Respiratory Review of 2013

Pulmonary Thromboembolism

장소 : 대전컨벤션센터 2층 그랜드볼룸

시간 : 2013. 4.6(토) 10:00~10:30AM

순천향대학교 구미병원 호흡기 내과 : 황 헌 규

Pulmonary thromboembolism

- Pulmonary Thromboembolism
- Clinical Course
- Treatment of PE (ACCP 9th Guideline)
- Optimal duration of anticoagulants
- Risk of bleeding on anticoagulants
- Recurrence of VTE and D-dimer
- Dose assessment interval (every 4 weeks vs 12 weeks)
- New anticoagulants
- Dabigatran-REMEDY, RESONATE
- Rivaroxaban-EINSTEIN PE
- Insurance in Korea
- Summary

PULMONARY THROMBOEMBOLISM

Pulmonary Embolism

- VTE = DVT and/or PE
- > 80% of PE originates in deep vein of leg (상수원)
- Incidence-PE : 70 per 100,000 population
  - Mayo : during 25-year period from 1966 through 1990

Dalen JE. Chest. 1986;89(5 Suppl) : 370S-3S.

Silverstein Achives of internal medicine. 1998;158(6):585-93

Pulmonary Embolism

- Incidence : per 100,000 pop
  - VTE=143, DVT= 93, PE=50
  - Norway, between 1995 and 2001

Naess, Journal of Thrombosis and Haemostasis 2007;5(4):692-9

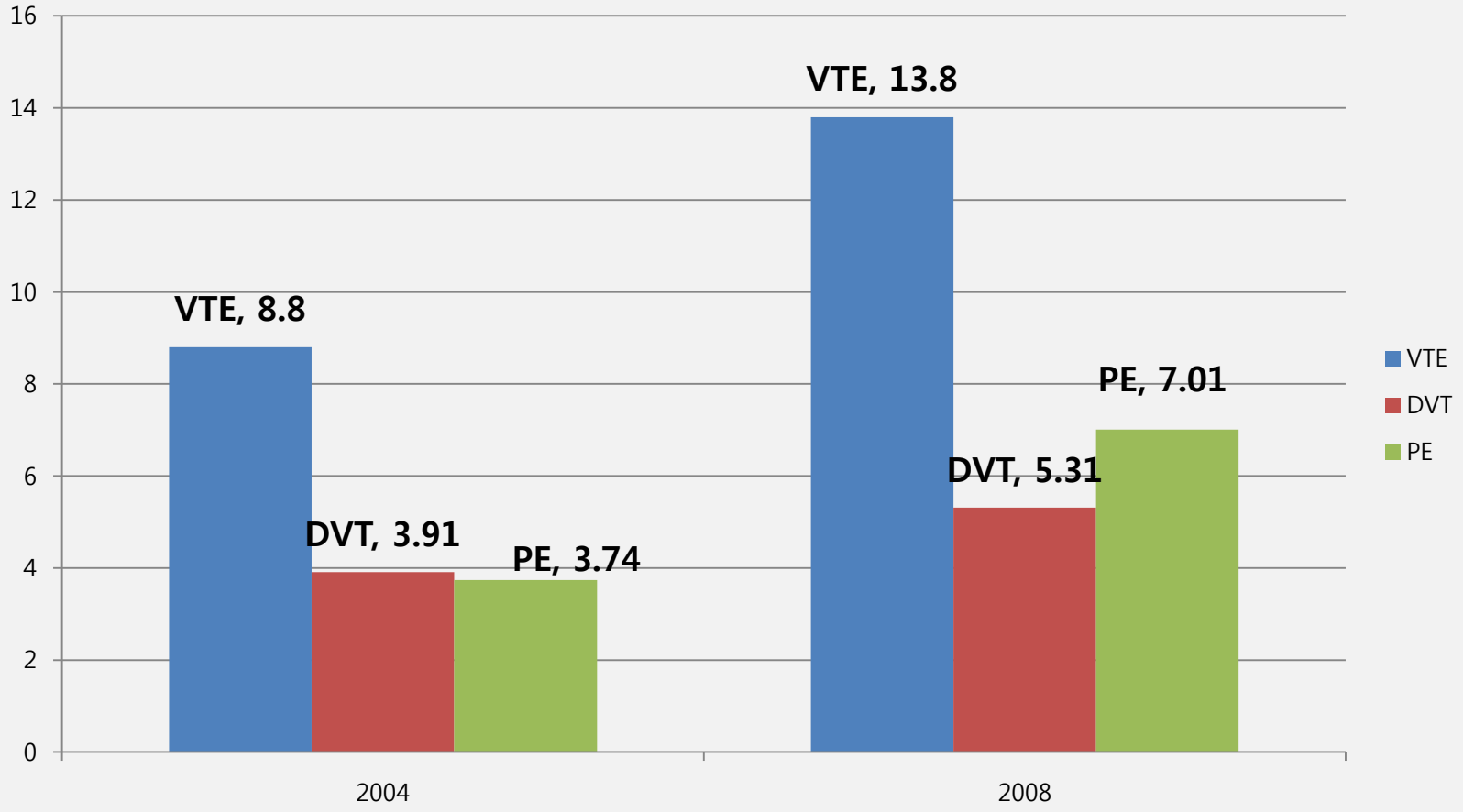
Incidence of PE in Korea

- VTE, DVT, and PE per 100,000

- 건강보험 심사평가원(심평원)
  - Korean Health Insurance Review and Assessment Service (HIRA) database

Jang et al, Journal of thrombosis and haemostasis 2011;9(1)

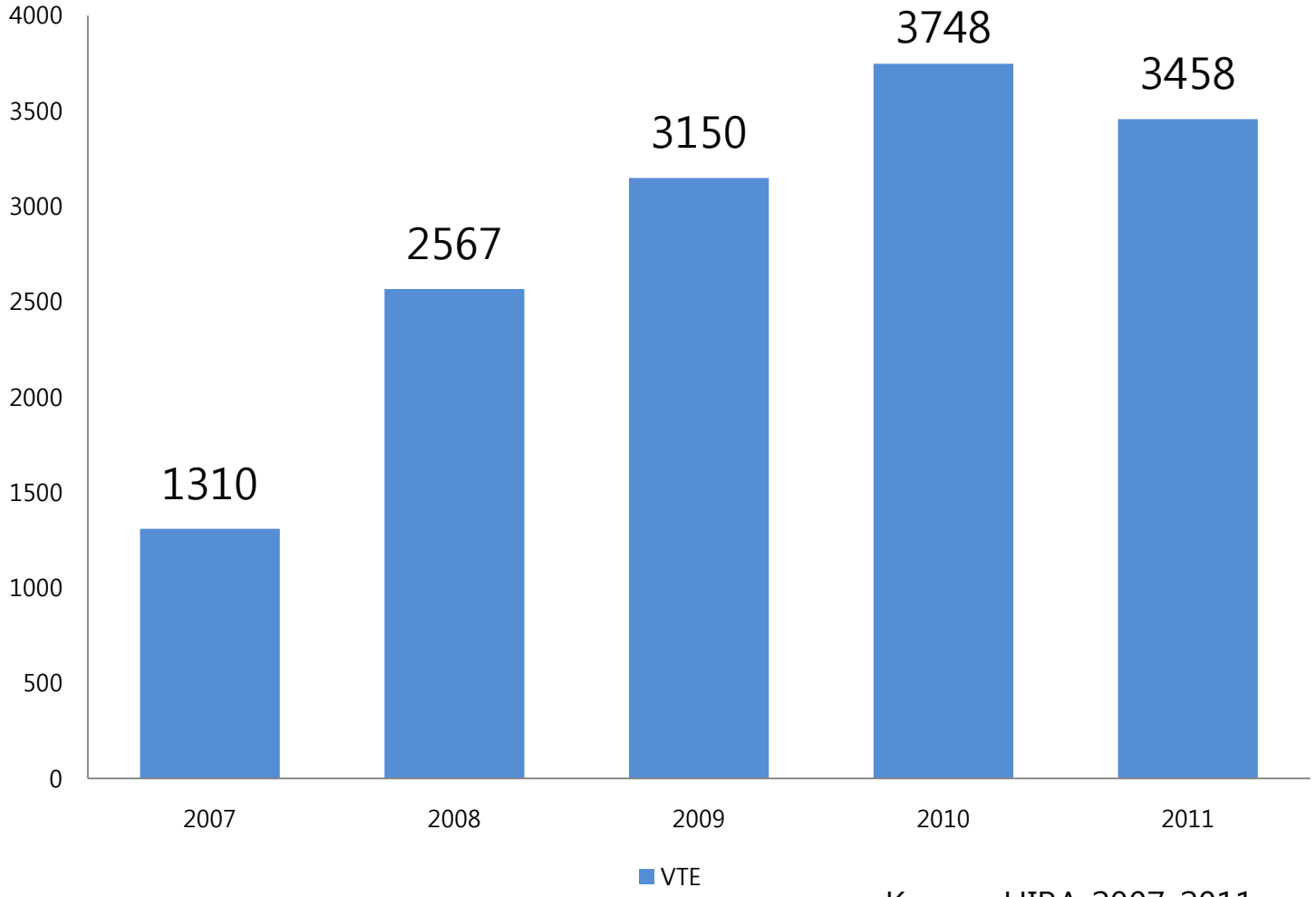
Thromboembolism in Korea



In western, incidence is 100~200 per 100,000.

