

# Is it beneficial or harmful to patients with PE to choose DOACs instead of warfarin?

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2018. 04. 21.

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호흡기내과/Thrombosis Clinic

김 양 기

# DOACs are beneficial?

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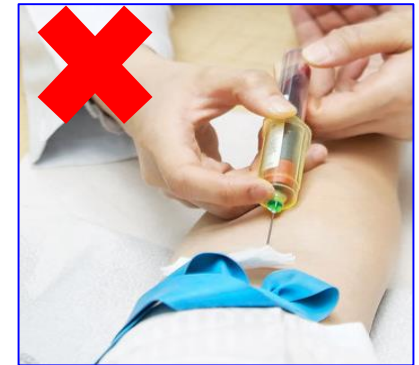
# Characteristics of DOACs

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**VAR** ~~IBLE~~

**FIXED**



**Tmax**

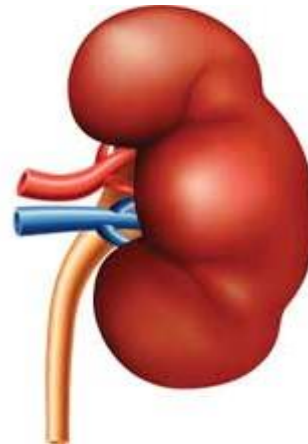
$\pm$  2 hours

Dabigatran : 80%

Rivaroxaban : 33%

Apixaban : 25%

Edoxaban : 35%



**Half life**

$\pm$  12 hours

# 식이의 제한 vs 자유로운 식사

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와파린



새로운 항응고제



# DOACs의 시기별 용량 (first 3 to 6 months)

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5-7 days

~ 21 days

~ 3 to 6 months

**Dabigatran**

Parenteral  
anticoagulant

150 mg bid

**Rivaroxaban**

15 mg bid

20 mg qd

**Apixaban**

10 mg bid

5 mg bid

**Edoxaban**

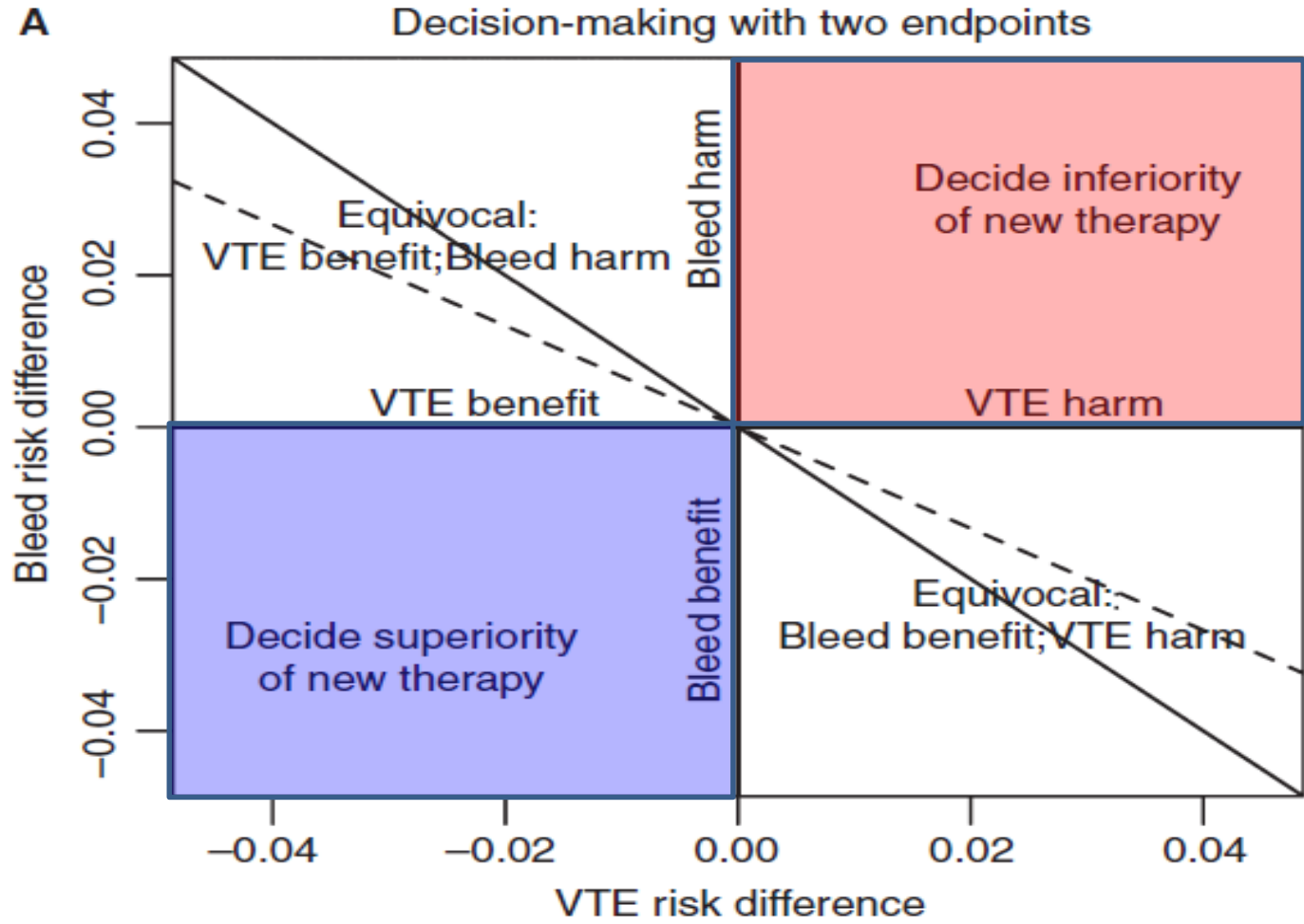
Parenteral  
anticoagulant

60 mg vs 30 mg qd



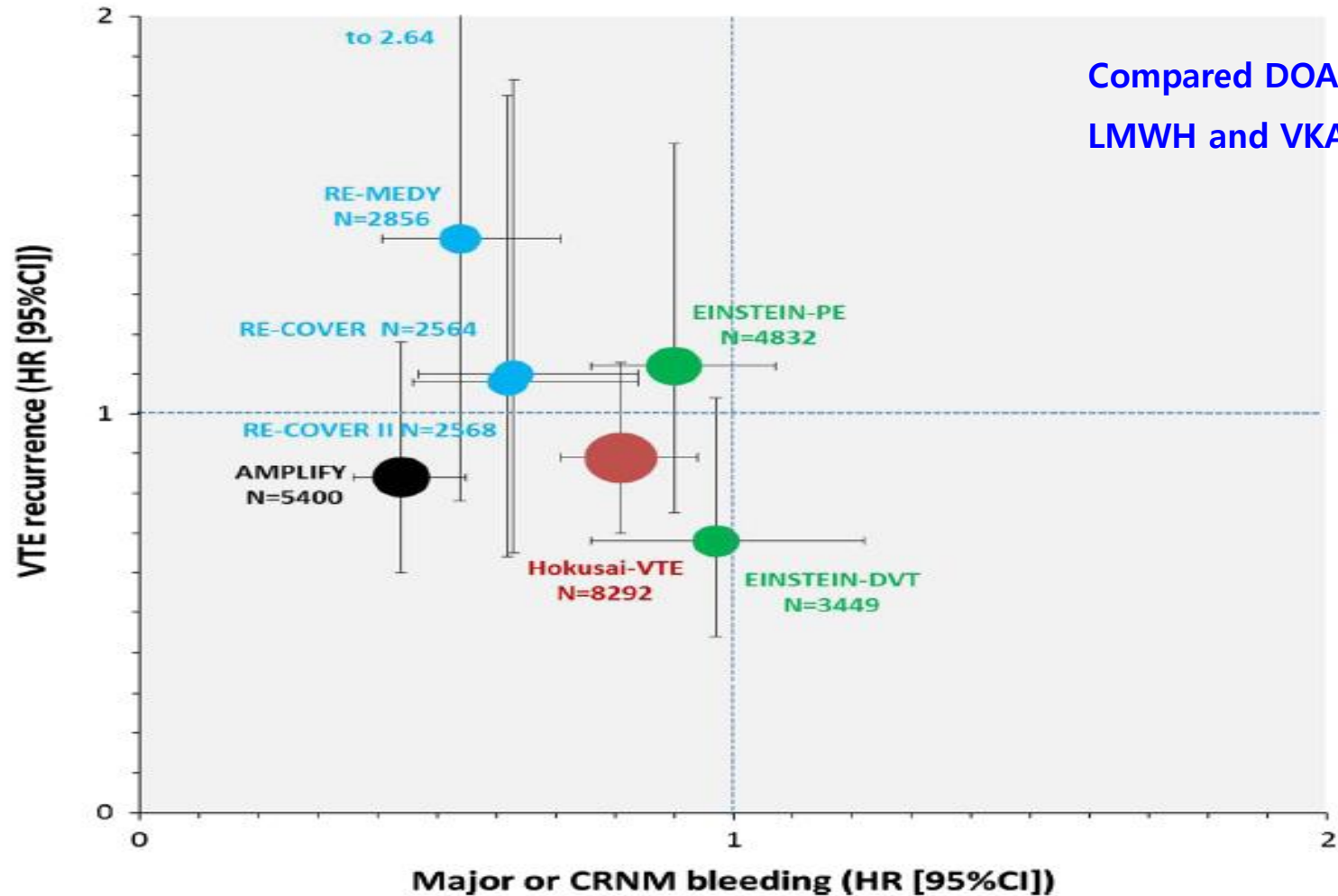
# Net Clinical Benefit

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# VTE recurrence & Rates of major or CRNMB in VTE studies

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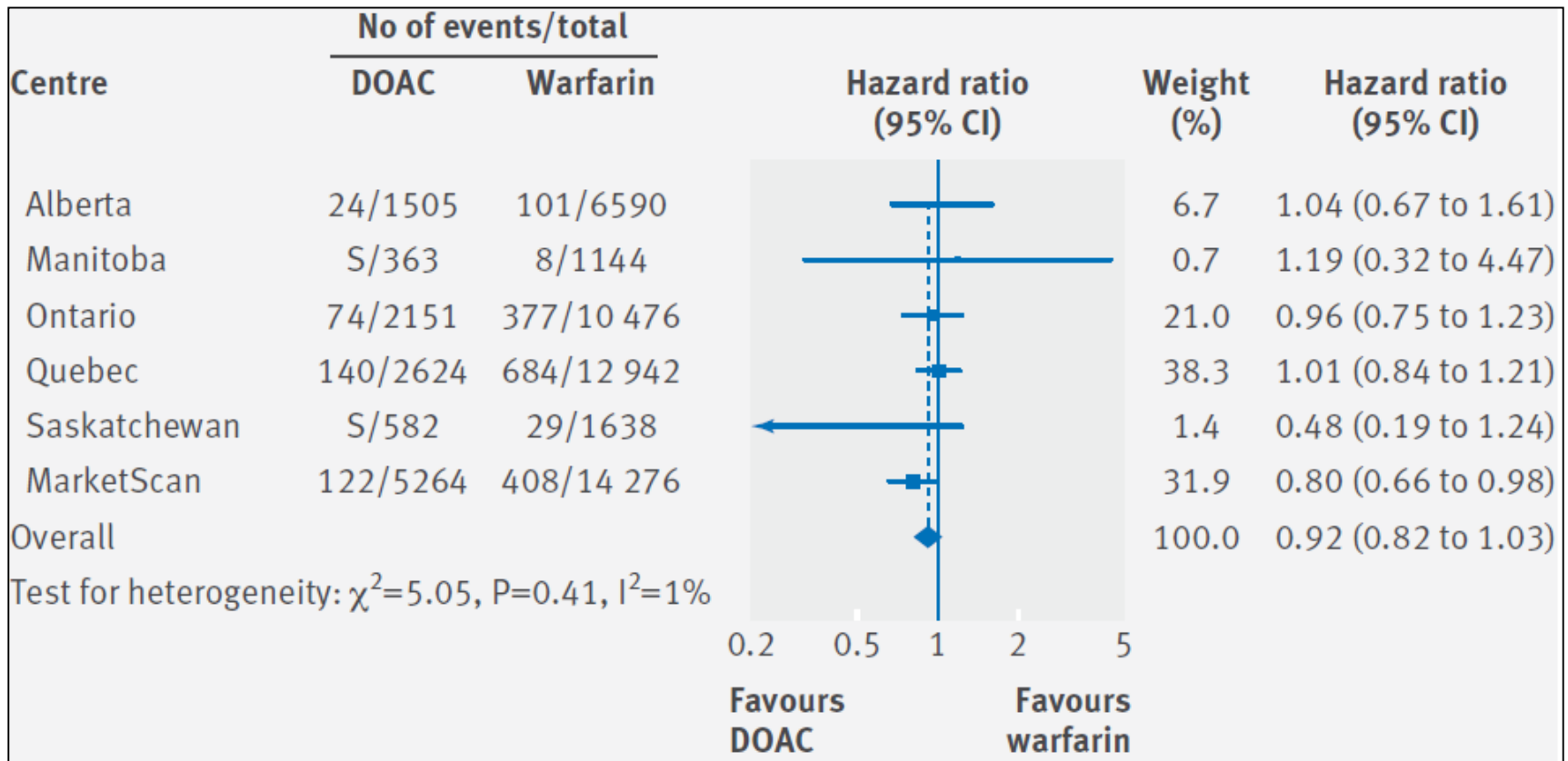


# Safety (major bleeding, DOACs vs Warfarin)

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**Multicentre, population based, observational study**

