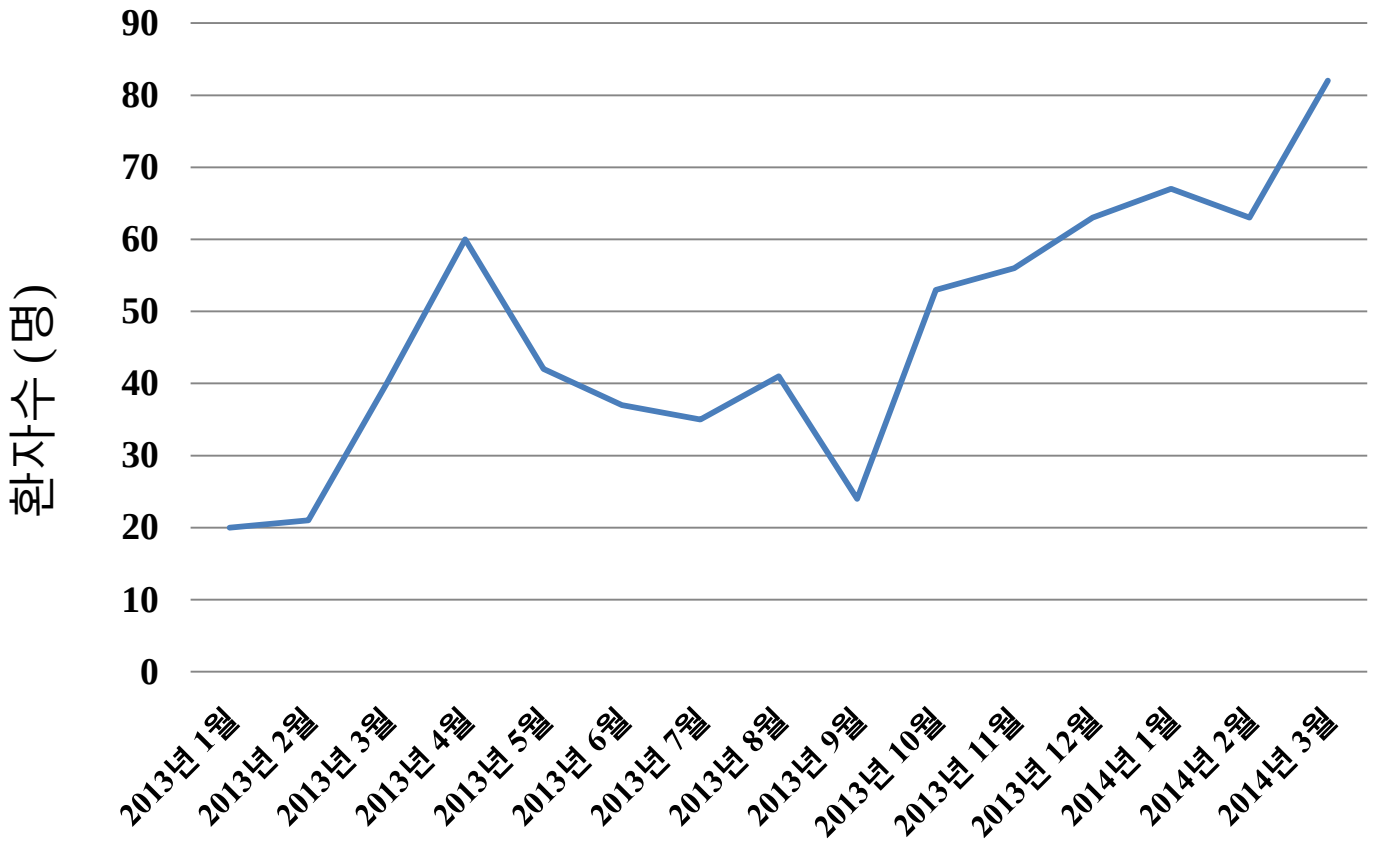
A Phase 2 Randomized, Double-Blind, Placebo-Controlled Trial Demonstrating Reversal Of Rivaroxaban-Induced Anticoagulation In Healthy Subjects By Andexanet Alfa (PRT064445), An Antidote For Fxa Inhibitors



- Conclusion

  - Dose dependently partially reverse the anticoagulant effects of rivaroxaban

Xarelto in Severance Hospital



Take-Home Message

• 뇌졸중 위험도가 낮은 환자를 제외하고, CHA_2DS_2-VASc 1 점 환자에서도 항응고 요법을 고려한다.

• NOAC이 warfarin 보다 안정성 및 효과가 좋아서 선호된다. 하지만 고령, 신기능 저하 환자에서 주의가 필요하다.

• NOAC 사용 중 발생하는 출혈은 대부분 시간이 지나면 호전되지만 심각한 출혈의 경우 혈액 투석 등 기타 조치가 필요하다.

Thank you for your attention!