Jang *J thrombo Haemost* 2011;9:85-91

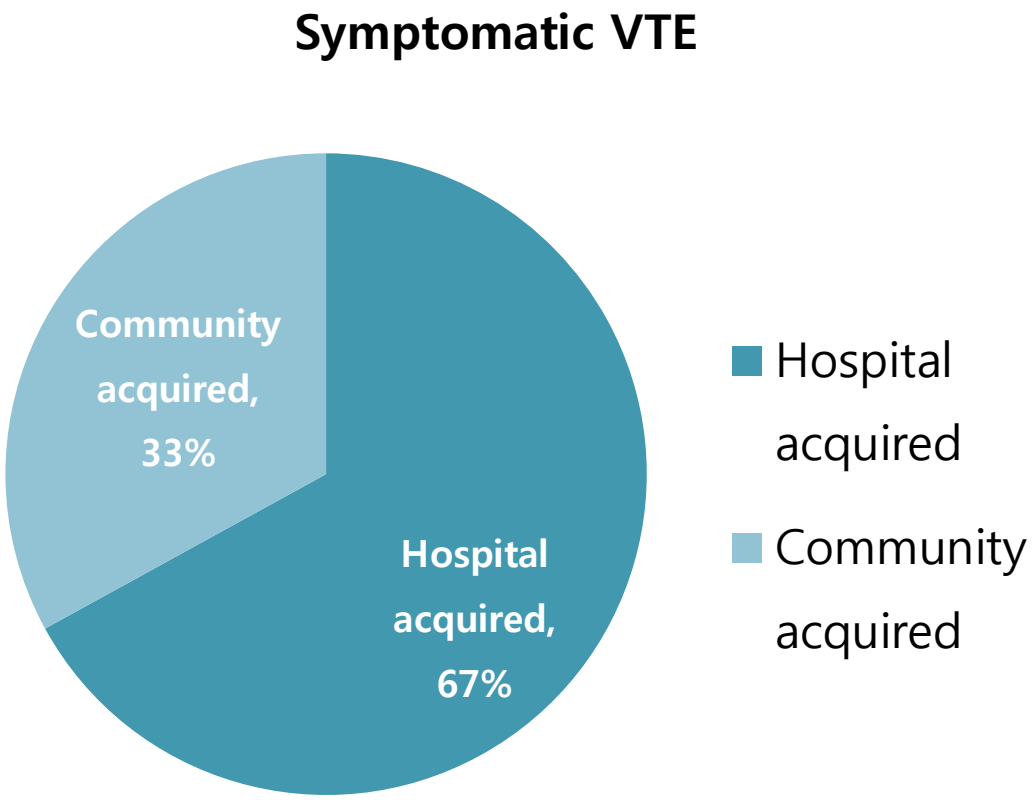
Incidence of VTE in Korea



Korean HIRA 2007-2011

CLINICAL COURSE OF VTE

Venous thromboembolism



Spencer Archives of internal medicine 2007;167(14):1471-5

Clinical Course of VTE

- 46% (Hip) , 76%(Knee) : postdischarge
- Clinical PE : in 26 to 67% of untreated proximal DVTs
- Mortality : 11% to 23%

- If treated, PE and mortality are 5% and 1%, respectively

Markel A. Seminars in vascular medicine 2005;5(1):65-74

Clinical Course of VTE

- Recurrent episode of VTE
  - PE after PE : 60%
  - PE after DVT : 20%
  - Pulmonary hypertension

Kearon et al., ACCP 9th guideline Chest 2012;141(2 Suppl):419S

Diagnosis of PE

- Embolism & DVT CT

Stein NEJM. 2006;354(22):2317-2327

- Negative D-dimer : helpful in exclusion
- False negative in >15% of pt with high probability

Kearon ACCP 8th 2008;133:454S-545S
Wells Seminars in thrombosis and hemostasis 2000;26(6):643-56
Wells. Jounal of thrombosis and thrombolysis 2006;21(1):31-40
Stin Radiology 2007;242(1):15-21

TREATMENT OF PE

Treatment of PE (ACCP 8th vs 9th)

- Initial Tx with parenteral Tx
- high clinical suspicion of acute PE
  - Tx with parenteral anticoagulants while waiting

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141

Treatment of PE (ACCP 8th vs 9th)

ACCP 8th : In patients with acute DVT, we recommend initial treatment with LMWH SC **once or twice daily**, as an outpatient if possible (Grade 1C), or as an inpatient if necessary (Grade 1A), rather than treatment with IV UFH.

ACCP 9th : In patients with acute DVT of the leg treated with LMWH, we **suggest once- over twice-daily** administration (Grade 2C) .

Kearon ACCP 8th Guideline Chest 2008. 133(6 Suppl)

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141

Treatment of PE (ACCP 8th vs 9th)

- ACCP 8th : For patients with objectively confirmed PE, we recommend short-term treatment with SC **LMWH** (**Grade 1A**), **IV UFH** (**Grade 1A**), **monitored SC UFH** (**Grade 1A**), **fixed-dose SC UFH** (Grade 1A), or SC **fondaparinux** (**Grade 1A**) rather than no such acute treatment.

- ACCP 9th : In patients with acute PE, we suggest **LMWH or fondaparinux over IV UFH** (Grade 2C for LMWH; Grade 2B for fondaparinux) and over **SC UFH** (Grade 2B for LMWH; Grade 2C for fondaparinux) **.**

Kearon ACCP 8th Guideline Chest 2008. 133(6 Suppl)

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141

Treatment of PE (ACCP 8th vs 9th)

- PE with hypotension
  - Systemic thrombolytic therapy
  - Initial Tx with IV UFH is preferred to use of SC.

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141

Treatment of PE (ACCP 8th vs 9th)

- ACCP 8th : In patients with acute PE, when a thrombolytic agent is used, we suggest **short infusion times (eg, a 2-h infusion**) over prolonged infusion times (eg, a 24-h infusion) (Grade 1B) .

  In patients with acute PE when a thrombolytic agent is used, we suggest administration **through a peripheral vein** over a pulmonary artery catheter (Grade 1B)

- ACCP 9th : Grade 2C

Kearon ACCP 8th Guideline Chest 2008. 133(6 Suppl)

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141

Treatment of PE

- IVC Filter in patient with acute PE on anticoagulants
  - It recommends **against** IVC filter(1A->1B)
  - If **contraindication** to anticoagulants, IVC filter recommended (1C->1B)

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141

Treatment of PE

- Standard Therapy
  - UFA or LMWH
  - Overlapped and followed by VKA
  - Limitation : Drug interaction, Injection, Monitor

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141

Buller Lancet 2012;379:123-9

Buller NEJM 2012;366(14):1287-97

Treatment of PE

- New oral anticoagulants(NOACs)
  - Directed against factor Xa
  - Against thrombin

Kearon ACCP Evidence-Based Clinical Practice Guidelines Chest 2012;141
Weitz Chest 2012;141(2 Suppl):e120S-51S
Mavrakanas Pharmacology & therapeutics 2011;130(1):46-58

