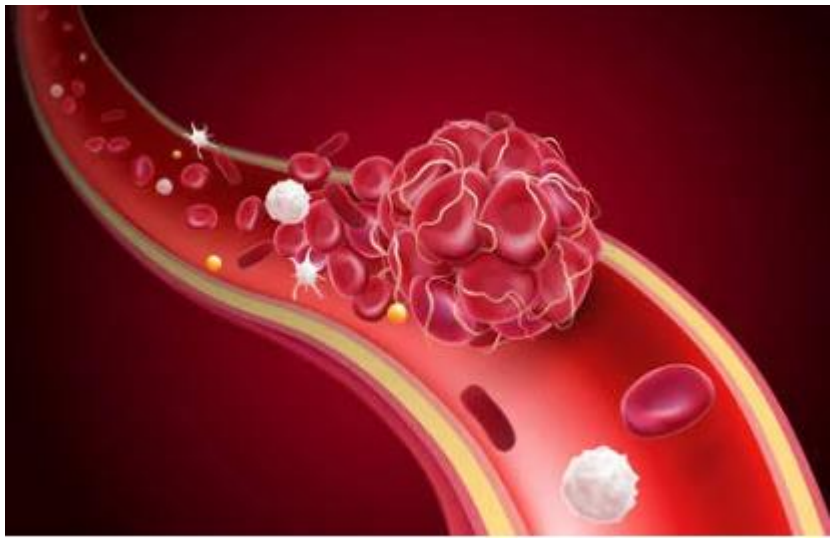
What should I do if blood clots and bleeding occur at the same time?