**59 525 VTE patients (12 489 DOAC users; 47 036 warfarin users) with matched cohort**





# DOACs의 시기별 용량 (after 3 to 6 months ~ )

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**Dabigatran**

150 mg bid

**Rivaroxaban**

20 mg vs 10 mg qd

**Apixaban**

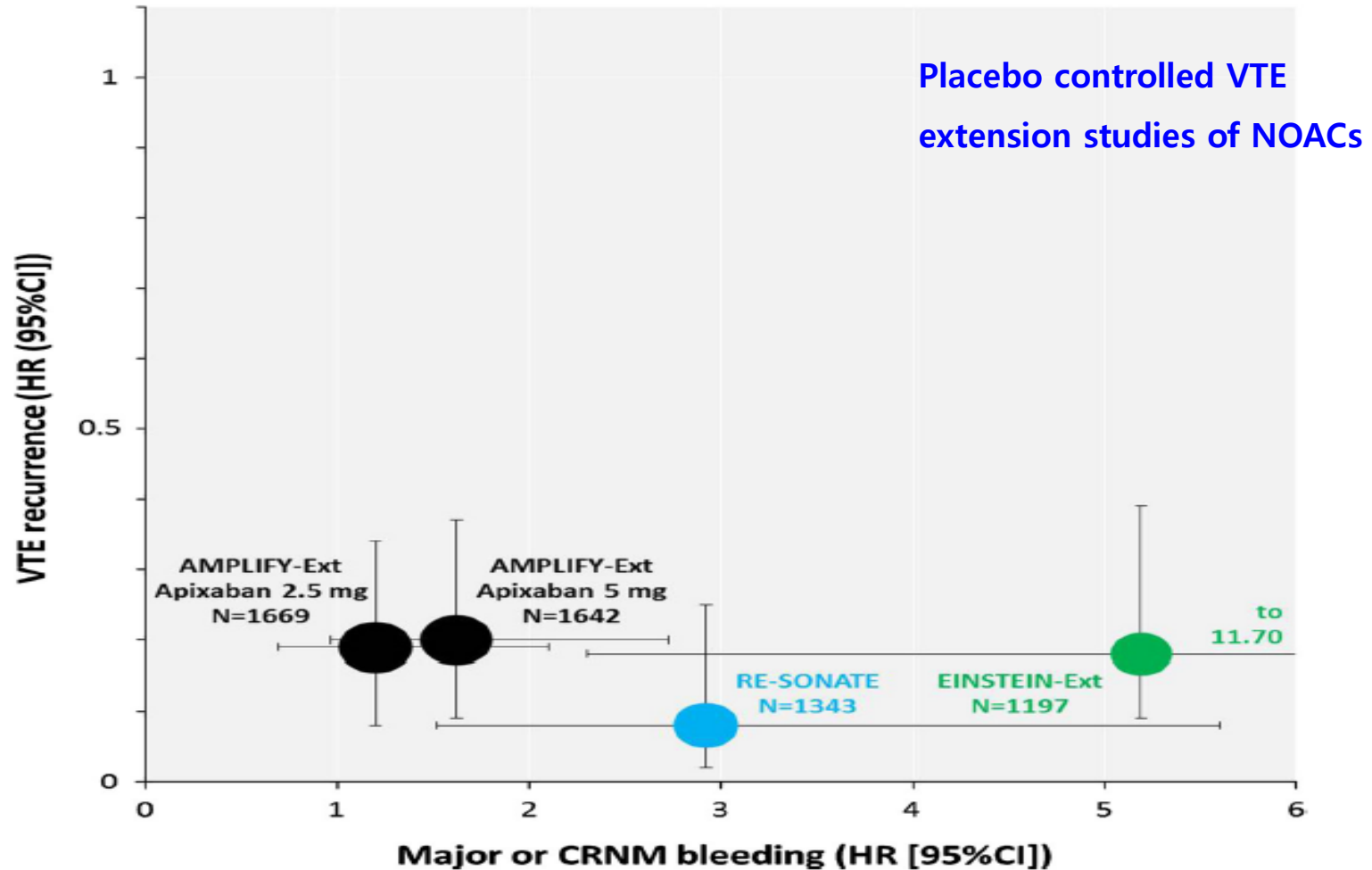
5 mg vs 2.5 mg bid

**Edoxaban**

60mg vs 30mg qd (?)

# VTE recurrence & Rates of major or CRNMB in VTE studies

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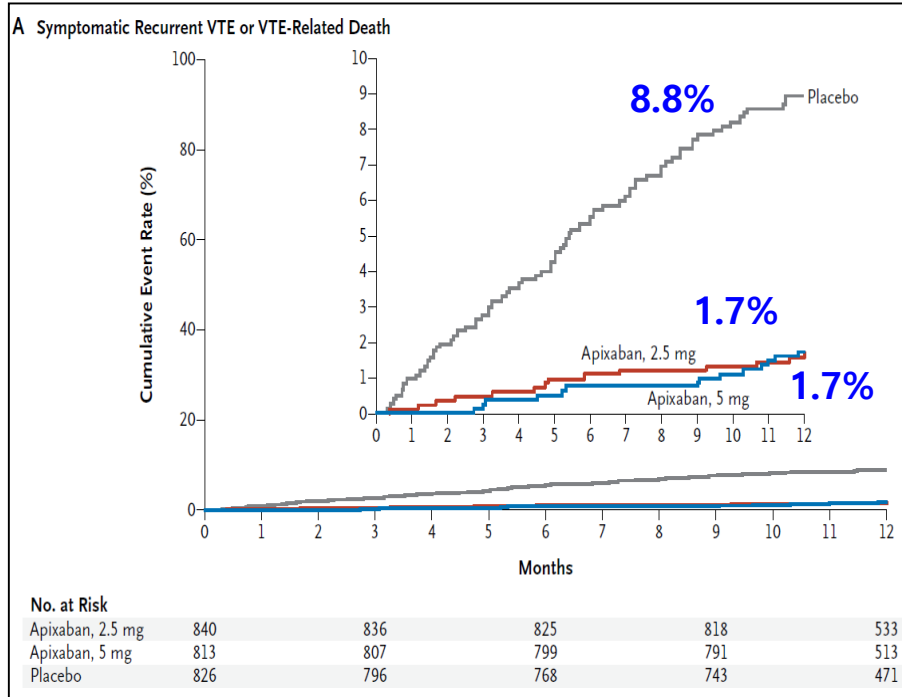
# Results of Apixaban vs Rivaroxaban [Extended]

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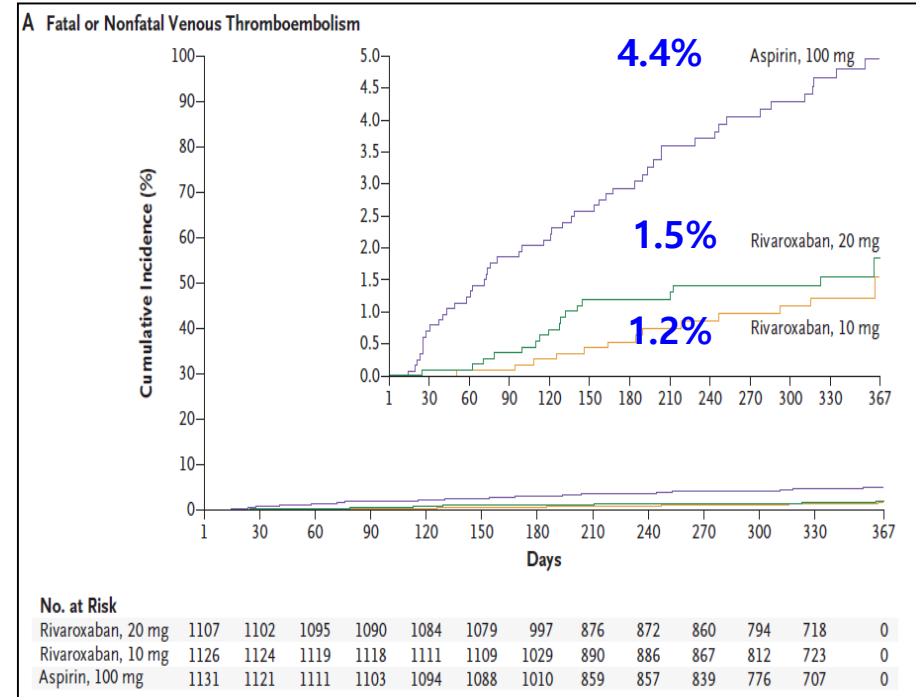
- 20 mg rivaroxaban vs. aspirin, HR 0.34; 95% CI 0.20 to 0.59
- 10 mg rivaroxaban vs. aspirin, HR 0.26; 95% CI 0.14 to 0.47
- $P < 0.001$  for both comparisons

## Efficacy

### Apixaban



### Rivaroxaban



**[Caution]** Excluded for patients who required extended treatment with therapeutic doses of anticoagulant agents

# Results of Apixaban vs Rivaroxaban [Extended]

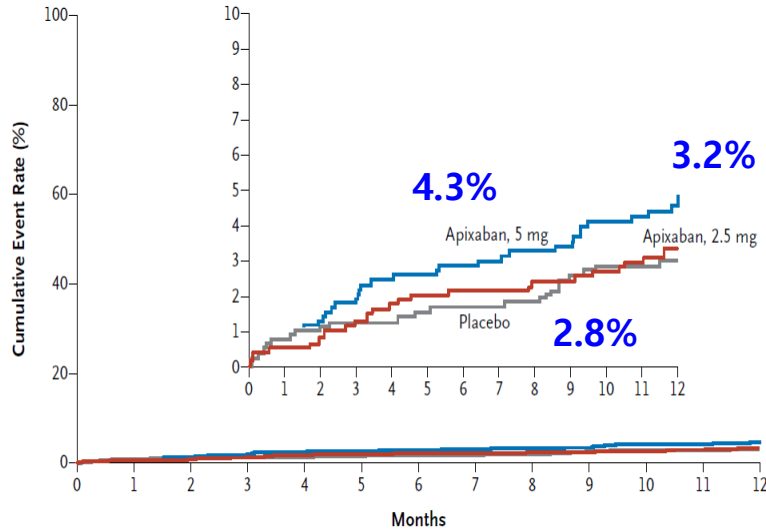
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## Safety

## Apixaban

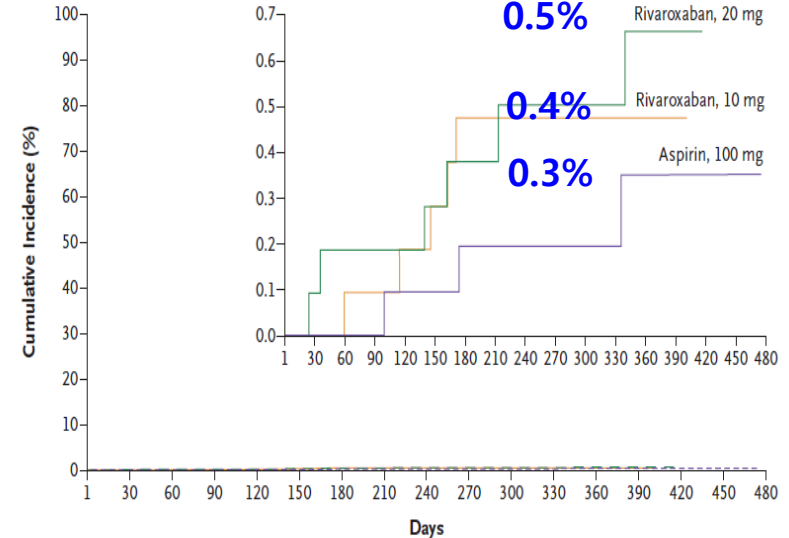
## Rivaroxaban

**B Major or Clinically Relevant Nonmajor Bleeding**



No. at Risk	0	3	6	9	12
Apixaban, 2.5 mg	840	786	759	737	354
Apixaban, 5 mg	811	751	716	689	331
Placebo	823	749	687	651	298