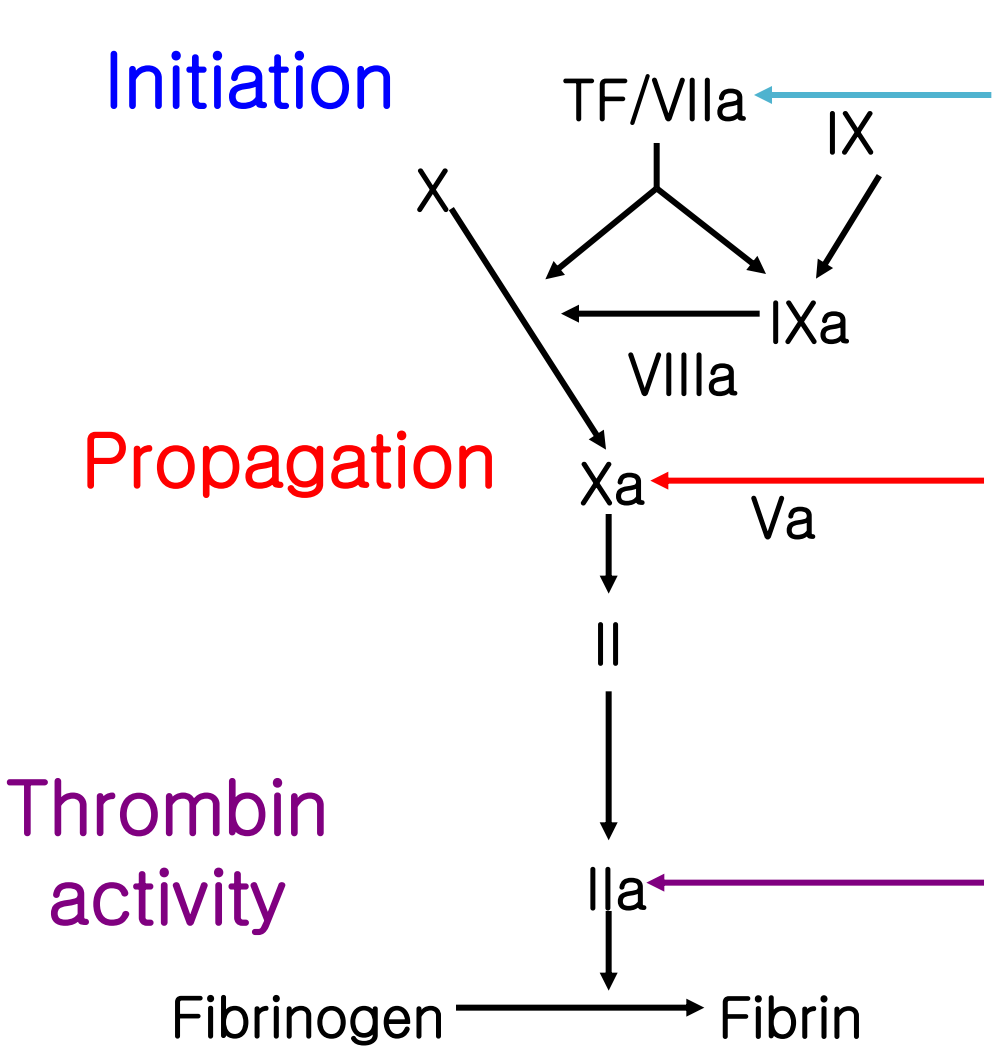
NEW ORAL ANTICOAGULANT AGENTS (NOACS)

A Brief history of anticoagulant therapy

- 1899 : Aspirin
- 1930s : **Unfractionated heparins (1936)** : antithrombin(AT) - dependent inhibition of factor Xa and IIa
- 1940s : **Vitamin K antagonists (Warfarin 1954)**: indirectly affect synthesis of multiple coagulation factors
- 1980s : **Low-molecular-weight heparin** : AT-dependent inhibition of factor Xa
- 2000s : **Direct factor IIa inhibitors (Dabigatran)**
  Direct factor Xa inhibitors (Rivaroxaban)
  Direct factor Xa inhibitors Apixaban (2011)

Alban S. Eur J Clin Invest. 2005;111:2671-2683

Novel anticoagulants and their targets

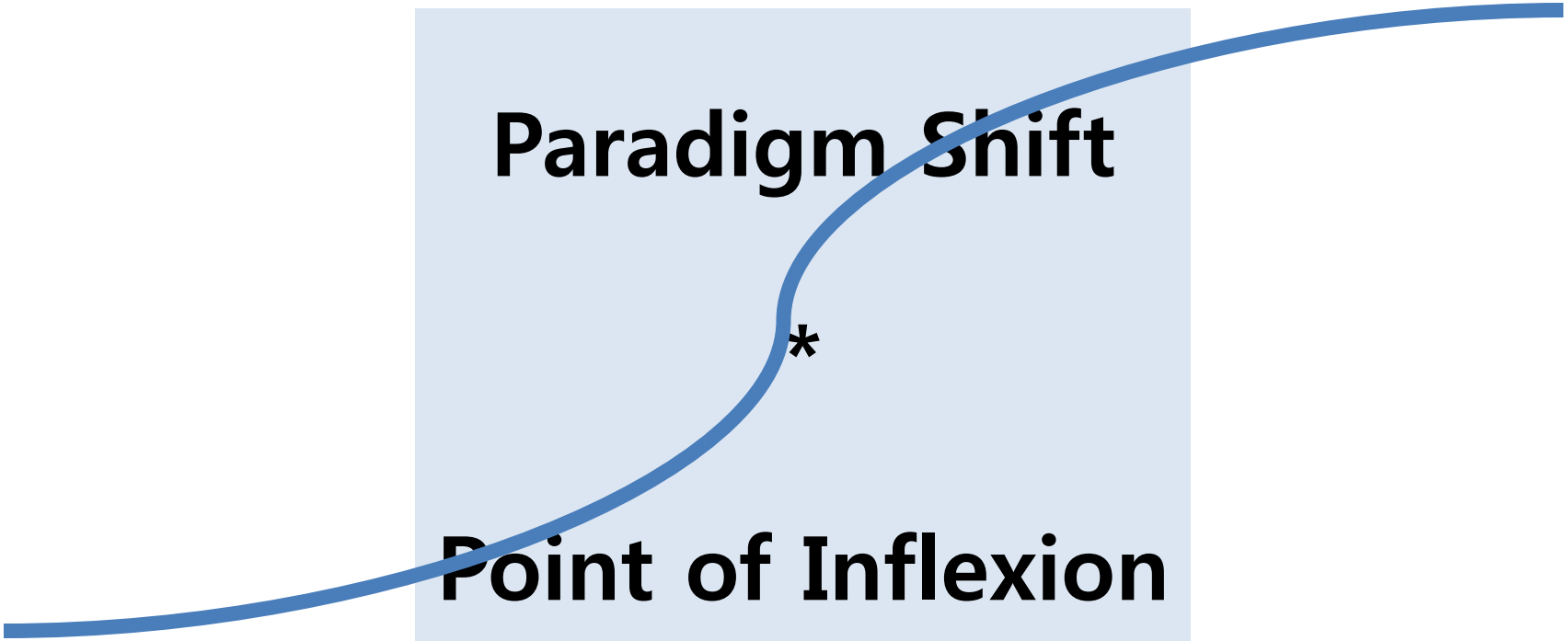


- Tissue factor pathway inhibitor (TFPI) (recombinant)
- Nematode anticoagulant peptide (NAPc2)
- Active-site-blocked Factor VIIa (FVIIai)

- Factor IXa inhibitors
- Direct Factor Xa inhibitors:
  - Rivaroxaban
  - Apixaban
  - YM150
  - DU-176b
  - Betrixaban
- Indirect Factor Xa inhibitors:
  - Fondaparinux
  - Idraparinux
  - Oral heparins
- Inhibitors of Factor VIIIa and Va
- Protein C
- Activated protein C (datrecogin alfa)
- Soluble thrombomodulin

- Hirudin
- Bivalirudin
- Argatroban
- Dabigatran
- Orally available heparins

Venous thromboembolism



Venous thromboembolism

Preventable Disease

A common cause of death in hospitalized patients

(150,000~200,000 VTE-related deaths per year in US)

Venous thromboembolism

- 호흡기내과에서 새로운 항응고제에 대한 관심은?
- PE from DVT
- DVT from OS surgery
- Prevention.
  - Pulmo-VTE-OS (consult)

OPTIMAL DURATION OF ANTICOAGULANTS

Cosideration

- Optimal duration
- Bleeding risk
- Recurrence

Duration of Anticoagulants

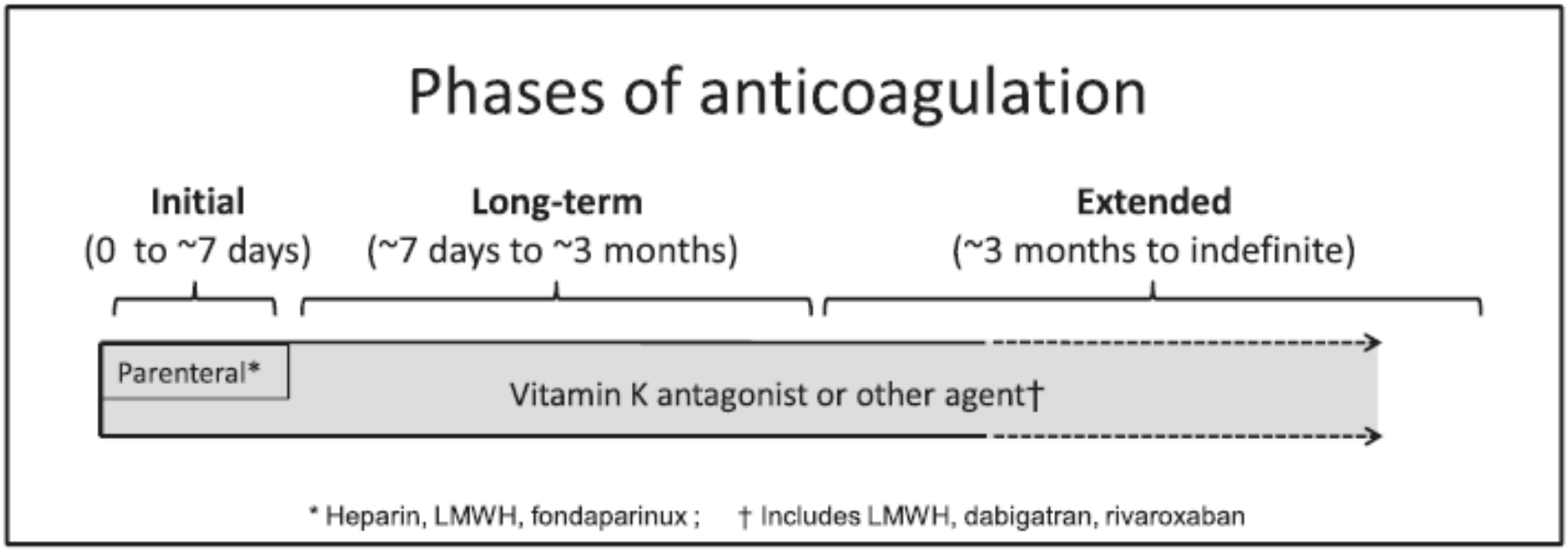


FIGURE 1. Phases of anticoagulation. LMWH = low-molecular-weight heparin.