호흡기알레르기 내과
중환자의학과
김진영

Dilemma

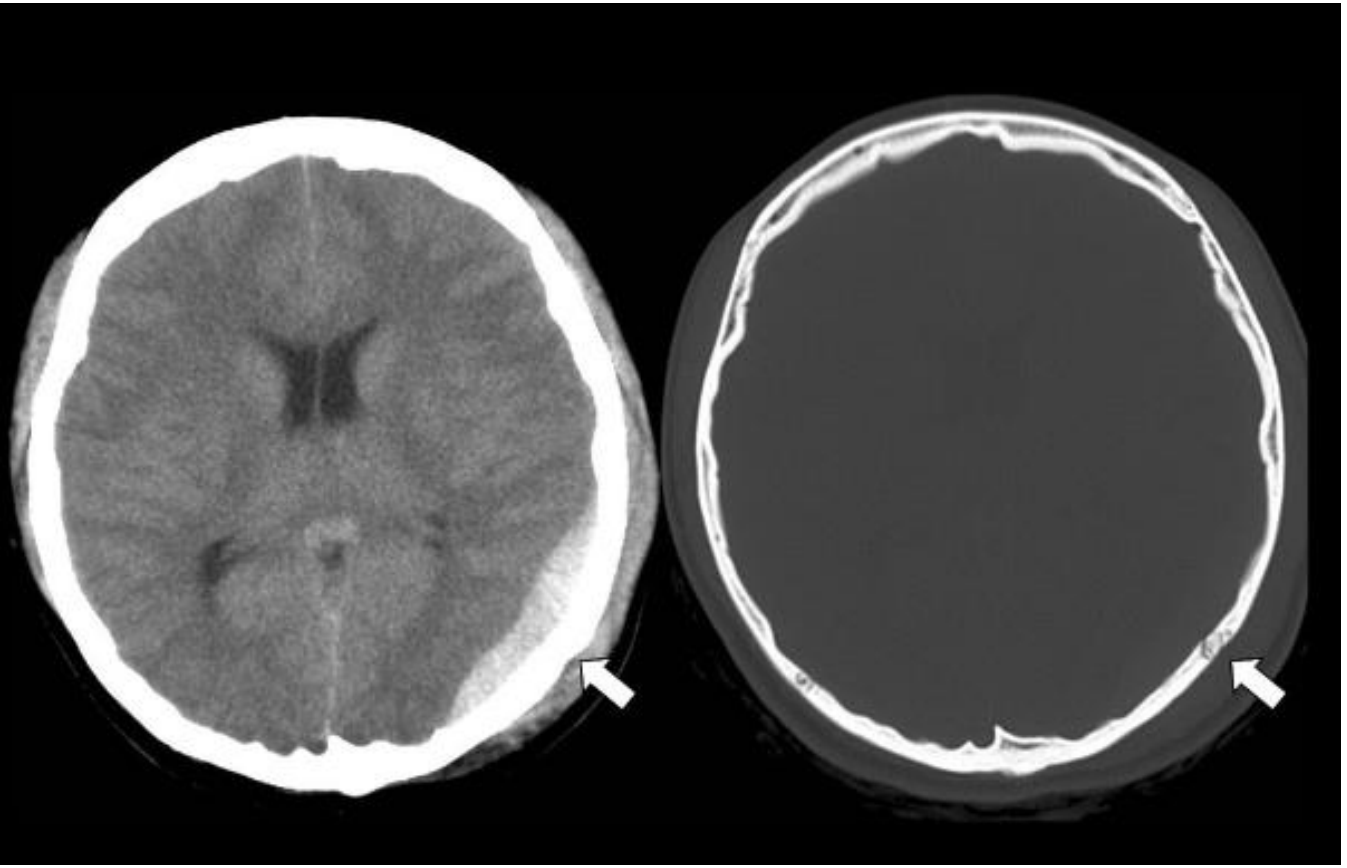


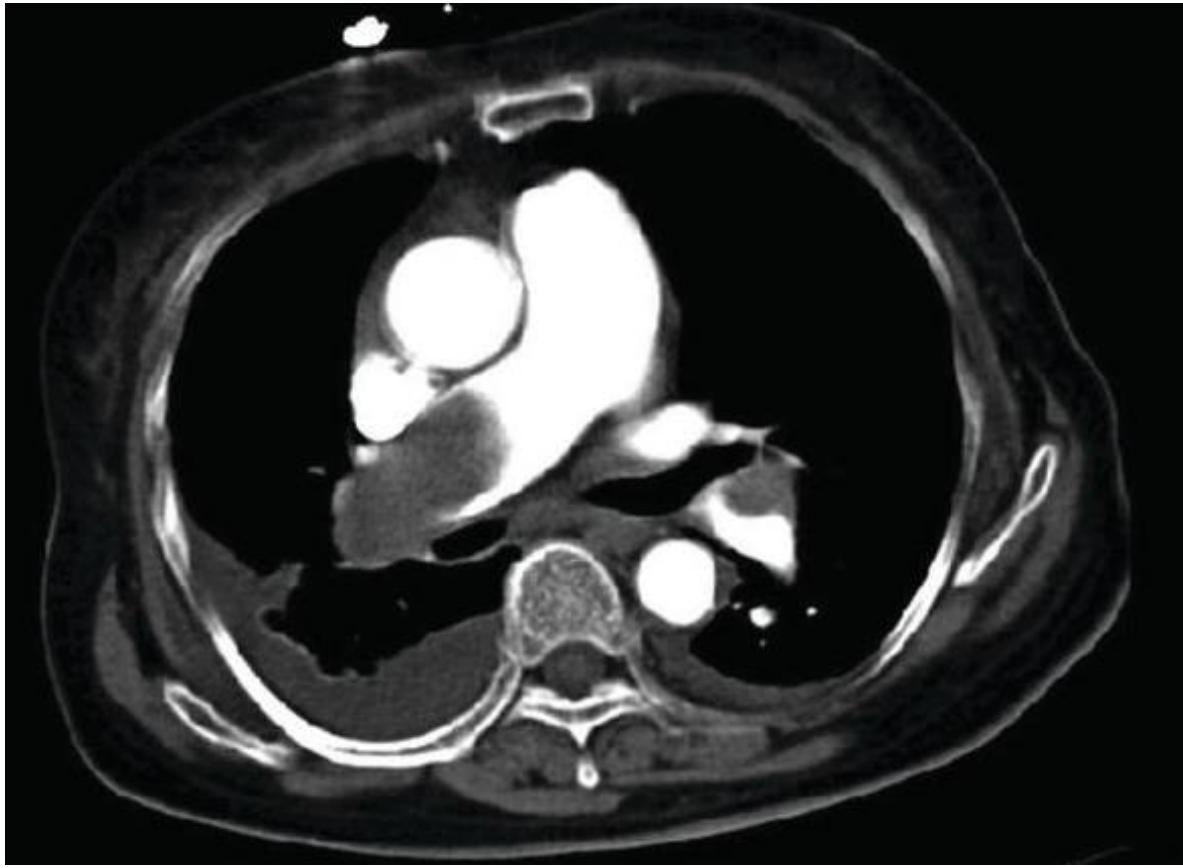
Case

- F/70
- Past Hx. : HTN, DM
- Chief complain : mental change onset today

- Present Illness
  - 내원 2일전 COVID 19 pneumonia infection 확진 후 가택 격리 중. 최근 기운이 없어 하루 중 대부분을 누워서 지내던 중. 