**B Major Bleeding**

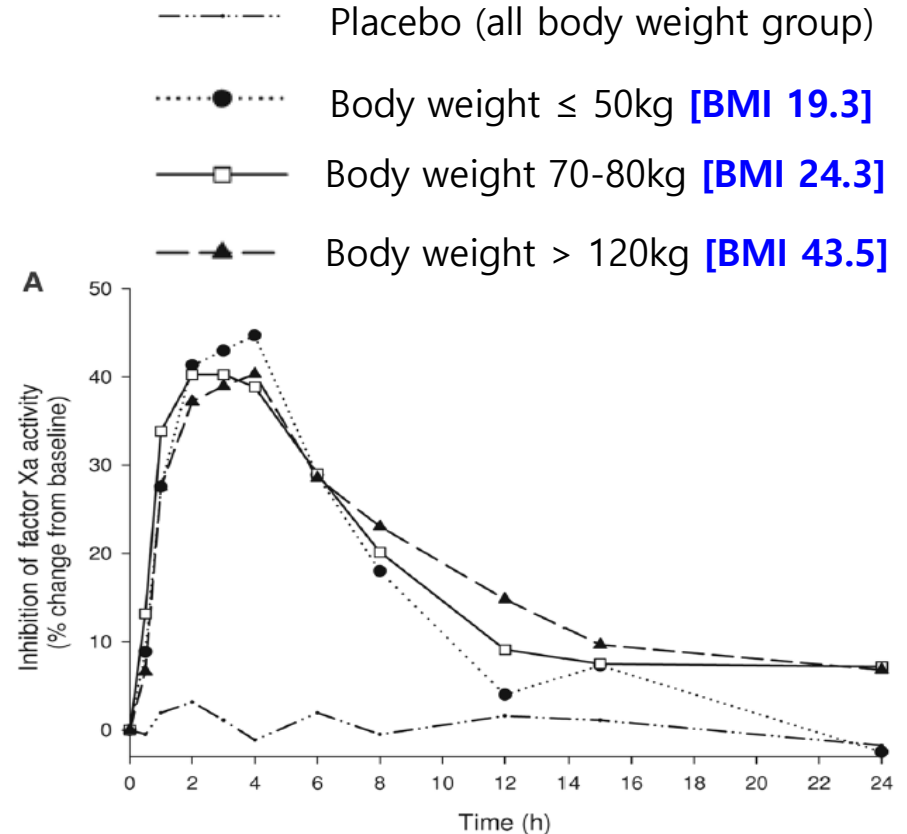
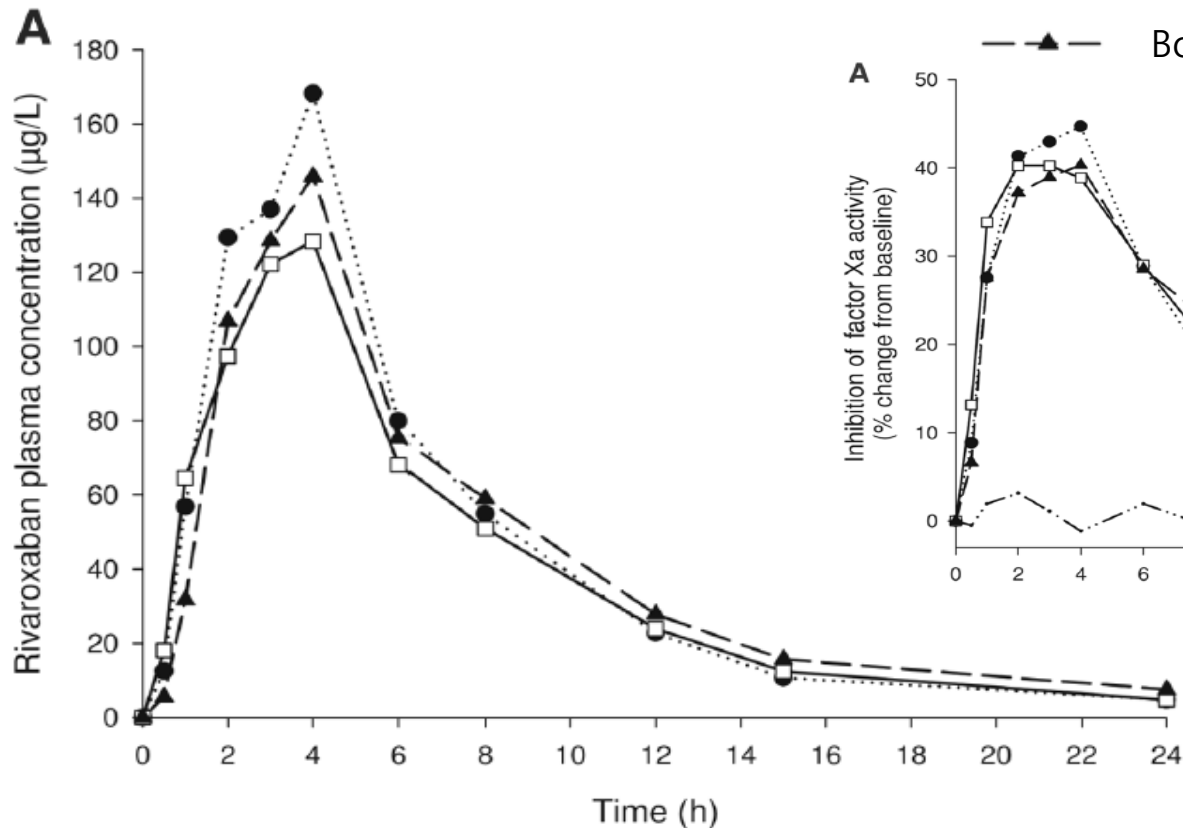


No. at Risk	0	30	60	90	120	150	180	210	240	270	300	330	360	390	420	450	480
Rivaroxaban, 20 mg	1107	1081	1063	1048	1036	1024	963	818	801	780	712	642	449	10	0	0	0
Rivaroxaban, 10 mg	1126	1103	1080	1070	1058	1046	988	823	812	790	733	653	469	8	0	0	0
Aspirin, 100 mg	1131	1096	1075	1058	1040	1023	970	800	791	768	709	645	445	5	2	2	0

# Body weight ✕ Rivaroxaban

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- Body weight  $\leq 50$ kg [BMI 19.3]
- Body weight 70-80kg [BMI 24.3]
- ▲ Body weight  $> 120$ kg [BMI 43.5]



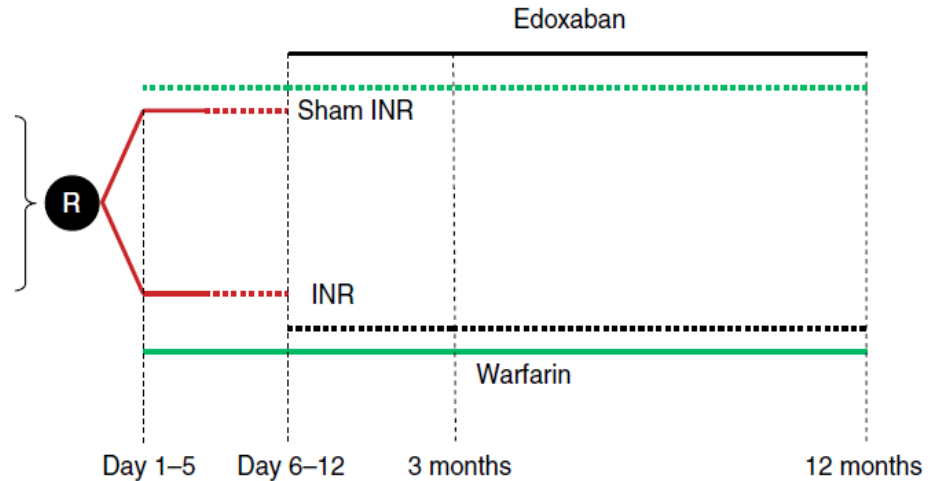
# Edoxaban

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표준용법  
및 용량

Objectively confirmed venous thromboembolism

- Stratified randomization for
  - Pulmonary embolism/ deep vein thrombosis
  - Dose adjustment
  - Risk factors



All patients receive initial heparin treatment for at least 5 days after randomization.

- Edoxaban
- ..... Placebo edoxaban
- Warfarin
- ..... Placebo warfarin
- Low-molecular-weight heparin

▶ 항응고 주사제 5일 이상 투여 후 60 mg qd

*J Thromb Haemost 2013;11(7):1287-94*

감량 적응증  
및 용량

**30 mg qd**

- moderate renal impairment ( $30 \leq \text{CrCL} \leq 50$  mL/min),
- body weight  $\leq 60$  Kg, or
- concurrently receiving the P-gp inhibitors (**Quinidine** or **Verapamil**).

*N Engl J Med 2013;369(15):1406-15*

# Edoxaban (first 3 to 6 months)

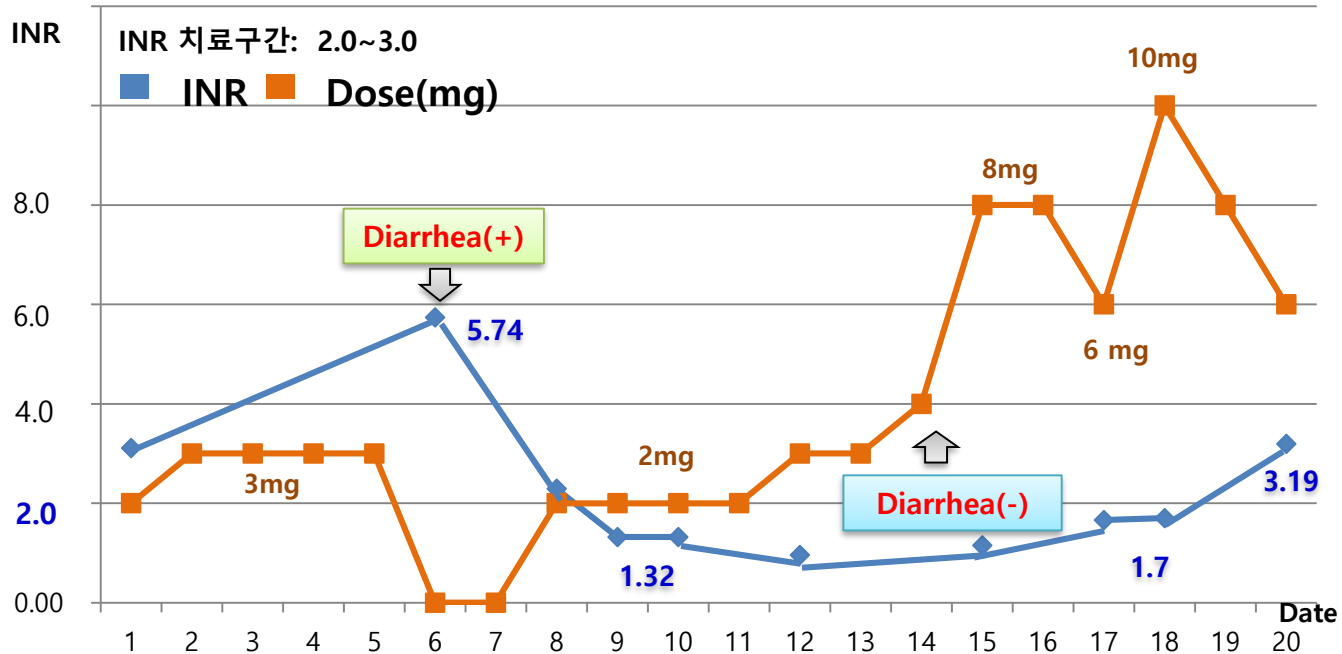
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	Exoxaban	warfarin	Hazard Ratio
<b>Recurrent VTE, n(%)</b>			
Total, n(%)	130/4118 (3.2)	142/4122 (3.5)	0.89 (95% CI 0.70-1.13)
<b>30mg, n(%)</b>	22/733 (3.0)	30/719 (4.2)	0.73 (95% CI 0.42-1.26)
<b>Major bleeding, n(%)</b>			
Total, n(%)	56/4118 (1.4)	66/4122 (1.6)	0.84 (95% CI 0.59-1.21)
<b>30mg, n(%)</b>	11/733 (1.5)	22/719 (3.1)	0.50 (95% CI 0.24-1.03)
<b>CRNMB, n(%)</b>			
Total, n(%)	349/4118 ( <b>8.5</b> )	423/4122 ( <b>10.3</b> )	<b>0.81</b> (95% CI 0.71-0.94)
<b>30mg, n(%)</b>	58/733 ( <b>7.9</b> )	92/719 ( <b>12.8</b> )	<b>0.62</b> (95% CI 0.44-0.86)

# L-tube feeding 과 Warfarin

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## 65/F, PEG insertion state

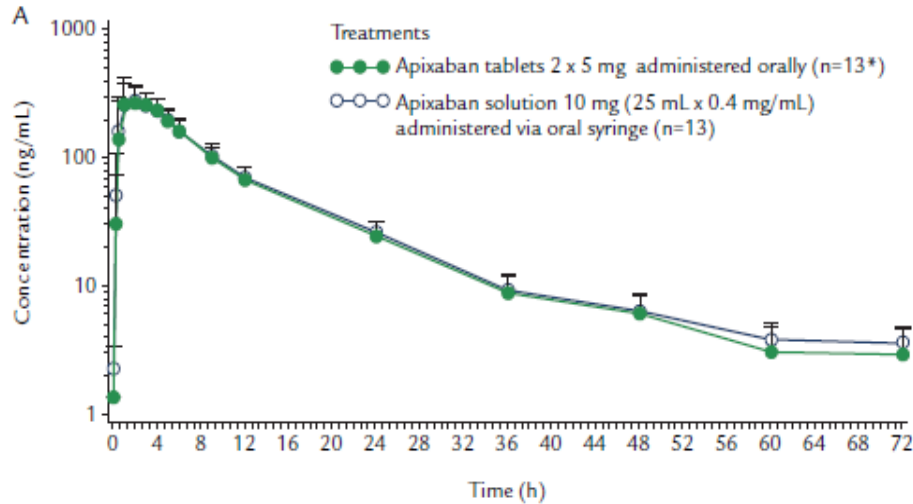


식이	그린비아 DM 150cc X 3회	그린비아 Fiber 300cc X 4회	메디웰 Fiber 300cc X 3회
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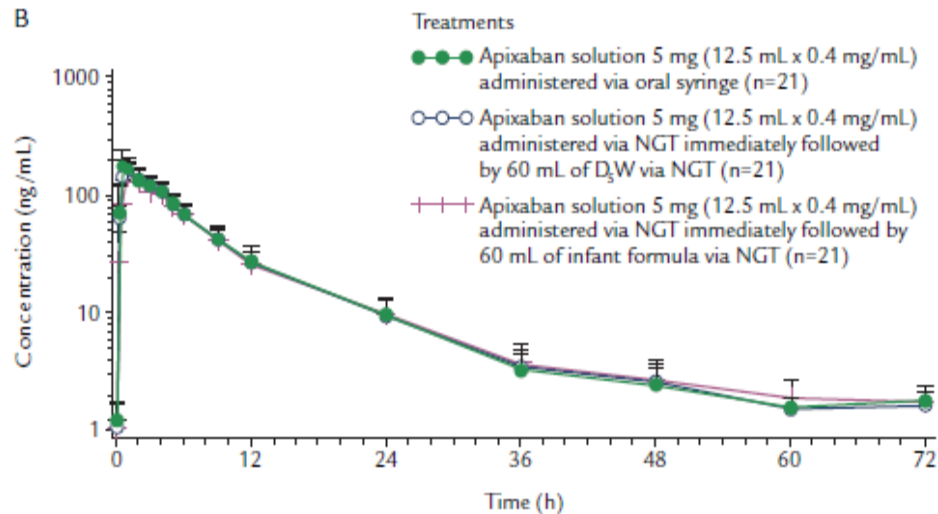
▶ 설사 후 Fiber formula feeding로 인한 INR 변화 (?)