Kearon et al., ACCP 9th Guideline. Chest 2012;141(2)(Suppl):e419S-3494S

Optimal Duration of Anticoagulants

Diagnosis	Duration if available
PE & Proximal DVT provoked by surgery	3 mo 1B
PE & Proximal DVT provoked by nonsurgical transient risk factor	3 mo 1B
Isolated distal DVT of leg provoked by surgery or nonsurgical transient risk	3 mo 1B

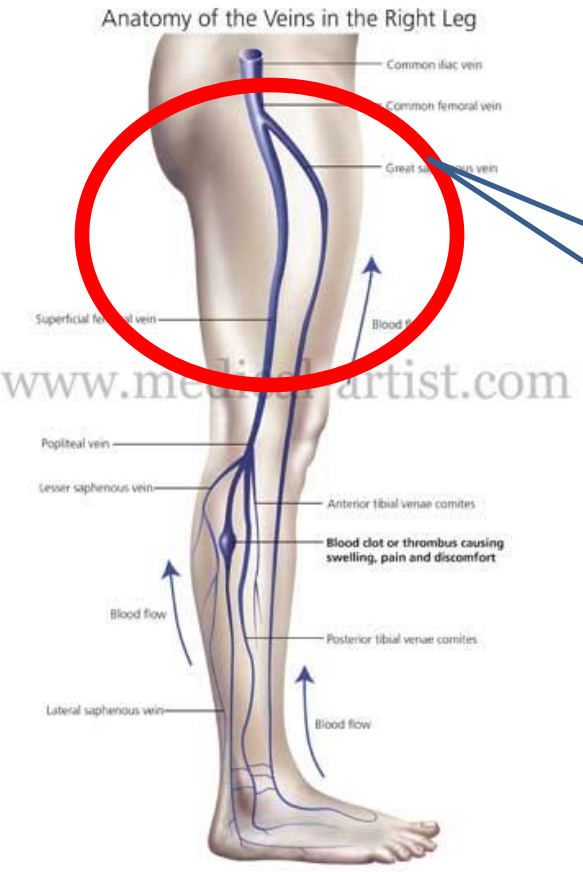
Schulman, Semin Thromb Hemost, 2013. **39**(2): p. 141-6.
Kearon ACCP 9th Guideline. Chest 2012;141(2)(Suppl):e419S-3494S

Optimal Duration of Anticoagulants

Diagnosis	Duration if available
Unprovoked PE & DVT of the Leg (isolated distal or proximal)	At least 3 mo 1B And Reassess
First VTE (**unprovoked** PE & proximal DVT of leg) with **low or moderate** bleeding risk	**Extended** (> 3mo) 2B & reassess at periodic interval
with **high** bleeding risk	3 mo 1B
First VTE (**unprovoked** distal DVT of leg) with **low or moderate** bleeding risk	3 mo 2B
with **high** bleeding risk	3 mo 1B
Second unprovoked VTE with Low or moderate risk of bleeding	**Extended (> 3mo)** **Low-1B, Moderate-2B**
with high risk of bleeding	3 mo 2B

Schulman, Semin Thromb Hemost, 2013. **39**(2): p. 141-6.
Kearon ACCP 9th Guideline. Chest 2012;141(2)(Suppl):e419S-3494S

Optimal Duration of Anticoagulants



First VTE(unprovoked PE & proximal DVT of leg) with **low or moderate** bleeding risk -> **Extended, 2B**

Schulman, Semin Thromb Hemost, 2013. **39**(2): p. 141-6.
Kearon ACCP 9th Guideline. Chest 2012;141(2)(Suppl):e419S-3494S

Risk Benefit ratio

- **High-risk** condition with **high risk** of bleeding
  - AF and high risk of ischemic stroke
  - Recurrent intracranial bleeding on anticoagulation

Schulman Seminar thrombosis and hemostasis. 2013;39(2):141-6

Risk Benefit ratio

- Low-risk condition with **high risk** of bleeding
  - Proximal, unprovoked DVT
    - **10% recurrence rate** of VTE **one year** after stopping
  - Recurrent, transfusion-required, **lower GI bleeds**
  - GI bleeding:2/3 of major bleeding on anticoagulants

Schulman Seminar thrombosis and hemostasis. 2013;39(2):141-6

Risk Benefit ratio

- **Low-risk** condition with **low risk** of bleeding
  - 60-year-old man
  - First unprovoked DVT
  - After 3 months of treatment
  - Risk of fatal PE : between 0.19 and 0.49% per year
  - Risk of recurrence : 10% the first year after stopping
  - Bleeding risk during extended Tx with warfarin 0.9 to 1.4% per year

Schulman Seminar thrombosis and hemostasis. 2013;39(2):141-6

Risk Benefit ratio

- **Very low-risk** condition
- Distal DVT and a transient and removable risk factors
- Surgery
- Risk of recurrence **: 1% per year** during 6 years of F/U

Schulman Seminar thrombosis and hemostasis. 2013;39(2):141-6

Risk of Bleeding

- Risk Indicators
  - ***Old age***
  - ***Renal dysfunction***
  - Recent history of major bleeding,
  - Previous stroke,
  - Anemia
  - Ethanol abuse

Schulman Seminar thrombosis and hemostasis. 2013;39(2):141-6
Loewen et al. Annals of hematology. 2011;90(10):1191-1200
Schulman Submitted to Circulation. on Feb, 2013

Risk of Bleeding

- Clinical prediction rules(CPRs)
  - For estimating bleeding risk in patients on oral anticoagulant therapy
- New CPRs
  - "RIETE"
  - "**HAS-BLED**"
  - Modified outpatient bleeding risk index (mOBRI)
  - Weak predictive accuracy
  - Not recommended for routine use in practice

Dahri Thromb Haemost. 2007;98(5):980-7

Loewen et al. Annals of hematology. 2011;90(10):1191-1200

HAS-BLED Score

	Clinical Characteristic	Score
H	Hypertension	1
A	Abnormal renal or liver function (1 each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly age	1
D	Drugs or alcohol (1 each)	1 or 2
	Maximum Score	9

Hypertension: SBP > 160 mmHg; Abnormal renal function: Chronic dialysis, renal transplant, serum creatinine ≥ 200µmol/L; Abnormal liver function: Chronic hepatitis, bilirubin > 2x upper limit of normal (ULN) in association with AST/ALT/ALP > 3 x ULN; Bleeding: Previous history, predisposition; Labile INRs: unstable/high INRs, in therapeutic range < 60%; Age > 65 years; Drugs/alcohol: Concomitant use of antiplatelet agents, non-steroidal anti-inflammatory drugs, etc.