내원 당일 아침 갑작스럽게 호흡곤란 호소 하면서 화장실 가던 중 넘어 지면서 세면대에 머리를 부딪히면서 의식을 잃은 상태로 보호자에 의해 발견되어 119 통해 본원 응급실 내원.

Case-image





Case-lab

- D-dimer 19.1 ug/ml
- Pro-BNP 1512.0 pg/ml
- Echocardiogram
  - moderate RV dysfunction with RAE
  - D-shape
- DVT sono
  - not exam

Hemostasis vs anti-coagulation

- Hemostasis
  1. Constriction of the blood vessel
  2. Formations of a temporary “platelet plug”
  3. Activation of the coagulation cascade
  4. Formation of “fibrin plug” or the final clot

- Anti-coagulation

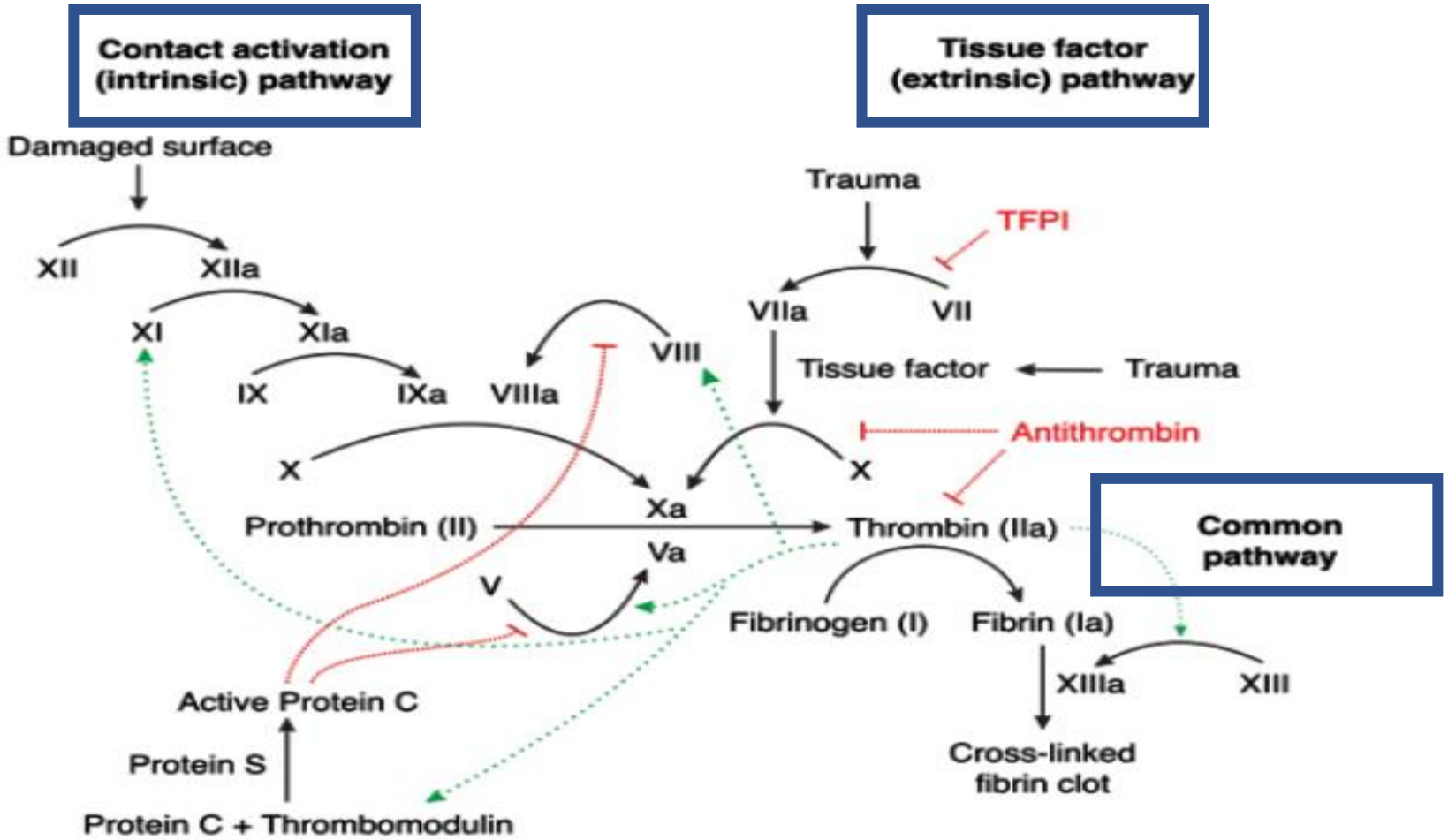
  - Derive their effect by acting at different site of the coagulation cascade.