# L-tube feeding 과 Apixaban

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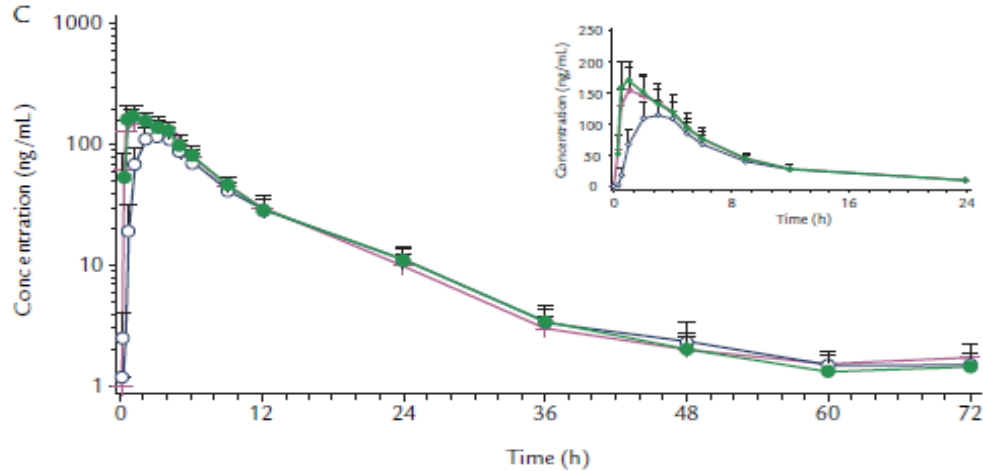
Tablet vs Oral solution



Oral solution vs  
Solution via NGT  
(DW vs Infant formula)

# L-tube feeding 과 Apixaban

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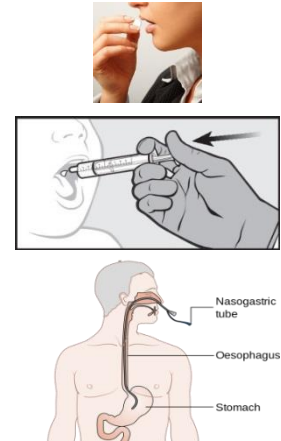


- Apixaban solution 5 mg (12.5 mL x 0.4 mg/mL) administered via oral syringe (n=20)
- Apixaban solution 5 mg (12.5 mL x 0.4 mg/mL) after Boost Plus® via NGT (n=20)
- + + + Apixaban 5 mg crushed tablet suspended in 60 mL D<sub>5</sub>W administered via NGT (n=21)



**Oral solution vs Solution via NGT vs Crushed tablet (DW) via NGT**

**Alternative methods of administering apixaban may be useful in certain clinical situations.**



## 주의사항

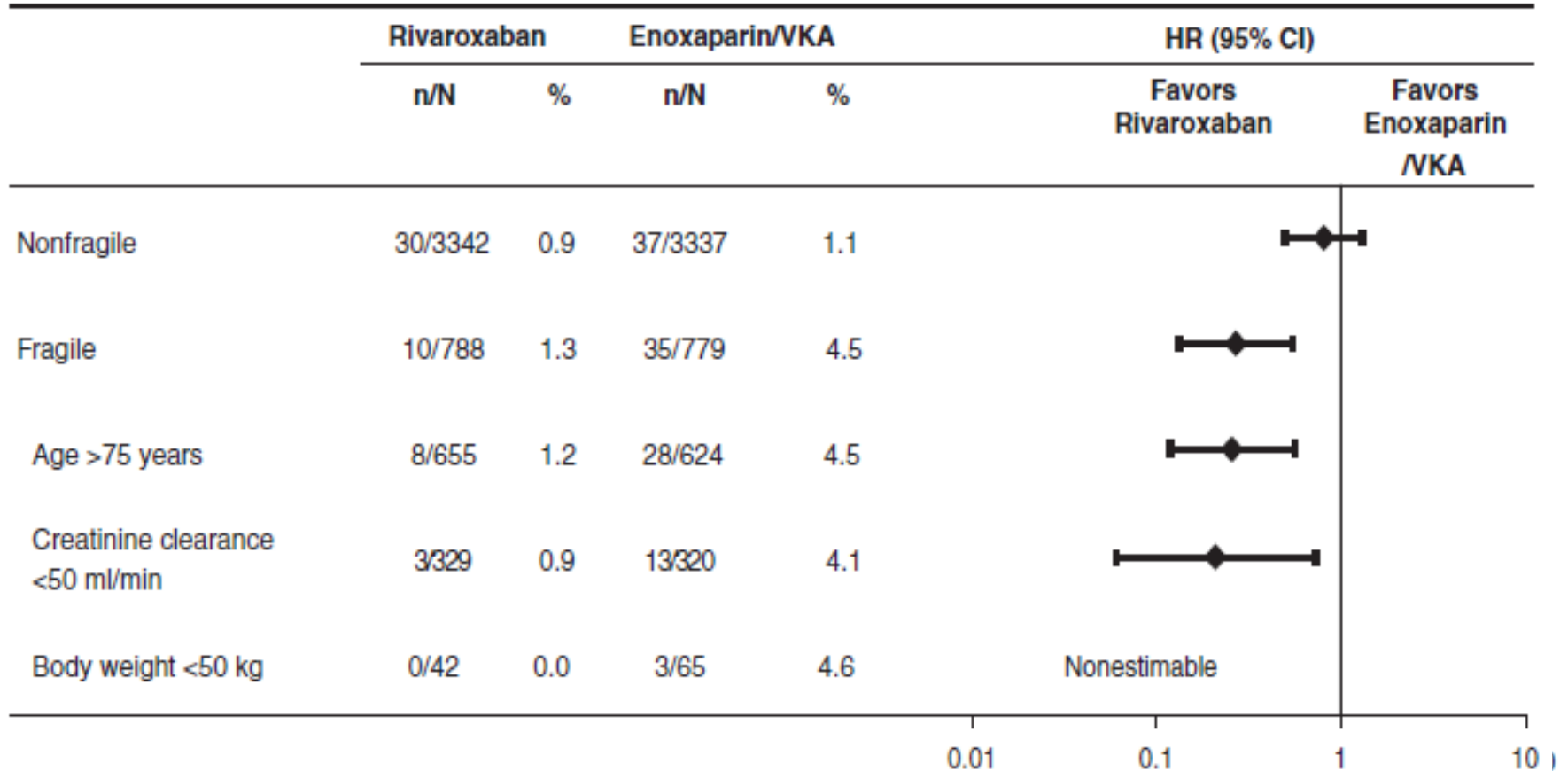
- ❖ The oral **bioavailability** of **dabigatran etexilate** **increases by 75%** when the pellets are taken **without the capsule shell** compared to the intact capsule formulation.
- ❖ **PRADAXA** capsules should therefore **not be broken, chewed, or opened before administration.**

# Rivaroxaban in fragile patients (VTE)

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Recurrent VTE

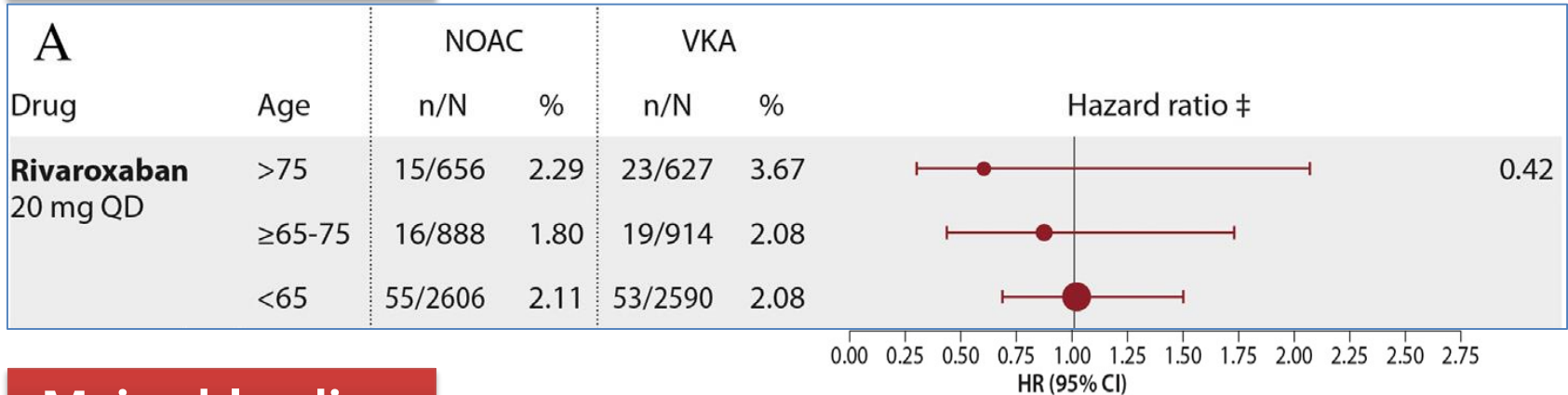
Major bleeding



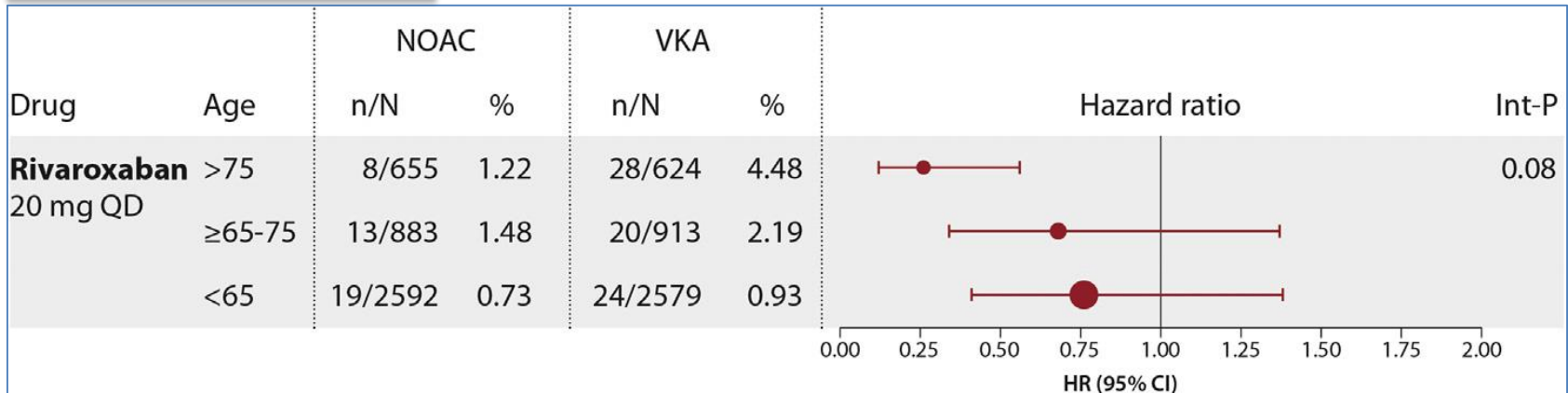
# Rivaroxaban in elderly patients (VTE)

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## Recurrent VTE



## Major bleeding



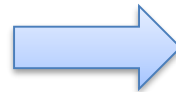
# Perioperative management in DOACs

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Recommended **time to interrupt** DOACs from last dose to anticipated procedure based on renal function

Renal function		Dabigatran	Rivaroxaban	Apixaban	Edoxaban
CrCl > 80 mL/min	Moderate bleeding risk	1day	1 day	1day	1day
	High bleeding risk	2days		2days	
CrCl 50-80 mL/min		3days	1day	2days	2days
CrCl 30-50 mL/min		4days	1day	3days	3days
CrCl 15-30 mL/min		5days	2days	N/A	3days

수술 혹은 시술 후 재투여시  
이것만은 꼭 기억!!!



**Tmax**

**± 2 hours**

# In case of overdose of Rivaroxaban

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자렐토 20mg 90알을 자살목적으로 먹고 응급실로 환자가 왔다. 복용 12시간 후 INR 은 7.38 이었다. 어떻게 진료하면 될까요?

Antidote ? 혹은 Reversal Agent?

Case Report

The X factor: Lack of bleeding after an acute apixaban overdose<sup>☆</sup>

Scott M. Leikin, D.O.<sup>a</sup>, Hina Patel, Pharm D<sup>b</sup>, Katherine L. Welker, M.D.<sup>c</sup>, Jerrold B. Leikin, M.D.<sup>d,\*</sup>