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

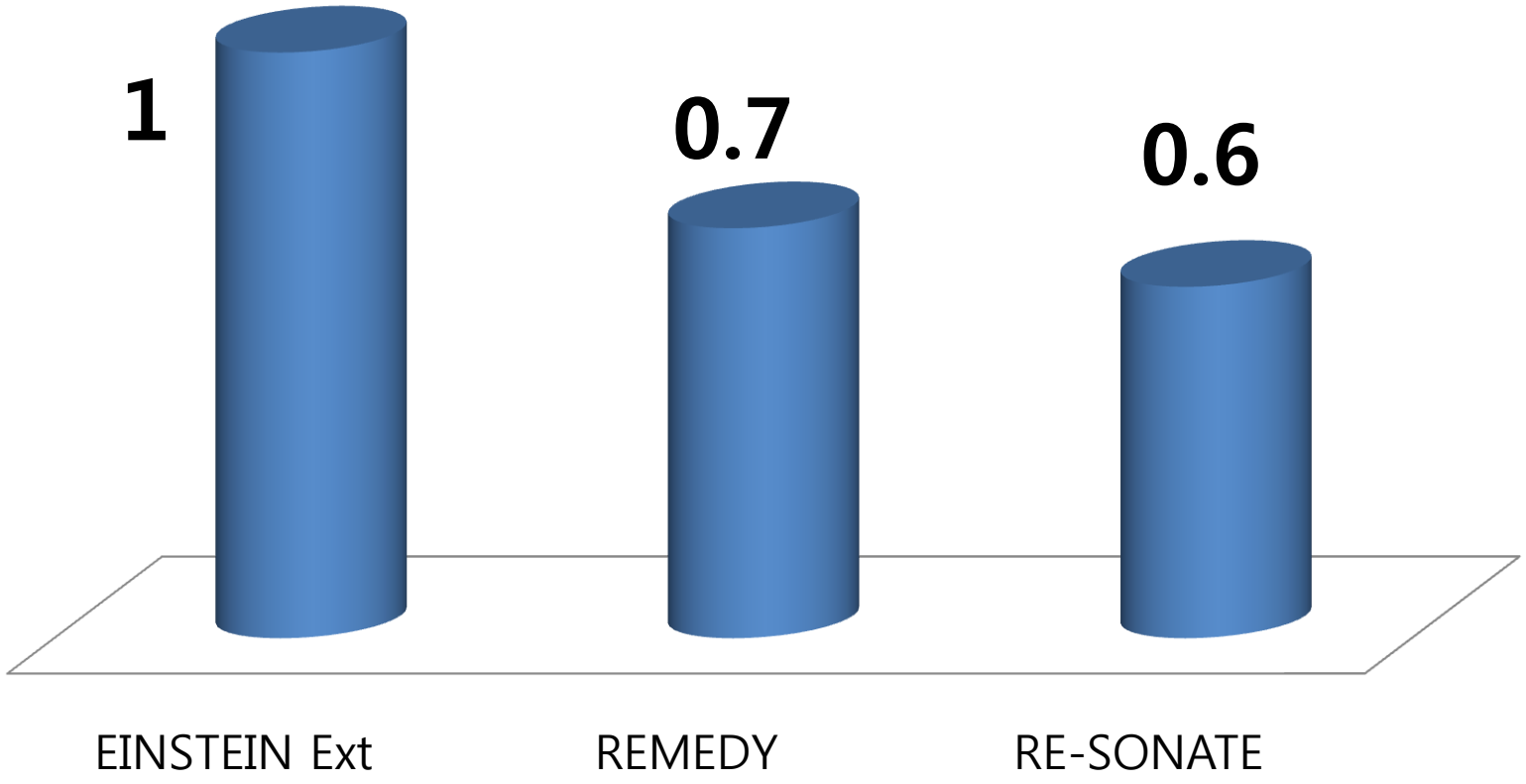
Risk of Bleeding

- "HAS-BLED"
  - Score >= 3 **; High risk**
  - Weak predictive accuracy
  - Not recommended for routine use in practice

Dahri Thromb Haemost. 2007;98(5):980-7

Loewen et al. Annals of hematology. 2011;90(10):1191-1200

Annualized risk of major bleeding of extended treatment mostly beyond the first 6 months



Management of major bleeding during Tx with dabigatran or warfarin

- Pooled analysis with 5 long-term phase III trials
- RE-LY, RE-COVER I, II, RE-MEDY, RE-SONATE
- 27,419 patients
- 1,034 individuals with 1,121 major bleed

- Pt with major bleeding on **dabigatran**
  - **Lower Ccr, older, shorter stay in ICU, lower mortality**

Schulman Submitted to Circulation. on Feb, 2013

D-DIMER & RECURRENCE OF VTE

Recurrence of VTE with anticoagulation

- Recurrence rate : 1.6~2.7 %

  Buller NEJM 2007;357(11):1094-104

- Recurrent VTE with rehospitalization
  - 50% of events in the first 3 months

Prandoni Annals of internal medicine 1996;125(1):1-7

Prandoni Blood. 2002;100(10):3484-8

D-dimer & Recurrence of VTE

- Annual risk of recurrent VTE
- Meta-analysis of seven studies
- Negative, 1-month D-dimer
- 3.5% (95% CI, 2.7 to 4.3)

Verhovse Annals of internal medicine 2008;149(7):481-90
Schulman Seminars in thrombosis and hemostasis 2013;39(2):141-6
Schulman Seminar in thrombosis and hemostasis. 2012;38(1):7-15

D-dimer & Recurrence of VTE

- **PROLONG** study
  - At least 3 months of anticoagulation
  - **Annualized risk of recurrence**
    - If D-dimer was negative at 1m after withholding warfarin, risk is **6.2%**
    - If D-dimer test was positive, risk was **15.0%**

Palareti NEJM. 2006;355(17):1780-9

D-dimer & Recurrence of VTE

- "DASH" rule
- 1880 Patients with unprovoked VTE
- For > 3 m with VKA
- To predict recurrence of VTE
- **1-month D-dimer, age, sex, hormone Tx**
- ROC area = 0.71

Tosetto Journal of thrombosis and haemostasis. 2012;10(6):1019-25

"DASH" rule

Characteristic	Score
D-dimer abnormal 30 d after stopping anticoagulant therapy	+2
Age <= 50	+1
Sex: male	+1
Hormone-use provoked VTE	-2
Final score	Annual risk (95% CI)
<= 1	3.1% (2.3–3.9)
2	6.4% (4.8–7.9)
>= 3	12.3% (9.9–14.7)

Tosetto Journal of thrombosis and haemostasis. 2012;10(6):1019–25
Schulman Seminars in thrombosis and hemostasis. 2013;39(2):141-6

“DASH” rule

- After Tx with VKA for at least 3 m
- Predict recurrence risk
- If a score <=1, low risk

- **Life-long anticoagulation** can be avoided in **half** of patients.

Tosetto Journal of thrombosis and haemostasis. 2012;10(6):1019-25

WARFAIN DOSE ASSESSMENTS EVERY 4 WEEKS VS 12 WEEKS

INR monitoring & Dose assessment

- ACCP : maximum interval of **4 weeks**
- 1998 British guideline
  - PT monitoring up to every **12 weeks** for **very stable patient**

Guidelines British journal of haematology 1998;101(2):374-87

INR monitoring & Dose assessment

- Recent Study
  - single center randomized phase II clincal trial
  - Comparison of every-12 weeks to every 4 weeks
  - **Noninferior** with respect to TTR
    - 74.1% vs 71.6
    - Within noninferiority margin of 7.5%
    - P-0.019

Schulman Annals of internal medicine 2011;155(10):653-9

NEW ORAL ANTICOAGULANT AGENTS (NOACS)

New Oral Anticoagulant Agents (NOACs)

- Dabigatran (Pradax)
- Apixaban
- Rivaroxaban (Xarelto)
- Fundaparinux

Warfarin vs New Agent

`	Warfarin	Dabigatran(Pradax)
Onset	Slow	Rapid
Monitoring	INR	No
Drug Interaction	Codarone, Rifampin, Antibiotics, etc	No major interaction
Dietary interaction	Vitamin K	No
Antidote	Vitamin K	No

Phase III Randomized Controlled Trials of New Anticoagulants for Indications Other Than VTE Prevention

Anticoagulant	Treatment of VTE Secondary Prevention	ACS	Prevention of stroke in patient with AF
Dabigatran etexilate vs VKA	RE-COVER I (2564) 2009년		RE-LY (18,113)
	RE-COVER II (2500)		RELY-ABLE (6000)
	RE-MEDY (2400) Published on Feb 2013		
	RE-SONATE (1800) Published on Feb 2013		
Rivaroxaban vs VKA	EINSTEIN-DVT (2900)	ATLAS (16 000)	Japanese AF (1280)
	EINSTEIN-PE (3300)		ROCKET-AF (14 000)
	EINSTEIN-Extension (1065)		

Eikelboom, *Circulation*. 2010;121:1523-1532

RE-COVER I II, RE-MEDY, RE-SONATE STUDY

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Extended Use of Dabigatran, Warfarin, or Placebo in Venous Thromboembolism

Sam Schulman, M.D., Ph.D., Clive Kearon, M.D.,
Ajay K. Kakkar, M.B., B.S., Ph.D., Sebastian Schellong, M.D.,
Henry Eriksson, M.D., Ph.D., David Baanstra, M.Sc.,
Anne Mathilde Kvamme, M.Sc.Pharm., Jeffrey Friedman, M.D.,
Patrick Mismetti, M.D., and Samuel Z. Goldhaber, M.D.,
for the RE-MEDY and the RE-SONATE Trials Investigators*

N ENGL J MED 368;8 NEJM.ORG FEBRUARY 21, 2013

RE-MEDY Study

- 2007-2009
- After completion of at least 3 months (**3-12 mo**) in RE-COVER I , II trial or Tx with approved agent
- Extended Secondary prevention (6 to 36 months)
- Additional informed consent.
- Dabigatran(**150mg** bid) vs **Warfarin (Active control group)**
- Submitted in late 2011
- Published on Feb 2013

Dabigatran 150mg bid	Warfarin
N = 506 N = 1430	N = 541 N = 1426

N Eng J med 361;24, p.2345
Schulman NEJM 2013;368(8):709-718

RE-MEDY Study

- Efficacy (Recurrent VTE)
  - 26 events (1.8%) vs 18 events (1.3) with warfarin
  - Noninferior (95% CI 0.78 to 2.64; p=0.01)

- Safety
  - 13 (0.9%) vs 25 (1.8%) (HR 0.52; 95% CI, 0.27 to 1.02)
  - Fewer major bleeding and significantly few CLNMB

N Eng J med 361;24, p.2345
Schulman NEJM 2013;368(8):709-718

RE-SONATE Study

- 2009-2010
- Long term prevention of recurrent symptomatic VTE
- Dabigatran vs Placebo (Placebo control)
- Phase III, multicentre, randomized, double-blind, event driven
- 6 months treatment
- In patient with confirmed symptomatic PE or proximal DVT treated for at least 3mo (6-13months, 200~400 days)
- Submitted in late 2011
- Published in Feb 2013.