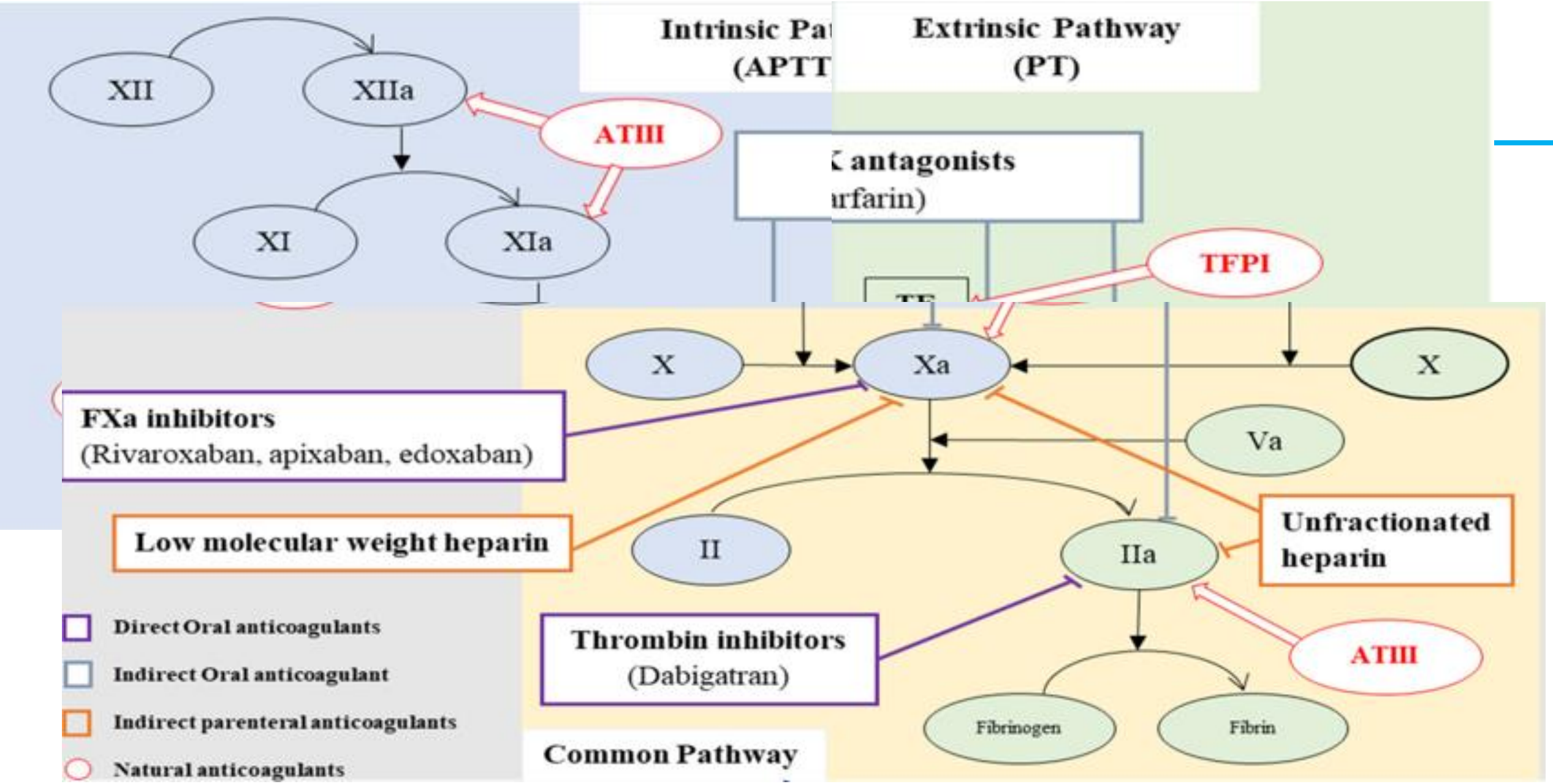
  1. Unfractionated Heparin
  2. Low Molecular Weight Heparin
  3. Vitamin K dependent Antagonists
  4. Direct Thrombin Inhibitors
  5. Direct Factors 10a Inhibitors