*Am J Emerg Med 2017;35(5):801.e5-801.e6*

## Massive intoxication with rivaroxaban, phenprocoumon, and diclofenac

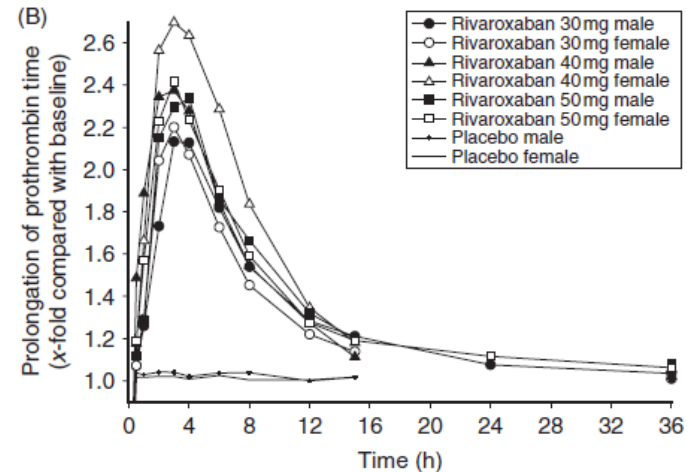
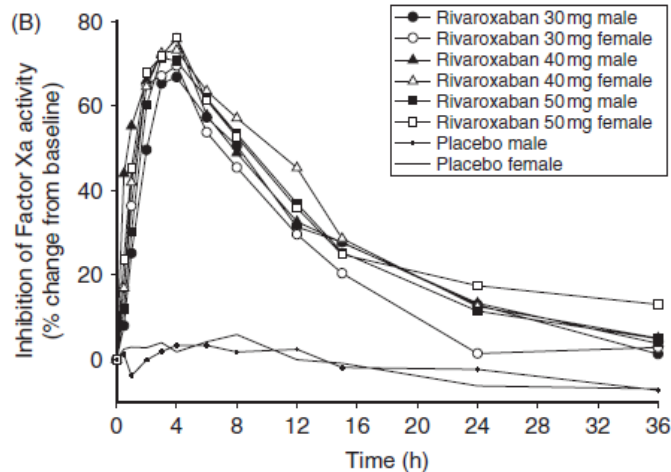
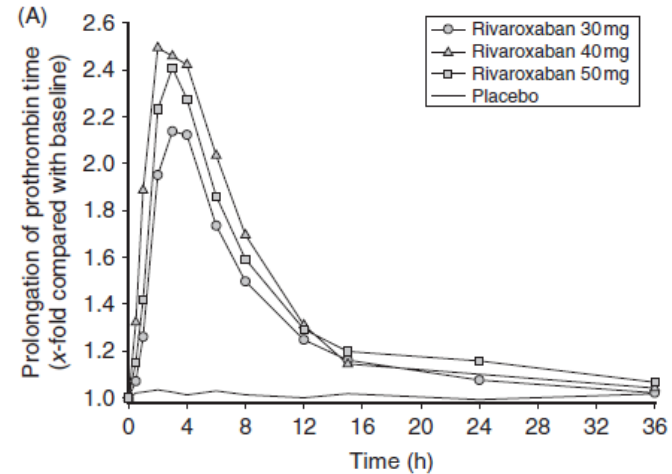
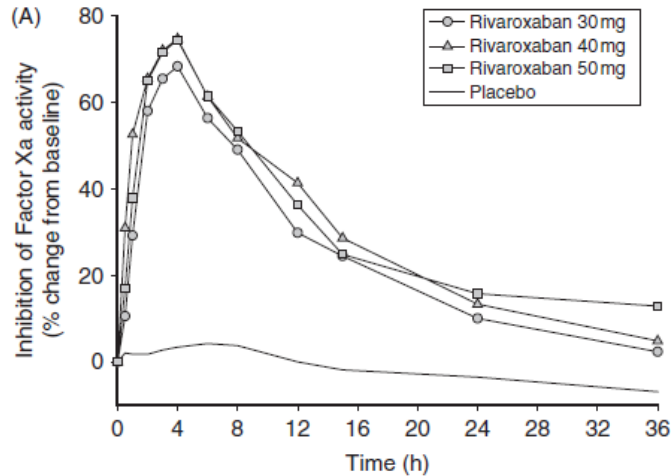
### A case report

Hella Pfeiffer, MD<sup>a,\*</sup>, Larissa Herbst, MD<sup>b</sup>, Bernd Schwarze, PhD<sup>c</sup>, Reinhold Eckstein<sup>a</sup>, Volker Weisbach<sup>a</sup>

*Medicine (Baltimore) 2016;95(44):e5343*

# In case of overdose of Rivaroxaban (ceiling effect)

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# In case of overdose of Rivaroxaban (ceiling effect)

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[According to the manufacturer] Rivaroxaban 은 과량 복용시 ceiling effect(천장효과)가 있어, **과량 복용 시에도 약물농도 및 효과가 무한대로 늘어나는 것이 아니라 통상 용량의 2-3배 이상은 안 오르는 것으로 알려져 있습니다.**( 600mg. 즉 30알x20mg을 먹어도 통상양의 2.5배정도인 50mg 정도 복용시의 약물 농도 정도만 상승함).

고령에서 약은 반감기가 약 12시간 전후 이므로, daily PT level검사를 시행하시고 경과 관찰하시기 바랍니다. 통상 **elimination half life의 약 5-6배인 60~72시간 후가 되면 흡수된 Rivaroxaban의 배설이 다 되어, PT level 이 정상화 될 가능성이 높아** 보입니다.

## ❖ F/U Prothrombin Time (INR) level

7.38['17-03-06, 11am] 90알 복용 12시간 후

→ 3.97['17-03-06, 6pm] 18시간 후

→ 1.80['17-03-07, 8am] 32시간 후

→ 1.26['17-03-08, 8am] 56시간 후

# Drug Information in Korea (회사의 권고에 따른 것임)

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Renal impairment (eGFR)		
Dabigatran	150mg bid	<b>[금지]</b> 중증 신장애 (CrCL<30mL/min)
Rivaroxaban	20mg qd	<b>[신중투여]</b> 신장애 (CrCl: 15-49mL/min)
Apixaban	5mg bid	<b>[신중투여]</b> 중증 신장애 (CrCl 15-29mL/min),
Edoxaban	60mg qd	<b>[금지]</b> 말기 신질환 (CrCL<15mL/min) 및 신장투석
Liver disease (Child Pugh Classification)		
Dabigatran	150mg bid	<b>[금지]</b> 간장애 또는 생존에 영향을 미칠 것으로 예상되는 간질환
Rivaroxaban	20mg qd	<b>[금지]</b> Child Pugh B 및 C 등의 임상적으로 의미있는 출혈 위험성과 관련된 간질환
Apixaban	5mg bid	<b>[신중투여]</b> 경증-중등도 간장애(Child Pugh A 또는 B)
Edoxaban	60mg qd	<b>[금지]</b> 혈액응고장애 및 임상적으로 의미있는 출혈 위험성과 관련된 간질환, 중증 간장애



**절대로 VTE 치료 용량과 혼동하시면 안됩니다 !!!!**

Standard dose regimens ▶ Reduced dose regimens			
	신기능장애	몸무게	나이
Dabigatran			
Rivaroxaban	CrCl < 50 mL/min		
Apixaban	sCr ≥ 1.5 mg/dL	weight ≤ 60kg	age ≥ 80 years
Edoxaban	CrCl 30–50 mL/min	weight ≤ 60kg	

**DOACs이 와파린을 모든 환자에서  
대신할 수 있는 것은 아닙니다**

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**와파린 용량조절을 잘 할 수 있는 방법을  
알아두어야 합니다. (질적 관리)**

# DOACs 이 대신할 수 없는 와파린 투여의 적응증

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- ❖ Rifampin 을 투여해야 하는 경우 (결핵, 골수염 등)
- ❖ 신기능 장애 ( < GFR 30 ml/min)
- ❖ 간기능 장애 (Child Pugh classification C)
- ❖ PE, DVT 이외 다른 장기에 발생한 정맥혈전증 (보험을 원하는 경우)
  - Mesenteric vein thrombosis (including portal vein thrombosis)
  - Cerebral venous sinus thrombosis
- ❖ 잦은 출혈합병증으로 target range 를 낮추어서 조절해야 하는 경우
  - ex) INR range 1.8-2.5

# Risk of bleeding with apixaban in patients with renal impairment

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Apixaban **reduces bleeding** compared with conventional anticoagulants in patients with **mild**, but **not moderate-to-severe, renal impairment**.

## Apixaban vs control (placebo, aspirin, or conventional anticoagulants) for major or clinically relevant nonmajor bleeding†

Population	Number of trials (n)	Weighted event rates		At a median 0.17 to 1.8 y of follow-up	
		Apixaban	Control	RRR (95% CI)	NNT (CI)
Mild renal impairment‡	6 (14 034)	2.7%	3.4%	20% (4 to 34)	148 (87 to 736)
Moderate-to-severe renal impairment§	6 (4999)	6.9%	6.8%	1% (-51 to 110)	Not significant

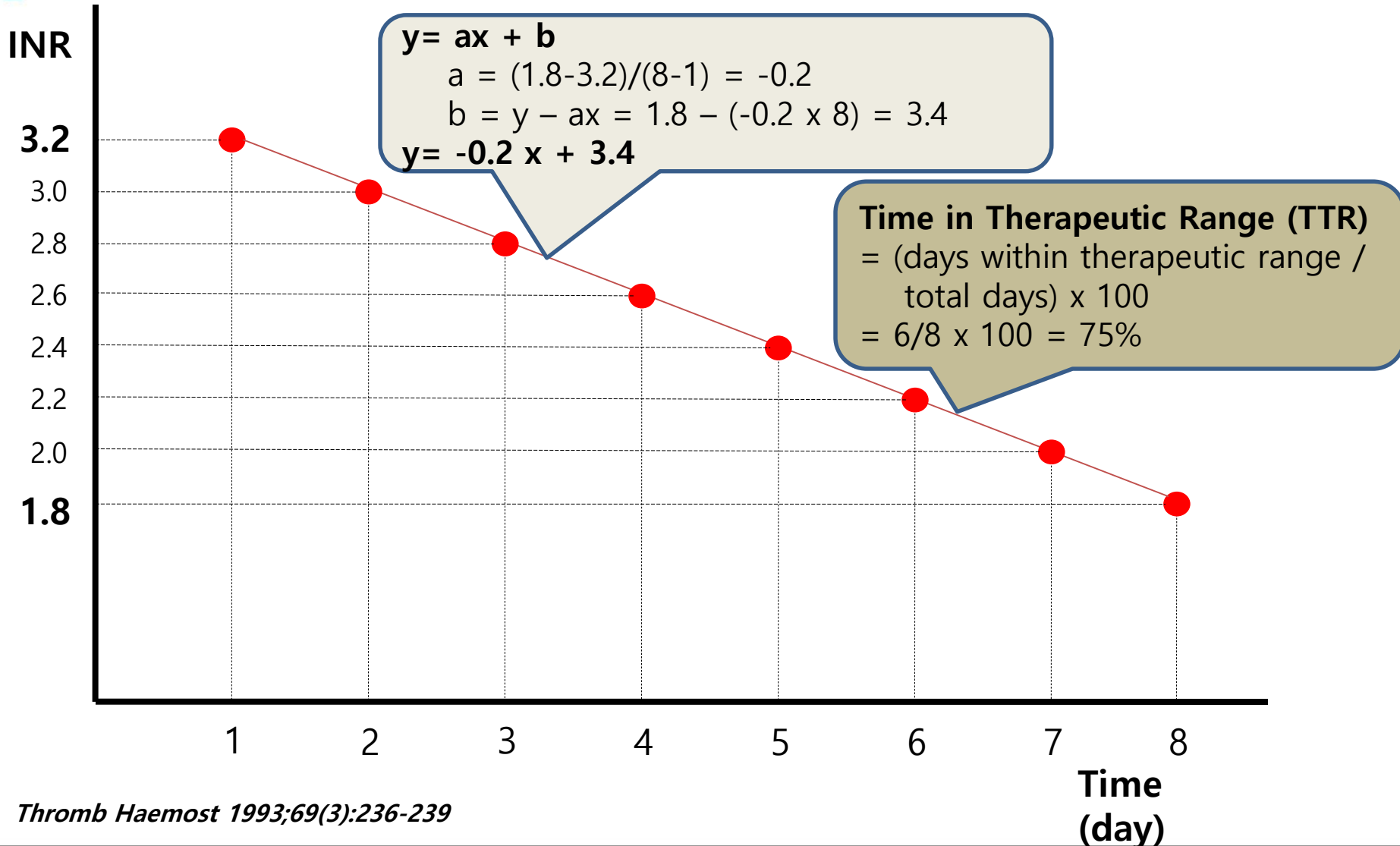
†Abbreviations defined in Glossary. RRR, RRI, NNT, and CI calculated from risk ratios and control event rates in article using fixed-effect (mild renal impairment) or random-effects (moderate-to-severe renal impairment) models.

‡Cockcroft-Gault equation creatinine clearance 50 to 80 mL/min.

§Cockcroft-Gault equation creatinine clearance < 50 mL/min.

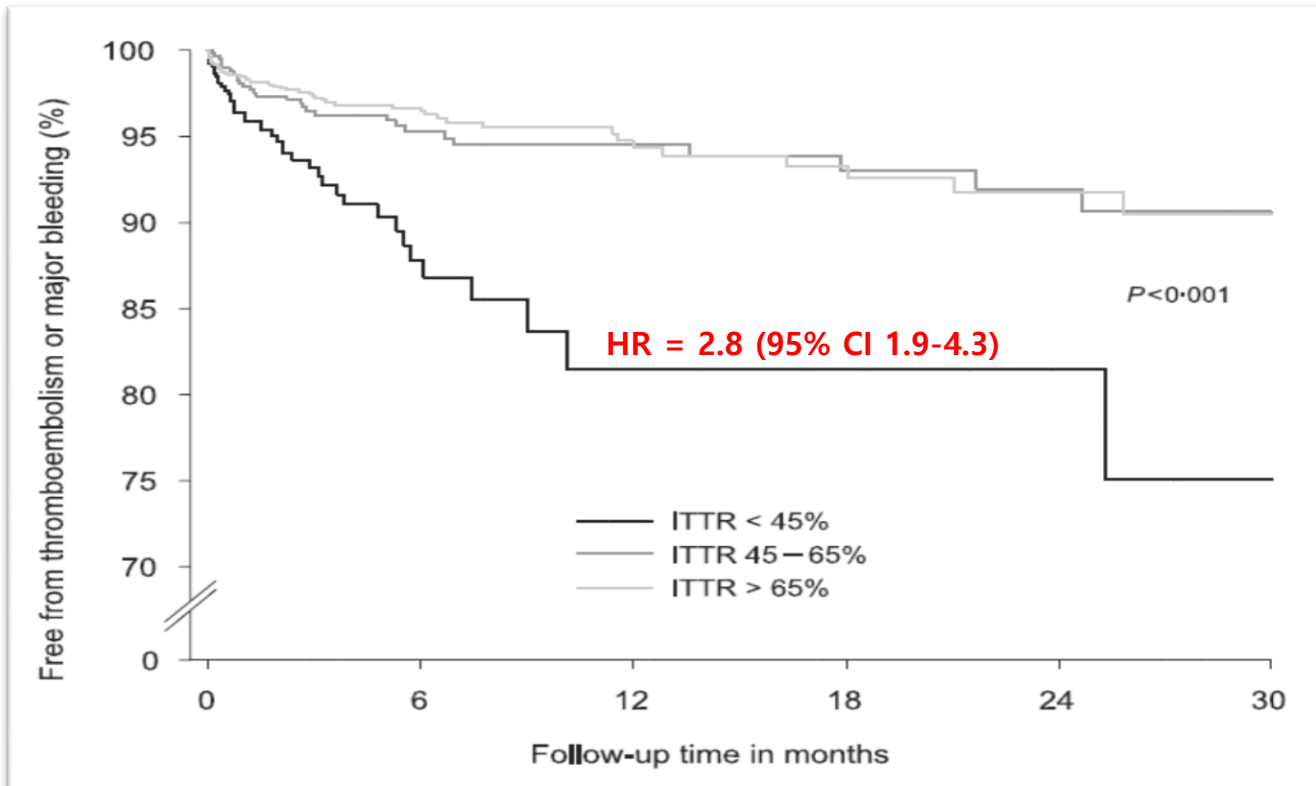
# 와파린의 질적관리 평가방법 (Rosendaal linear interpolation)