Schulman NEJM 2013;368(8):709-718

RE-SONATE Study

- Efficacy (Recurrent VTE)
  - Significantly reduced the recurrent and fatal VTE
  - 3 of 681 (0.4%) vs 37of 662 (5.6%) in placebo group
  - HR, 0.08; 95% CI, 0.02 to 0.25; p<0.001)

- Safety
  - Significantly higher risk of major or CRNMB
  - Major bleeding 2 (0.3%) vs 0 in placebo group
  - CRNMB 36 (5.3%) vs 12 (1.8%) in placebo group
  - HR, 2.92; 95% CI, 1.52 to 5.60)

Schulman NEJM 2013;368(8):709-718

Acute coronary syndrome

- RE-LY study for atrial fibrillation
  - Higher risk of acute coronary syndrome with dabigatran
  - Further Analysis : no significant

Connolly NJEM 2010;363:1875-6
Hohnloser Circulation 2012;125:669-76
Schulman NEJM 2013;368(8):709-718

- Meta-analysis of seven noninferiority trials
  - Significantly higer risk of MI or acute coronary syndrome with dabigatran

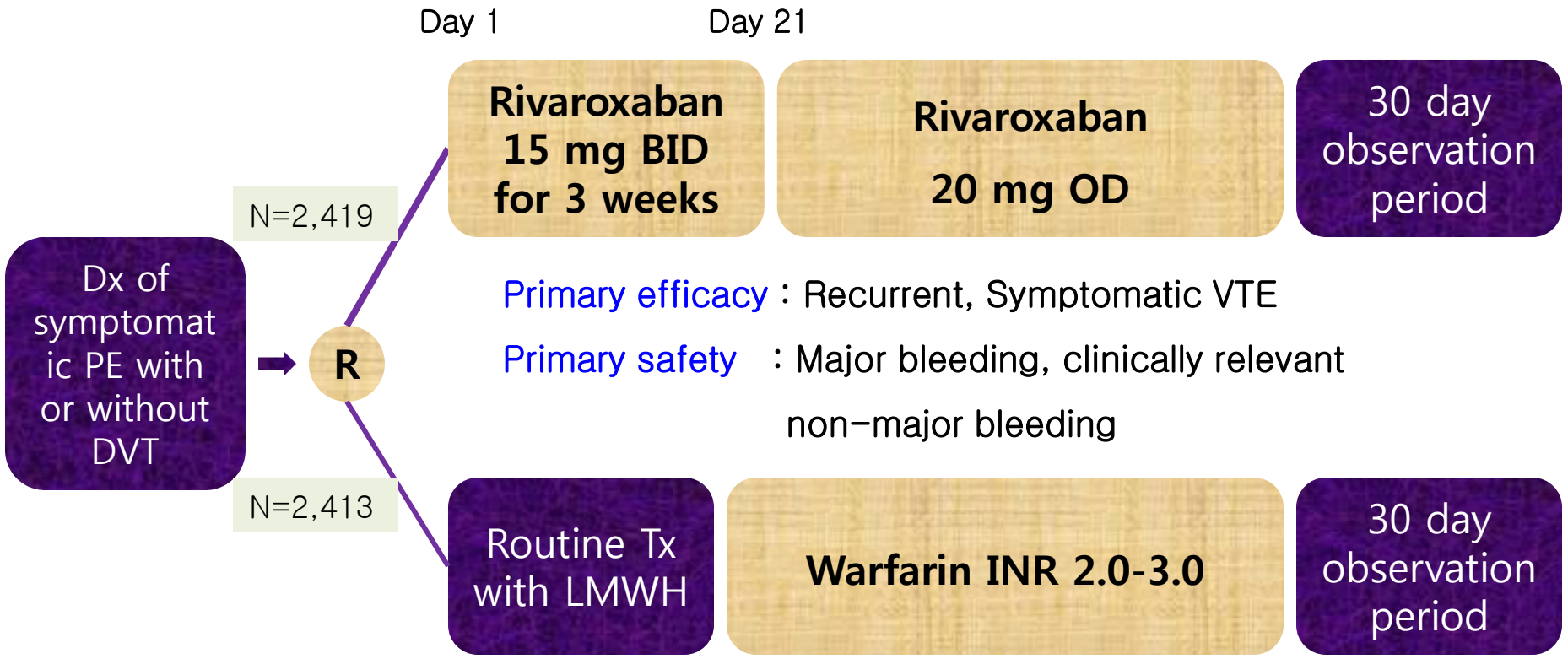
Uchino Arch Intern Med 2012;172:397-402

EINSTEIN STUDY DVT, EXT, PE

EINSTEIN-PE study design

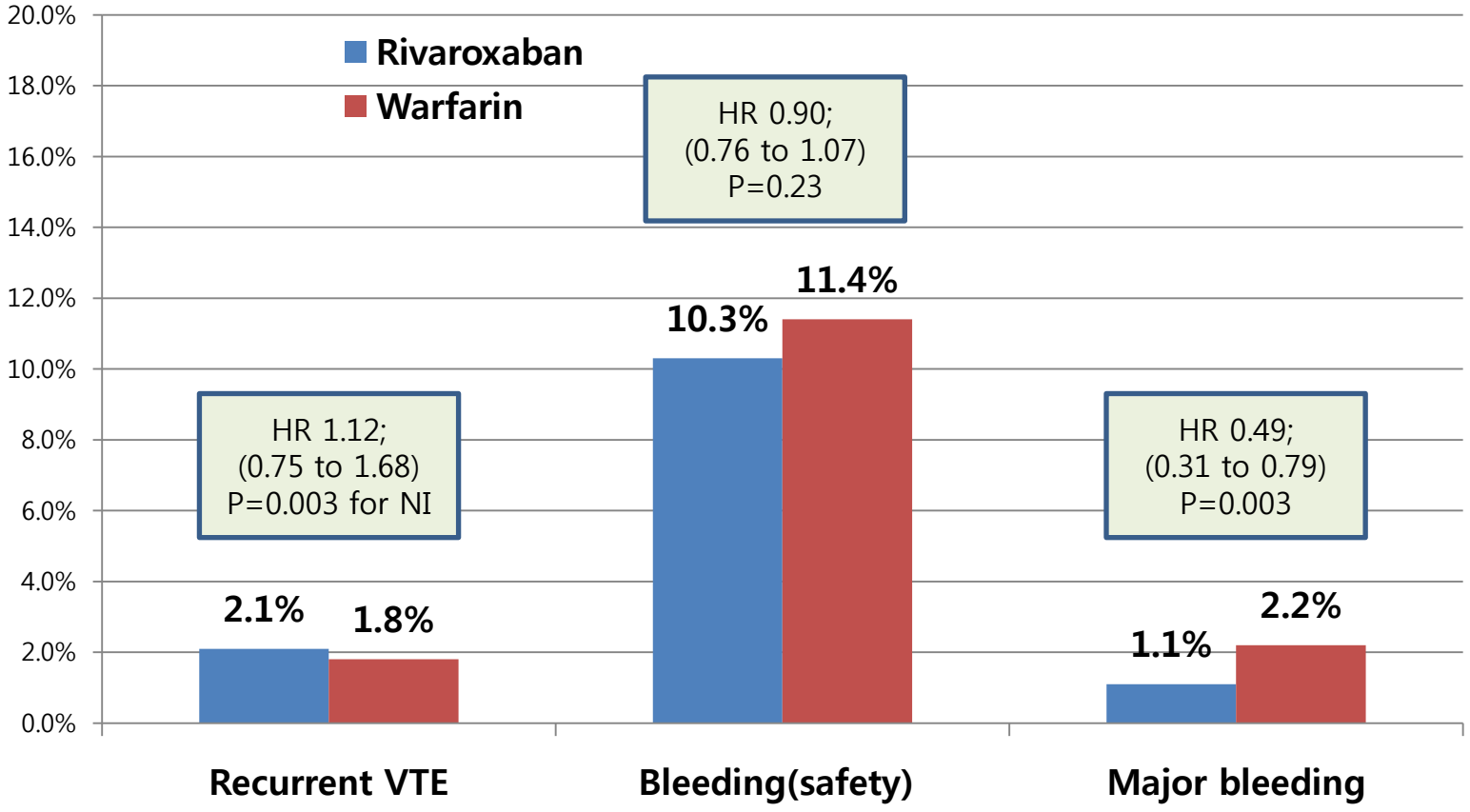
4832 pts : Rivaroxaban vs Warfarin

From March 2007 through Mar 2011 , Published on April, 2012
Acute symptomatic PE with or w/o DVT
Pre-defined treatment period: 3, 6 or 12 ,