1.LaPelusa A, Dave HD. Physiology, Hemostasis. [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.

2.Umerah Co, Momodu II. Anticoagulation. [Updated 2022 Jul 18]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.

Coagulation Cascade





Chandika P, Tennakoon P, Kim T-H, Kim S-C, Je J-Y, Kim J-I, Lee B, Ryu B, Kang HW, Kim H-W, Kim Y-M, Kim CS, Choi I-W, Park WS, Yi M, Jung W-K. Marine Biological Macromolecules and Chemically Modified Macromolecules; Potential Anticoagulants. *Marine Drugs*. 2022; 20(10):654.

What is your treatment choice?

1) Anti-coagulation without bleeding control

2) Bleeding control without anti-coagulation

3) Anti-coagulation with bleeding control

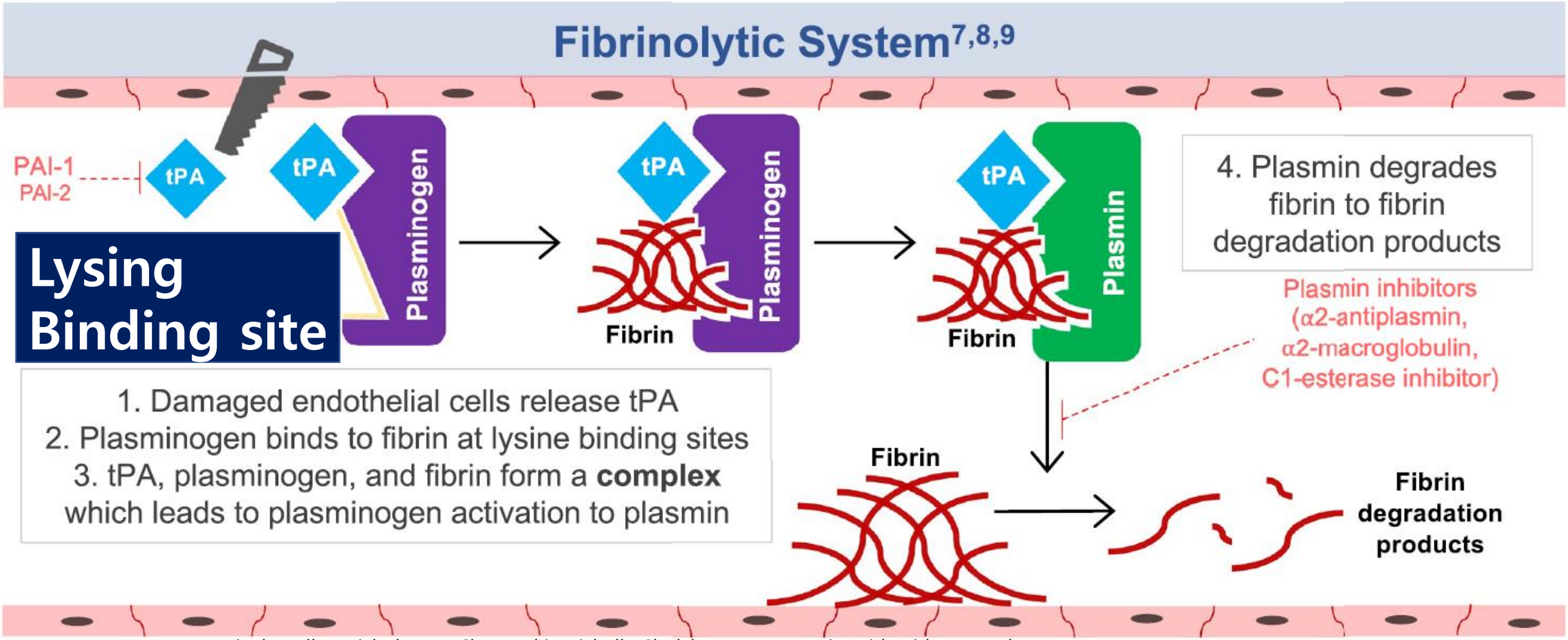
4) No treatment

What is bleeding control

Typical hemostats	Bleeding sites	Comments
Intravenous infusion		
Coagulation factor concentrates: fibrinogen, recombinant factor VII, prothrombin complex [33–36]	Extremity/junctional/truncal hemorrhage	Used clinically and in remote operational environments, showing logistic benefits, requiring more randomized controlled trials for clinical benefits
Dried plasma [37, 38]	Extremity/junctional/truncal hemorrhage	Used prehospitally and on the battlefield, suggesting a survival advantage to severely bleeding patients
Tranexamic acid [39–42]	Extremity/junctional/truncal hemorrhage	Used prehospitally and on the battlefield, suggesting a survival advantage to severely bleeding patients
Platelet substitutes/synthetic platelets [46–48]	Extremity/junctional/truncal hemorrhage	Under development
Synthetic polymers: polySTAT [49–51]	Extremity/junctional/truncal hemorrhage	Under development, improved survival compared to an albumin control in a rat femoral artery injury

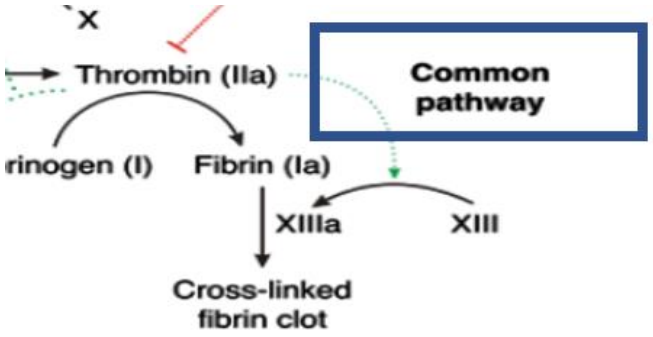
Peng HT. Hemostatic agents for prehospital hemorrhage control: a narrative review. Mil Med Res. 2020 Mar 25;7(1):13