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# Influence the quality of OAC management on clinical outcomes (VTE)

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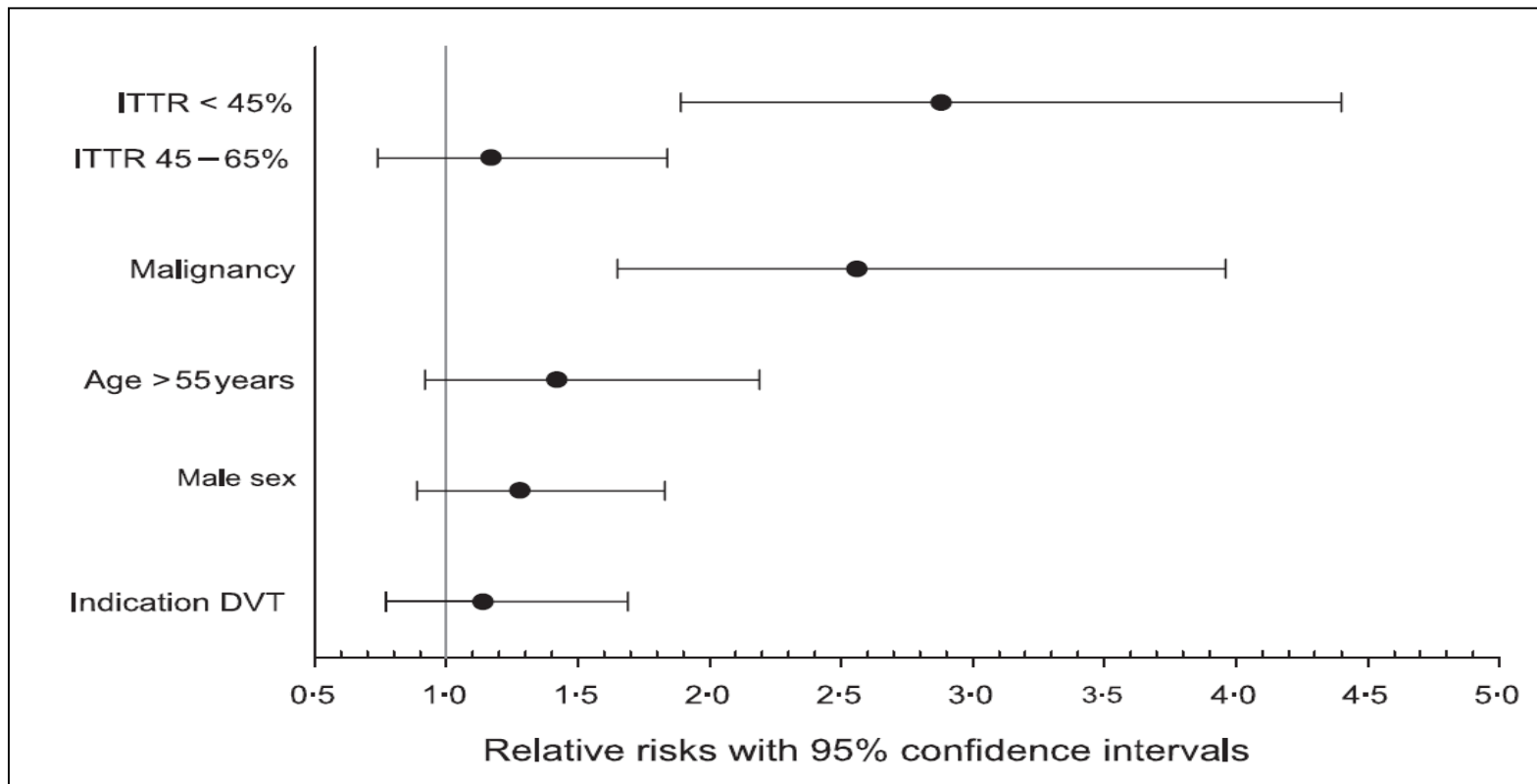


The two highest quartiles (65-80% and 80-100%) were combined.

The risk of recurrent thromboembolism was related to the **total time at which INR values were below the target range** in individual patients, rather than **incidental low INR values**.

# RR of the composite of recurrent thromboembolism and major bleeding,

for time within therapeutic range (reference group > 65%)



**Both iTTR and malignancy**

**were strong independent predictors of clinical outcome.**

# TTR and Time to risk of adverse events [ACTIVE-W]

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Country	Patients per TTR Quartile (Low to High), n				Mean TTR	Clopidogrel+Aspirin		OAC		Clopidogrel+ASA vs OAC		
	1	2	3	4		Events	%/y	Events	%/y	RR	95% CI	P
South Africa	55	43	0	0	46.3	5	8.42	8	14.94	0.57	0.19–1.75	0.33
Brazil	188	25	25	8	47.1	13	9.38	14	9.43	1.01	0.47–2.15	0.98
Russia	188	28	0	41	53.4	13	7.92	7	4.16	1.88	0.75–4.70	0.18
Poland	313	224	86	18	55.3	18	4.71	19	4.94	0.95	0.50–1.81	0.87
Belgium	4	128	9	0	58.7	11	11.91	6	6.72	1.81	0.67–4.90	0.24
United States	135	460	363	116	62.9	59	8.02	48	6.6	1.25	0.85–1.83	0.26
Netherlands	65	98	163	49	64.0	15	6.65	7	3.17	2.12	0.86–5.20	0.10
Argentina	40	79	76	106	64.5	10	6.02	10	5.9	1.03	0.43–2.48	0.94
Czech Republic	11	110	64	48	66.8	7	4.67	5	3.32	1.45	0.46–4.56	0.53
Italy	23	15	107	21	67.2	8	7.46	4	3.83	1.94	0.59–6.46	0.28
Canada	45	259	480	316	68.5	61	8.94	34	4.89	1.88	1.23–2.86	0.003
Germany	0	149	261	171	69.3	22	5.82	15	3.95	1.51	0.78–2.90	0.22
Australia	5	12	54	145	74.5	18	12.92	5	3.76	3.60	1.34–9.71	0.01
United Kingdom	2	34	59	199	74.8	12	7.03	7	3.97	1.79	0.71–4.55	0.22
Sweden	0	0	28	96	77.8	11	14.42	4	5.33	2.86	0.91–8.97	0.07

ASA indicates acetylsalicylic acid; RR, relative risk. Rows are ordered by mean TTR.

# Warfarin dosing algorithm (Maintenance)(INR 2.0-3.0)

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INR	Action
$\leq 1.5$	Increase weekly dose by <b>15%</b> ; repeat INR in <b>7-14 days</b>
<b>1.51 - 1.99</b>	If falling or low on two or more occasions, increase weekly dose by <b>10%</b> ; repeat INR in <b>7 - 14 days</b>
<b>2.00 - 3.00</b>	No change
<b>3.01 - 3.99</b>	If rising or high on two or more occasions, decrease weekly dose by <b>10%</b> ; repeat INR in <b>7 - 14 days.</b>
<b>4.00 - 4.99</b>	Hold for 1 day ; decrease weekly dose by <b>10%</b> ; repeat INR in <b>7-14 days.</b>

# Management with warfarin (example)

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Date	요일	INR	tablet strength(mg)	Mon	Tue	Wed	Thu	Fri	Sat	Sun	Weekly dose(mg)	다음 INR 검사일	% change of weekly dose	
2012-01-06	금	1.27	2					4	4	3	22	3	2012-01-09	38
2012-01-09	월	1.91	2	3	2	3	2	3	2	3	36	4	2012-01-13	64
2012-01-13	금	2.38	2	3	2	3	2	3	2	3	36	7	2012-01-20	0
2012-01-20	금	4.81	2	2	2	2	2	3	2	2	30	6	2012-01-26	-17
2012-01-26	목	1.58	2	2	3	2	3	2	3	2	34	7	2012-02-02	13
2012-02-02	목	3.4	2	2	3	2	2	2	2	2	30	7	2012-02-09	-12
2012-02-11	토	2.32	2	2	3	2	2	2	2	2	30	13	2012-02-24	0
2012-02-23	목	2.37	2	2	3	2	2	2	2	2	30	28	2012-03-22	0
2012-03-22	목	3.14	2	2	2	2	2	2	2	2	28	28	2012-04-19	-7
2012-04-19	목	2.18	2	2	2	2	2	2	2	2	28	28	2012-05-17	0
2012-05-17	목	2.12	2	2	2	2	2	2	2	2	28	28	2012-06-14	0
2012-06-14	목	1.96	2	2	2	2	3	2	2	2	30	28	2012-07-12	7
2012-07-12	목	3.04	2	2	2	2	3	2	2	2	30	28	2012-08-09	0
2012-08-09	목	2.48	2	2	2	2	3	2	2	2	30	35	2012-09-13	0
2012-09-13	목	2.31	2	2	2	2	3	2	2	2	30	35	2012-10-18	0

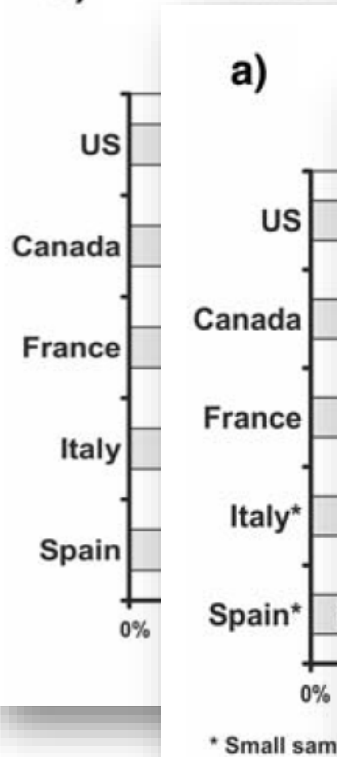
Continue ....

2016-12-26	월	2.76	2	2	1	2	2	1	2	1	22	56	2017-02-20	0
2017-02-20	월	2.43	2	2	1	2	2	1	2	1	22	56	2017-04-17	0
2017-04-19	수	2.6	2	2	1	2	2	1	2	1	22	63	2017-06-21	0
2017-06-21	수	2.58	2	2	1	2	2	1	2	1	22	56	2017-08-16	0
2017-08-16	수	2.07	2	2	1	2	2	1	2	1	22	63	2017-10-18	0
2017-10-18	수	2.06	2	2	1	2	2	1	2	1	22	56	2017-12-13	0

# Frequency of INR monitoring

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**b)** Time to next INR when last INR in range 2.0-3.0