N Engl J Med 2012 366: 1287 – 1297

EINSTEIN-PE Study



N Engl J Med 2012 366: 1287 – 1297

Demographics of EINSTEIN-PE

Limited: **≤25% of vasculature of a single lobe**	309 (12.8)	299 (12.4)
Intermediate	1392 (57.5)	1424 (59.0)
Extensive: **multiple lobes and >25% of entire pulmonary** vasculature	597 (24.7)	576 (23.9)
Not assessable	121 (5.0)	114 (4.7)
Concurrent symptomatic deep-vein thrombosis — no. (%)	606 (25.1)	590 (24.5)
Hospitalized — no. (%)	2156 (89.1)	2160 (89.5)
Admitted to intensive care unit — no. (%)	311 (12.9)	289 (12.0)
Time from onset of symptoms to randomization — days		
Median	4.0	4.0
Interquartile range	2.0–8.0	2.0–9.0
Cause of pulmonary embolism — no. (%)†		
Unprovoked	1566 (64.7)	1551 (64.3)
Recent surgery or trauma	415 (17.2)	398 (16.5)
Immobilization	384 (15.9)	380 (15.7)
Estrogen therapy	207 (8.6)	223 (9.2)
Active cancer	114 (4.7)	109 (4.5)

EINSTEIN-PE

- Efficacy & Safety : noninferior

Buller NEJM 2012;366(14):1287-97
Buller Blood 2008;112(6):2242-7
Bauersachs NEJM 2010;363(26):2499-510

EINSTEIN-PE

- Same dose of rivaroxaban without monitoring ?
  - Subgroup analysis
  - Regardless of age, sex, obesity, renal function, extent of PE

Buller NEJM 2012;366(14):1287-97

Is there no remaining role for warfarin?

- Severe renal impairment (e.g. CrCl <30 ml/min)
- Patients who require treatment with a drug that is contraindicated
- Another indication for warfarin (e.g., mechanical heart valve)
- Cannot afford one of the new the new oral anticoagulants
- Skip
- Adherence
- Antidote

Korea going to Aged Society

- **Aging** society **as of 1999**
  - More than **7%** (> 65 year old)
- **Aged** society **in 2020**
  - More than **15%**

- Speed is extraordinary

M. J. Jang, et al. *J Thromb Haemost,* 9 (2011), 85-91.

Korean Guideline

- 2nd Edition in April, 2013 - Impending
- 1st Edition in 2009

INSURANCE IN KOREA

Rivaroxaban (Xarelto)

	Prevention of VTE in OS surgery	**Treatment and secondary prevention of VTE**	**Prevention of Stroke in non-valvular AFib**
Rivaroxaban	Y (Canada, Europe) Y (Korea in 2009)	Y (Europe in Dec 2011) Y (Korea in Feb 2012) @Insurance in Jan 2013 for VTE @인정비급여 on Feb26, 2013	Y (USA in Nov 2011) Y (Europe in Dec 2001) Y (Korea in Feb 2012) *ROCKET AF

Rivaroxaban (Xarelto) in Korea

	Prevention of VTE in OS surgery	**Treatment and secondary prevention of VTE**	**Prevention of Stroke in non-valvular AFib**
Rivaroxaban	In 2009	In Feb 2012 @Insurance in Jan 2013 for VTE @인정비급여 on Feb26, 2013	In Feb 2012

Dabigatran(Pradax)

	Prevention of VTE in OS surgery	**Treatment of VTE**	**Prevention of Stroke in non-valvular AFib**
Dabigatran	Y (Europe in 2008) Y (Canada in 2010) Y (USA in 2010)	*RECOVER 2009 *REMEDY 2011 *RESONATE 2011 @Published in Feb 25, 2013 in NEJM	Y (Canada) Y (USA in 2010) **Y (Europe 2011)** *RE-LY

Case

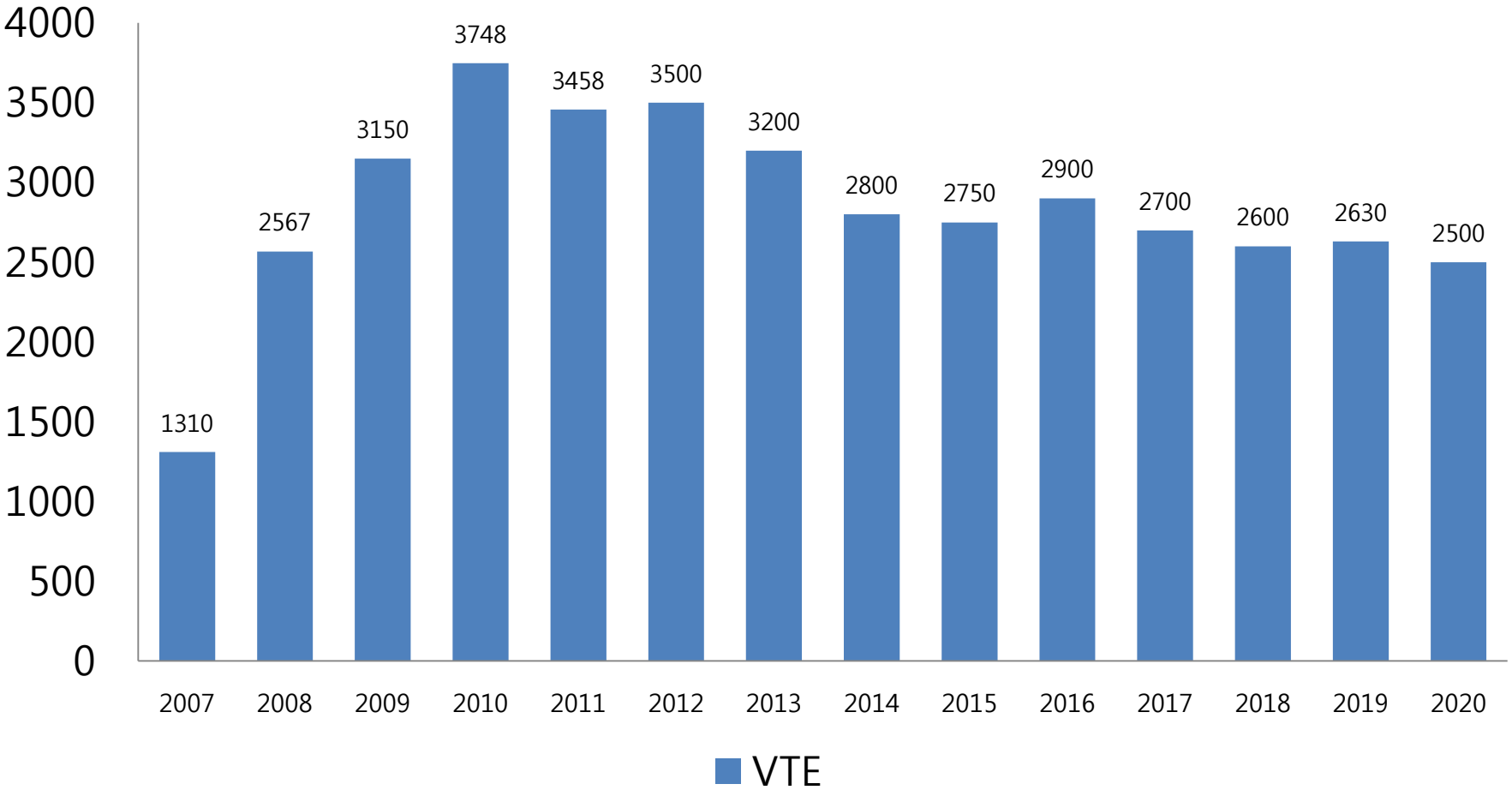
- 59세 여자
- GB empyema 수술 후 혈압강하
- Thrombolytics & Heparin
- Anticoagulants of VKA for 2mo
- Alopecia
- NOACs on Dec 24, 2012.

SUMMARY

SUMMARY

- PE Treatment
- Prophylaxis of DVT in Hospital
- NOACs

Future Prospect for Incidence of VTE in Korea



Imaginary News

- Gradual reduction in incidence of VTE in Aged Society, Korea

NBC News Today, April, 2020

경청해 주셔서 감사합니다.