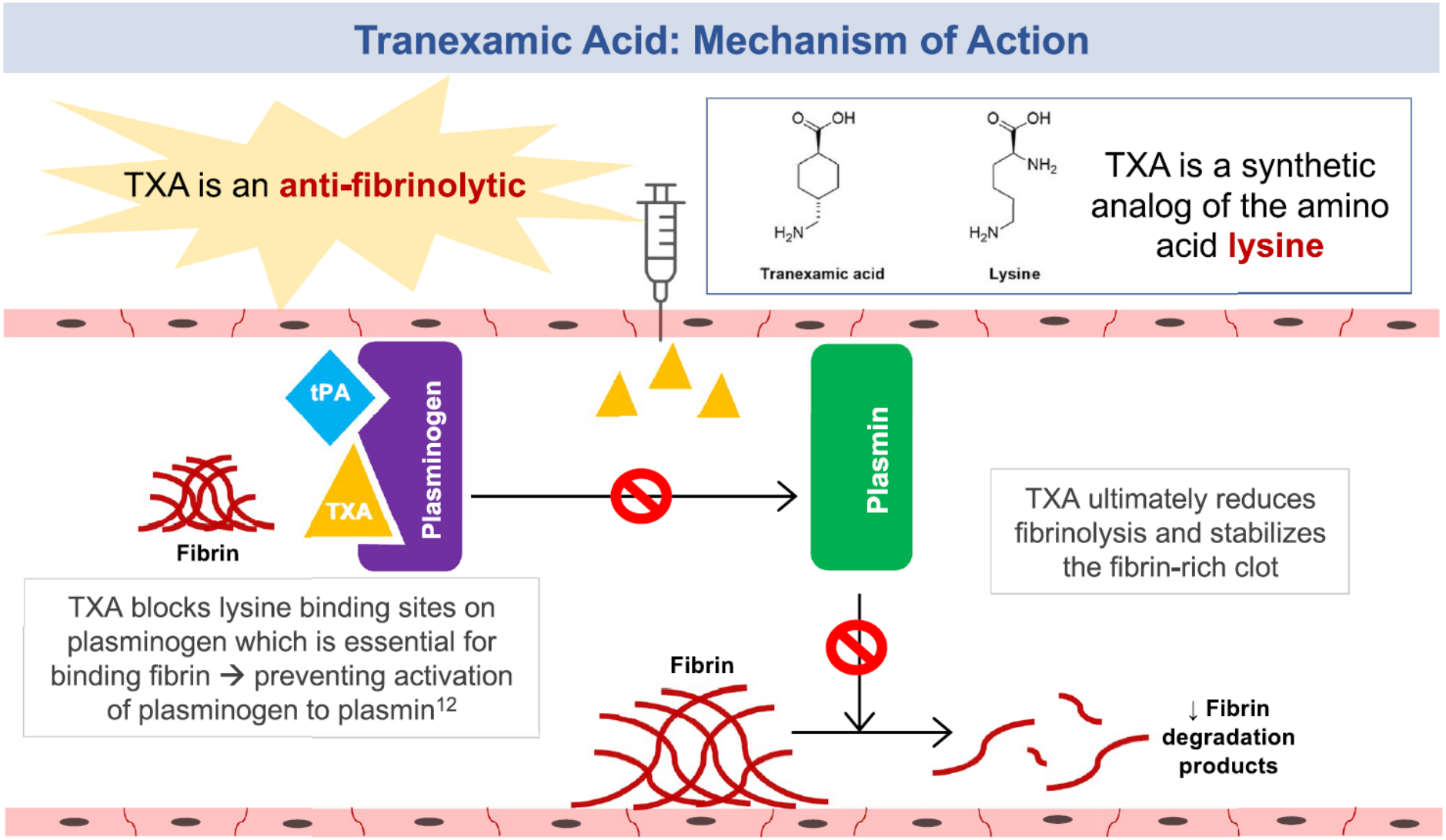
The mechanism of Tranexamic acid (1)



Nicole Relke, Nicholas L.J. Chornenki, Michelle Sholzberg, Tranexamic acid evidence and controversies: An illustrated review,Research and Practice in Thrombosis and Haemostasis, Volume 5, Issue 5,2021,

The mechanism of Tranexamic acid (2)





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Hemostasis vs anti-coagulation

- Q1) Which one is more important?
- Q2) When I start medication for anti-coagulation?
- Q3) Which medication is more safe and efficacy for anti-coagulation?
- Q4) What about dose of anti-coagulation? Same dose or not ?