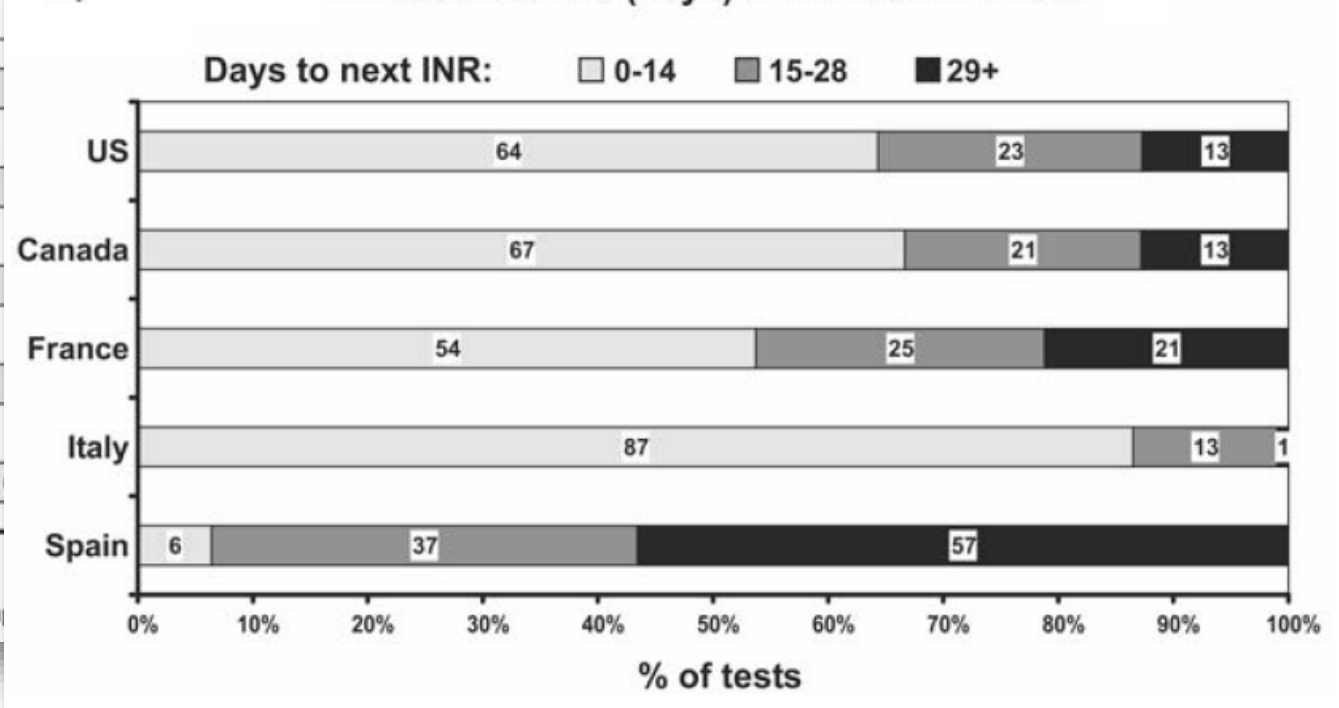


**a)** Time to next INR (days) when last INR < 1.5



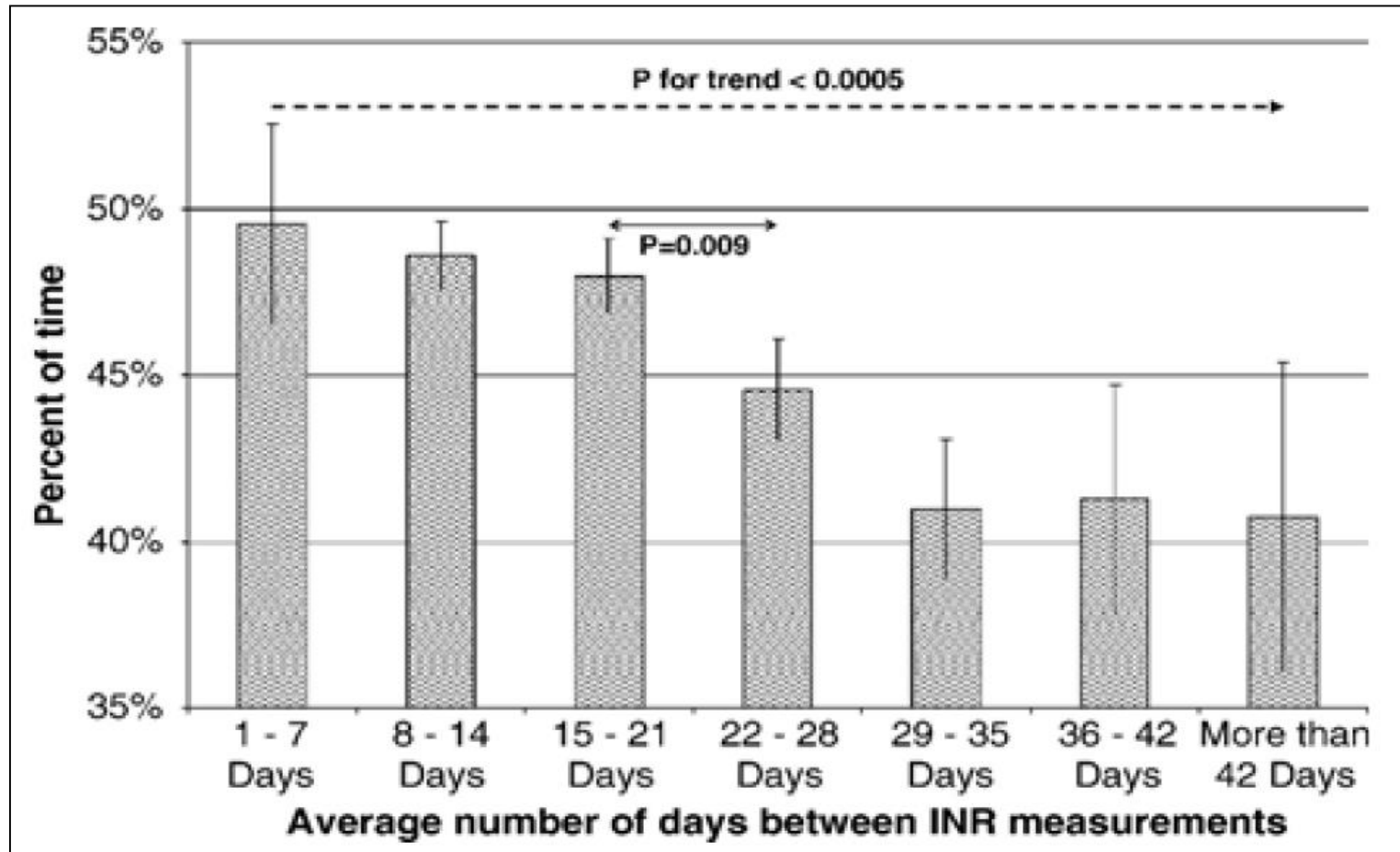
\* Small sam

**c)** Time to next INR (days) when last INR > 3.5



# Frequency of monitoring and Quality of OAC

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## 항응고제 치료시 주의해야할 식품정보 와파린

항응고제 치료를 하시는 분들은 원활한 체내 혈액응고 작용을 위해 식사 내에서 과량의 비타민K 섭취는 제한하고 영양소가 골고루 포함된 식사를 하도록 합니다.

**비타민 K**는 지용성 비타민으로 우리 몸속에서 혈액응고 및 골대사와 관련된 많은 단백질을 활성화 시키는 조효소로 작용하며 뼈를 건강하게 하며 심장 질환에 도움을 주기도 하지만, 반대로 항응고제 치료를 하시는 분들에게 있어서는 원활한 체내 혈액응고 작용을 방해할 수 있으므로 비타민 K 섭취시 주의해야 합니다.

### ★ 항응고제 치료시 주의사항

1. **비타민K 섭취량은 한국인 1일 총분 섭취 기준량 정도가 일정하게 공급되도록** 식사를 계획 합니다. (한국인 영양섭취 기준 성인남성 총분섭취량 75 $\mu$ g/일 성인여성 65 $\mu$ g/일, 한국영양학회, 2005)  
※ 본원에서 제공되는 1일 식단구성 예 참조
2. **녹색잎 채소류 중 시금치, 근대, 쑥갓, 부추, 호박잎, 미나리와 케일과 브로콜리, 양배추 등의 양채류 일부 식품에는** 비타민K가 다량 함유되어 있으므로 **섭취시 주의가** 필요합니다.  
(※ **비타민 K** 고함량 식품 분류 표 참조)
3. **해조류 중 김의 경우** 생식하기 보다는 **구워서 섭취**하는 것이 **비타민K** 섭취를 85%가량 줄일 수 있게 됩니다.  
(※ 제7차 식품성분표, 농촌자연개발 연구소, 2006년)
4. **식사 내에** 비타민K가 들어있는 모든 식품을 완전히 피할 필요는 없습니다. 다만 **과량을** 매일 섭취하거나 **주의해야할 식품들을 한 끼 식사에 동시에 구성**되지 않도록 합니다.
5. **모든 종합비타민제에는** **비타민K가** 함유되어 있으므로 **비타민제**를 추가로 섭취 하시고자 하신다면 **반드시 의료진에게** 문의하신 후 복용하도록 합니다.
6. **항응고제** 치료가 안정적으로 유지되지 않는다면 **평소** 섭취하고 있는 **식사 내용**을 상세히 기록하여 **영양사의 상담**을 받도록 합니다.
















### ★ **비타민 K** 고함량 식품의 분류(식품 100g당)

식품명	비타민K	식품명	비타민K	식품명	비타민K ( $\mu$ g)
케일	210	유채	260	쑥(생것)	340
쑥갓(생것)	250	근대(생것)	830	쑥(삶은것)	380
쑥갓(삶은것)	460	근대(삶은것)	327	비름	1,140
냉이	330	부추(삶은것)	330	녹차, 가루차	4,000
시금치(생것)	270	순무잎(생것)	340	홍차, 잎	1,500
시금치(삶은것)	320	순무잎(삶은것)	370		
호박잎(삶은것)	108	브로콜리, 생것	160	미나리	160
고비, 마른것(생것)	120	브로콜리, 삶은것	150	부추, 생것	180
양배추(생것)	78	양배추(삶은것)	76		

※ 녹차(가루차)와 홍차(잎)에는 **비타민K**가 많이 함유되어 있으나 **침출액**의 경우 아직 보고된 자료가 없으므로 **향후 연구**가 필요한 사항입니다.

\* 출처 : 식품성분표(제7차 개정판, 농촌자연개발 연구소, 2006년)

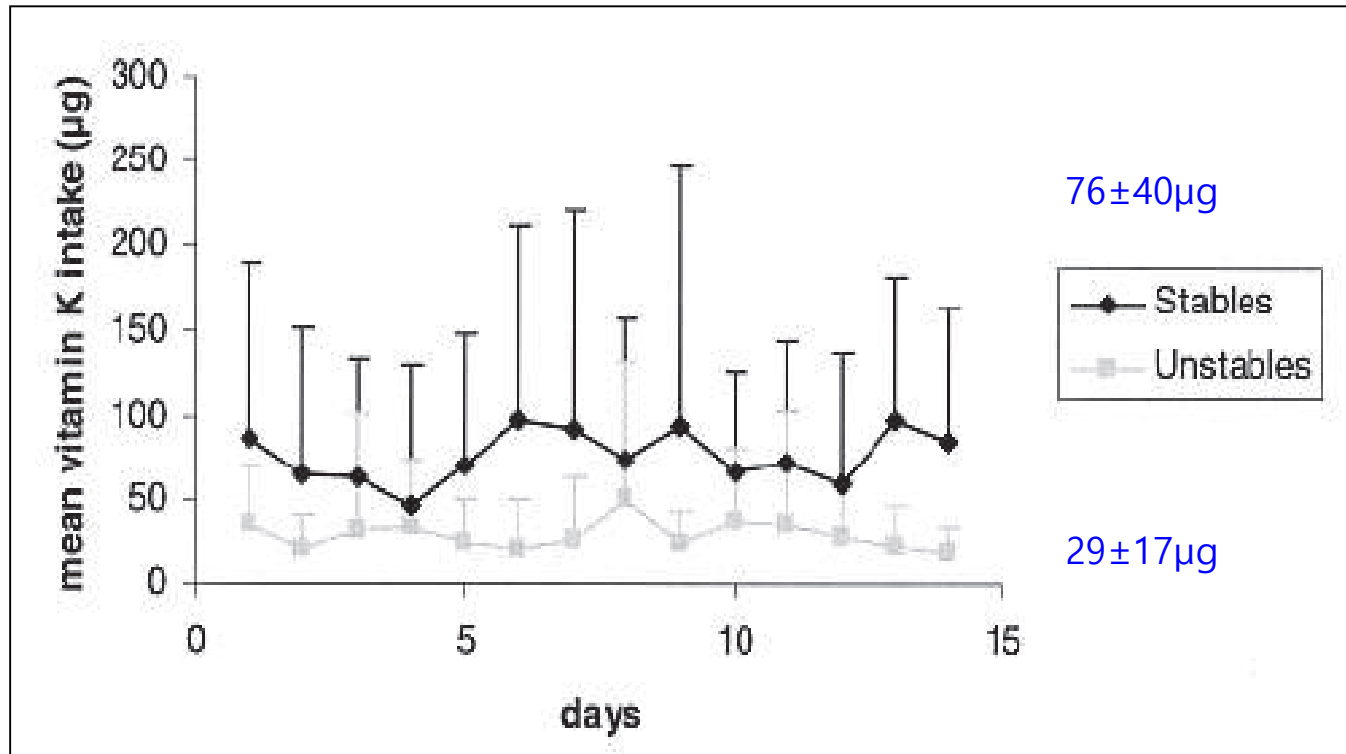
### ★ **평소 자주 섭취하게 되는** **비타민K** 함유 식품 표기(1 serving당)

식품명	식품 표기	식품명	식품 표기	식품명	식품 표기
 <b>배춧잎 70g</b> 798 $\mu$ g □	 <b>시금치나물 70g</b> 189 $\mu$ g □	 <b>미나리나물 70g</b> 112 $\mu$ g □			
 <b>근대나물 70g</b> 581 $\mu$ g □	 <b>유채나물 70g</b> 182 $\mu$ g □	 <b>브로콜리 70g</b> 112 $\mu$ g □			
 <b>순무잎 70g</b> 238 $\mu$ g □	 <b>쑥갓나물 70g</b> 175 $\mu$ g □	 <b>고비나물 70g</b> 84 $\mu$ g □			
 <b>쑥 70g</b> 238 $\mu$ g □	 <b>케일 70g</b> 147 $\mu$ g □	 <b>호박잎 70g</b> 76 $\mu$ g □			
 <b>냉이무침 70g</b> 231 $\mu$ g □	 <b>부추나물 70g</b> 126 $\mu$ g □	 <b>양배추나물 70g</b> 55 $\mu$ g □			