Prophylaxis in OS Dept (2012.7~)

- 2 차발표 (2013.2.27 : 총 28명중 16명)
- 2명-Enoxaparin사용안함
- 1명-Warfarin Bridging
- 2명- Septic arthritis, THA

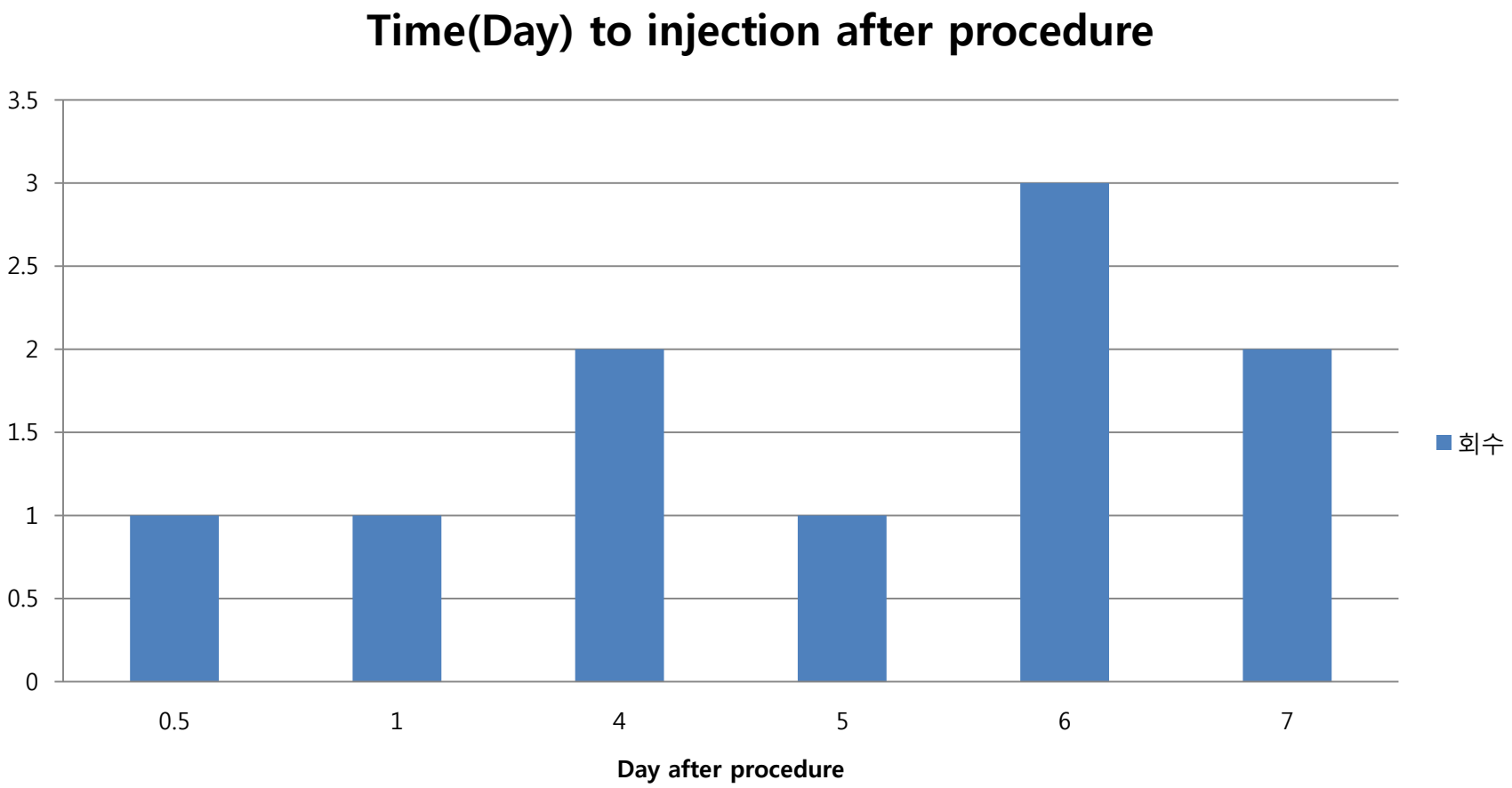
Prophylaxis in OS Dept (2012.7~2013.1)

Male (Female)	5(11)
Age(Mean+SD)	78.8±5.9
Name of operation	
Bipolar hemiarthroplasty	8
CR & IF	7
Open reduction & IF	1
Preop LMWH injection	14(87.5%)
Interval between procecure and postop injection Mean (Range) day	1.84.72 ±1.98
Number of injection after operation (Mean+SD)	9.4+
VTE (PE)	1
CVA	1
Major bleeding	1

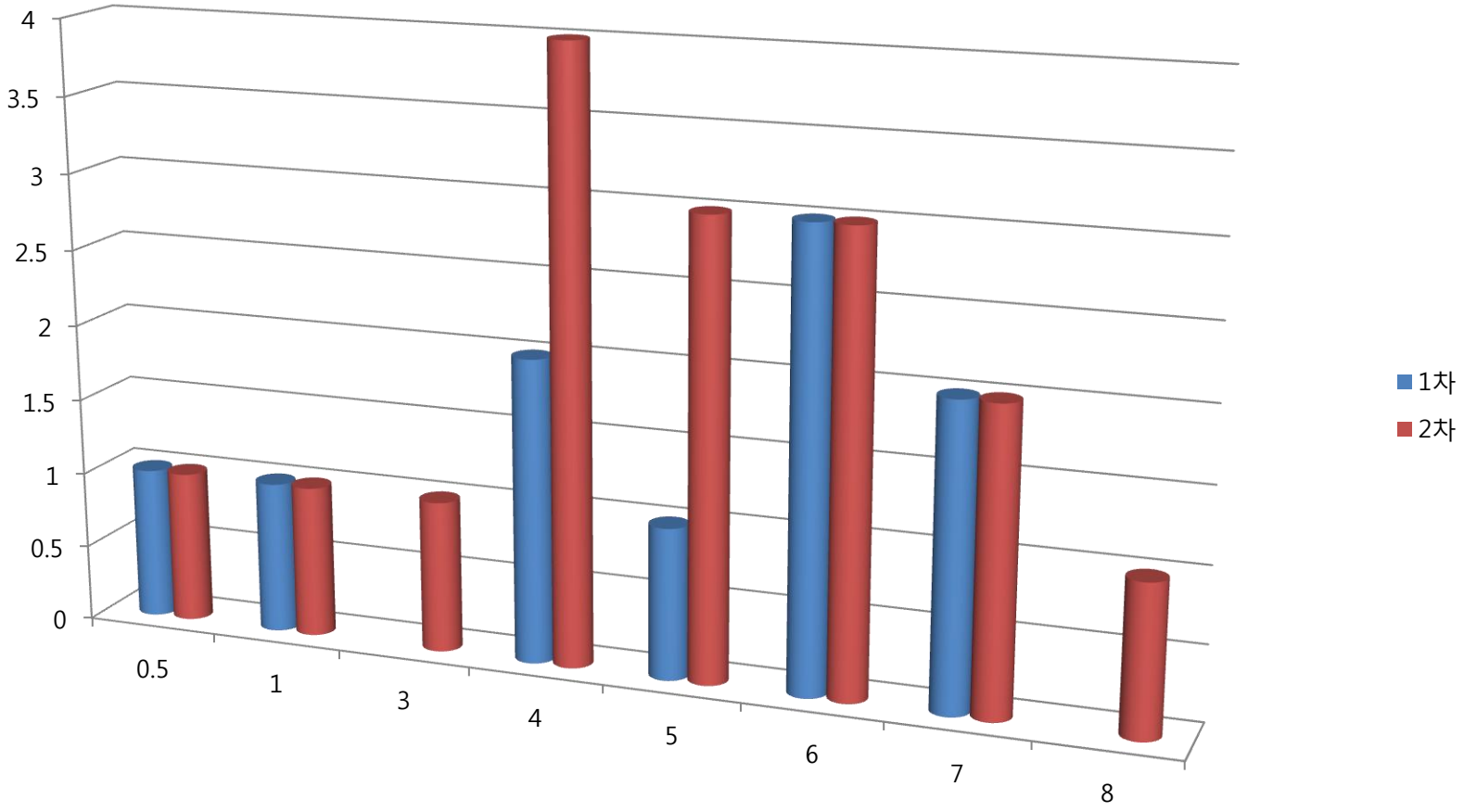
Prophylaxis in OS Dept (2012.7~2013.1)

	Total N=16	Group 1 N=10	Group 2 N=6
Male (Female)	5 (11)	4 (6)	1 (5)
Age(Mean+SD)	78.8 ± 5.9	79±6.4	78.5±5
Site of femur fracture Right(left)			
Right	11	5	6
Left	5	5	0
Name of operation			
Bipolar hemiarthroplasty	8	3	5
Closed reduction & internal fixation	7	6	1
Open reduction & internal fixation	1	1	0
Preop LMWH injection (%)	14(87.5%)	8 (80%)	6 (100%)
Interval between procecure and postop injection Mean (Range) day	4.72 ± 1.98	3.55 ±1.52	6.67±0.75
Number of injection after operation (Mean+SD)	9.4 ± 1.8	9.2±1.54	9.67±2.21
VTE (PE)	1	0 (0%)	1 (16.7%)
CVA	1		
Major bleeding	1	0 (0%)	1 (16.7%)

Prophylaxis in OS Dept (2012.7~9)



Prophylaxis in OS Dept (2012.7~2013.1)



Event after Major Surgery

- Major bleeding
  - Post op Day 3 : transfusion of 3 units
- Pulmonary embolism(LMWH postop D6)
  - Post op Day 2
  - Preoperative injection(+)
- Cerebral infarction
  - Postop Day 5 injection
  - Postop Day 16 (+)

Conclusion

- Limitation : Small data
- No one bleeding Cx in Group 1
- Prophylaxis with LMWH be started 6 to 8 hr after proper wound closure to prevent VTE.