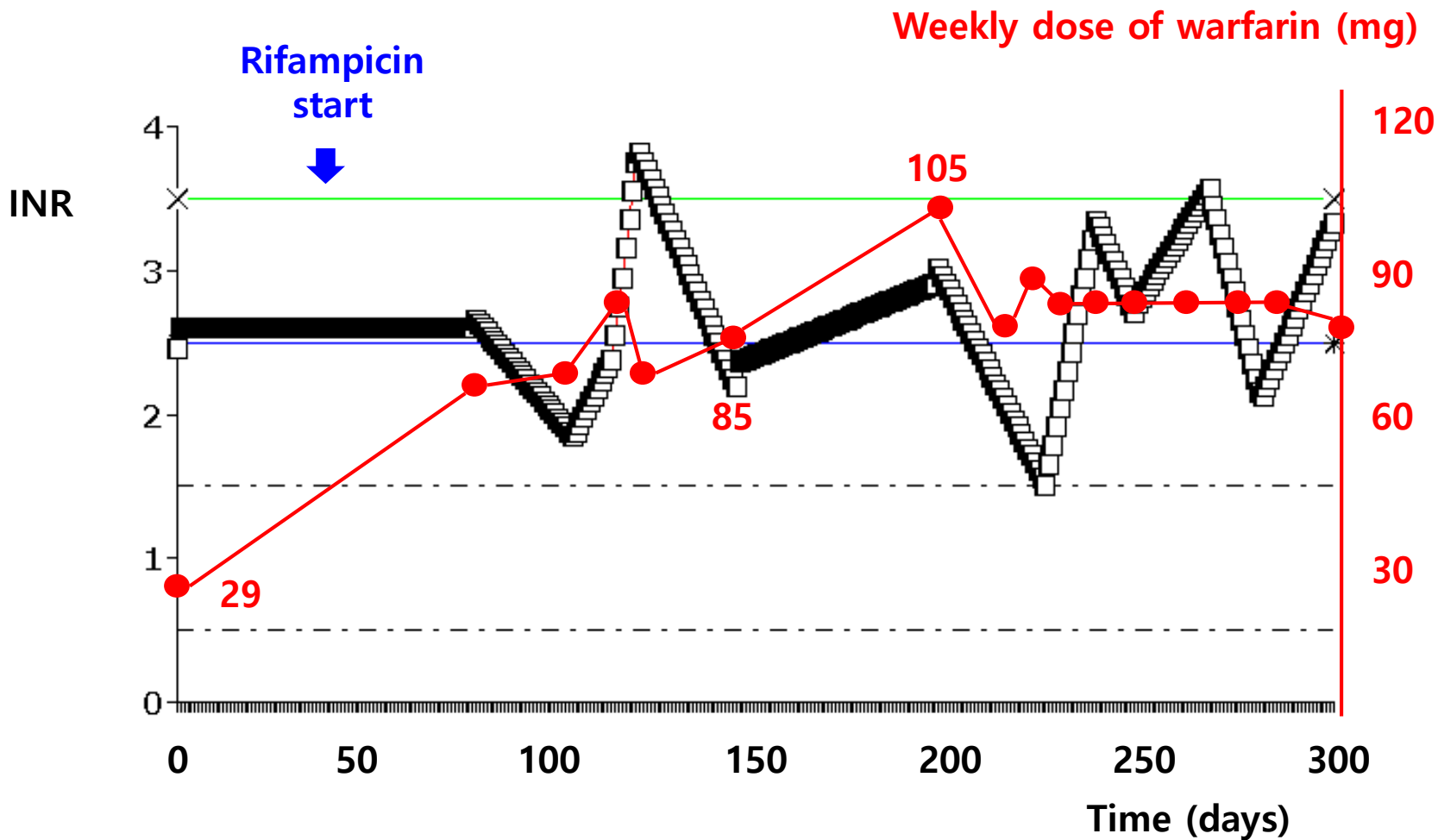
분량(g) : **가식부 조리전 무개입**

# Dietary intake of vitamin K in unstable vs stable control of OAC

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**Daily supplementation with oral vitamin K in unstable patients could lead to a more stable anticoagulation response to warfarin.**



# 증례 II

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## Rifampicin 600mg (2014.01.25.~ 10.20.)

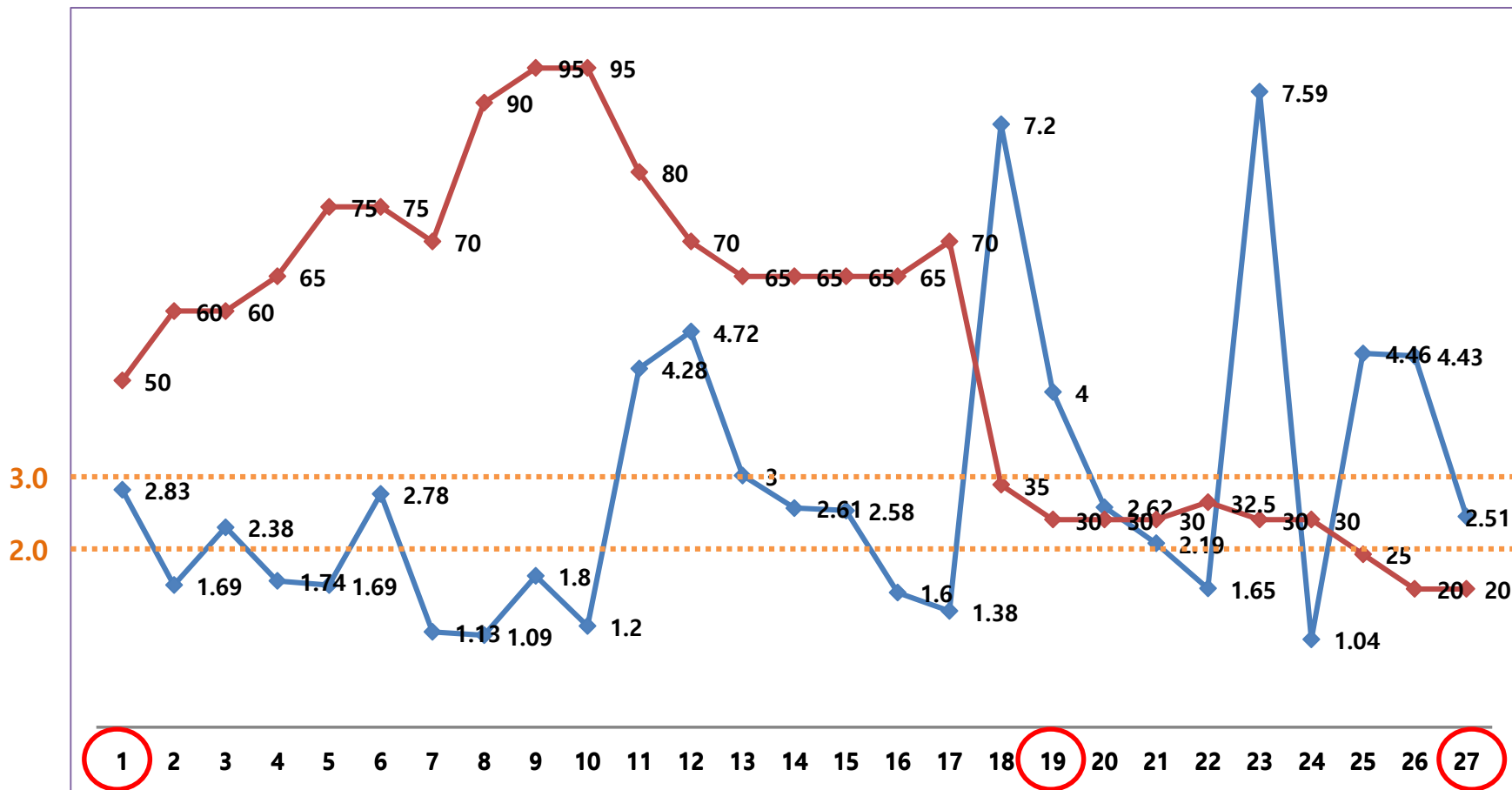


Weekly dose (mg)



INR

Outpatient management only



2014.02.07.

2014.10.20.

2015.03.25.

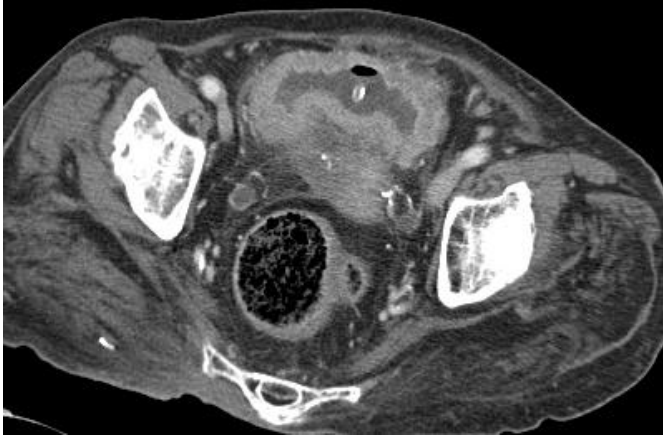
# DOACs are harmful?

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# Unmet Clinical Needs (hematuria)

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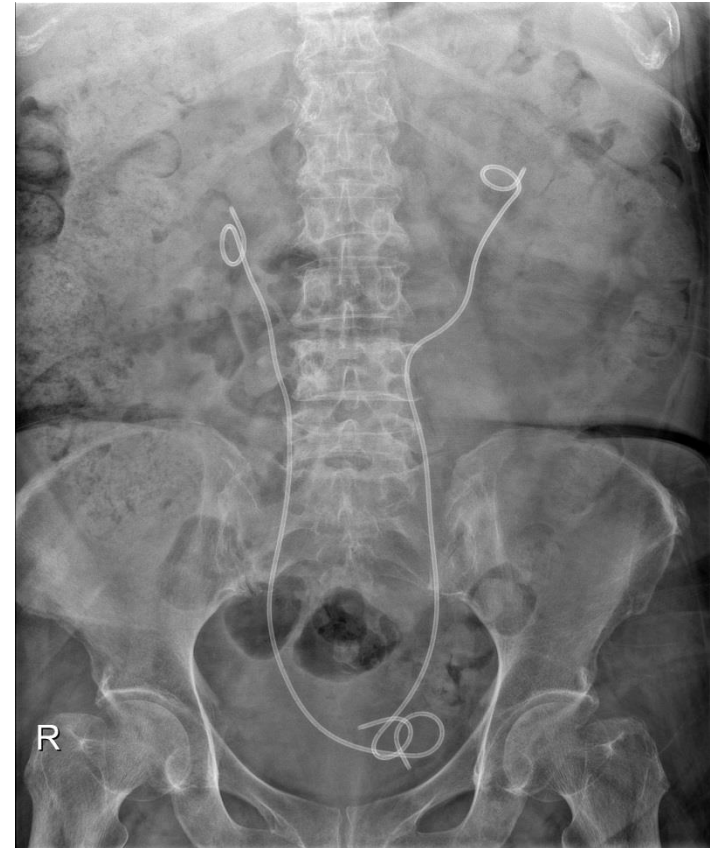
83/F, Chronic cystitis with foley catheter



68/M, Renal stone, Lt with hydronephrosis

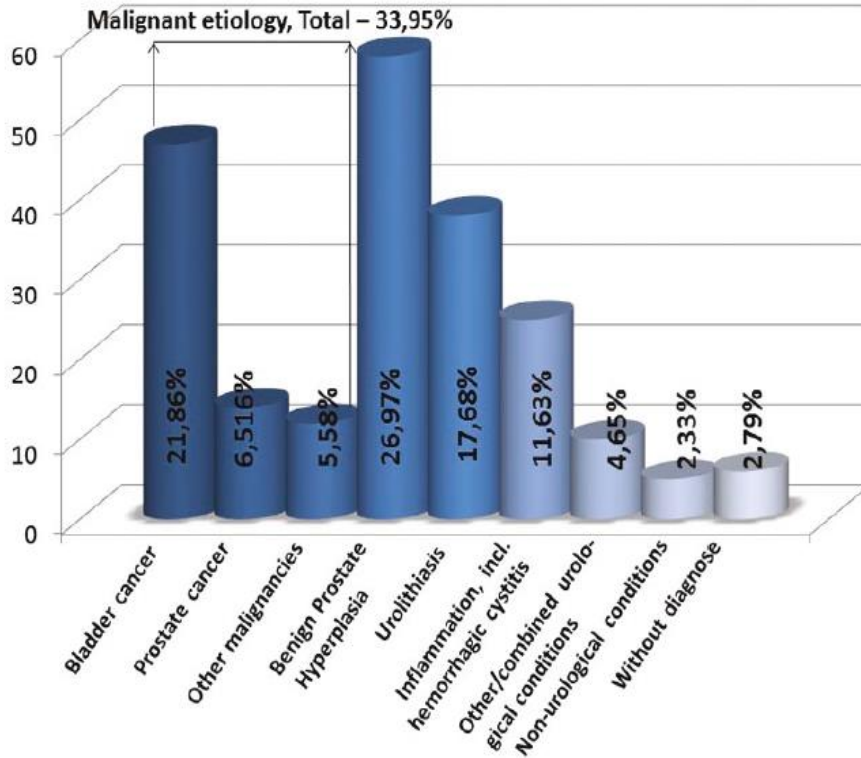


57/F, Ovarian ca with ureter invasion

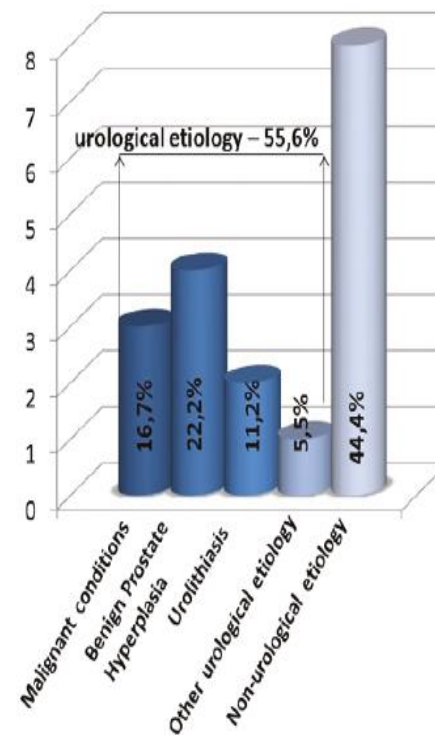


# Distribution of patients with hematuria according to etiology

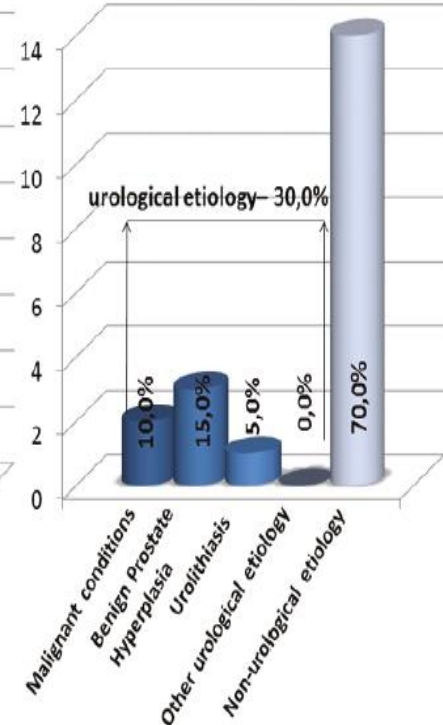
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INR < 4



INR > 4



▶ 혈뇨의 원인 진단 후 항응고제 치료 결정? 어떻게? 그럼 혈전은?

**경청해주셔서 감사합니다**

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