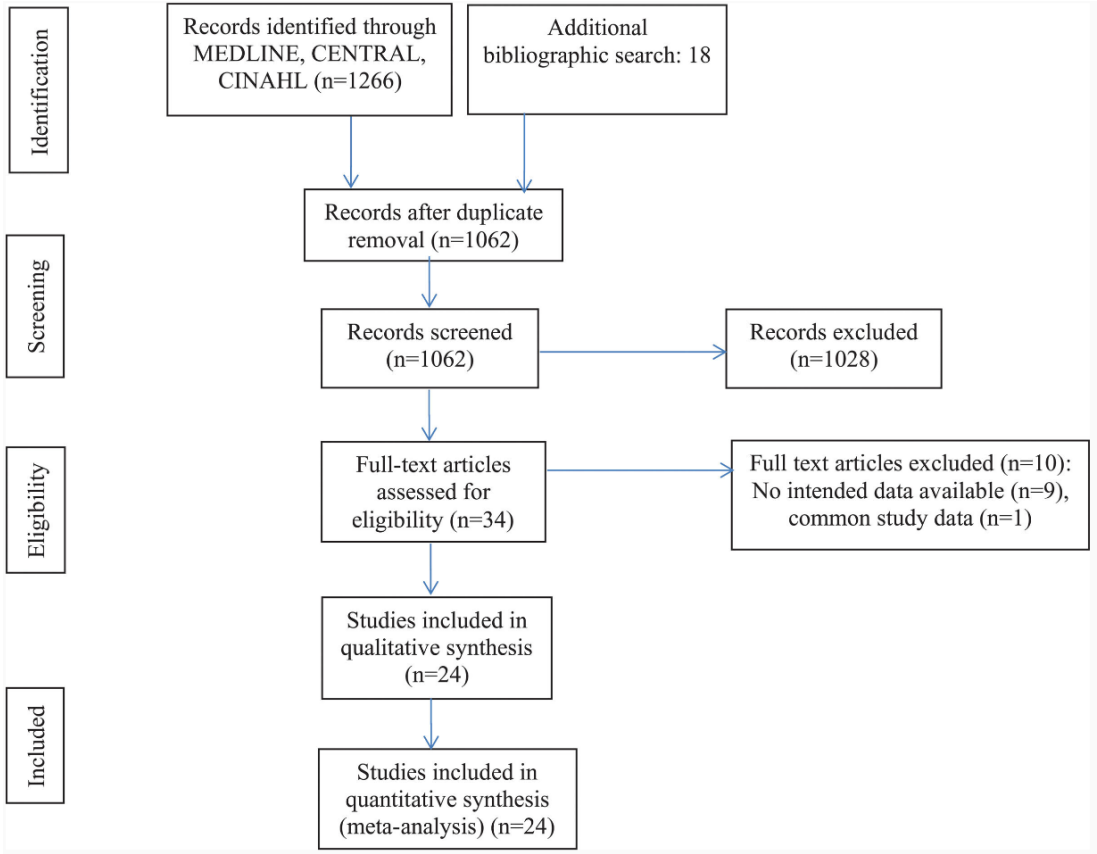
Mortality (1)

Prevalence, Characteristics, and Outcomes of Undetermined Intracerebral Hemorrhage: A Systematic Review and Meta-Analysis

Konark Malhotra ✉, Christina Zompola, Aikaterini Theodorou, Aristeidis H. Katsanos, Ashkan Shoamanesh, Himanshu Gupta, Simon Beshara, Nitin Goyal, Jason Chang, ... See all authors

Originally published 4 Aug 2021 | https://doi.org/10.1161/STROKEAHA.120.031471 | Stroke. 2021;52:3602–3612

Other version(s) of this article



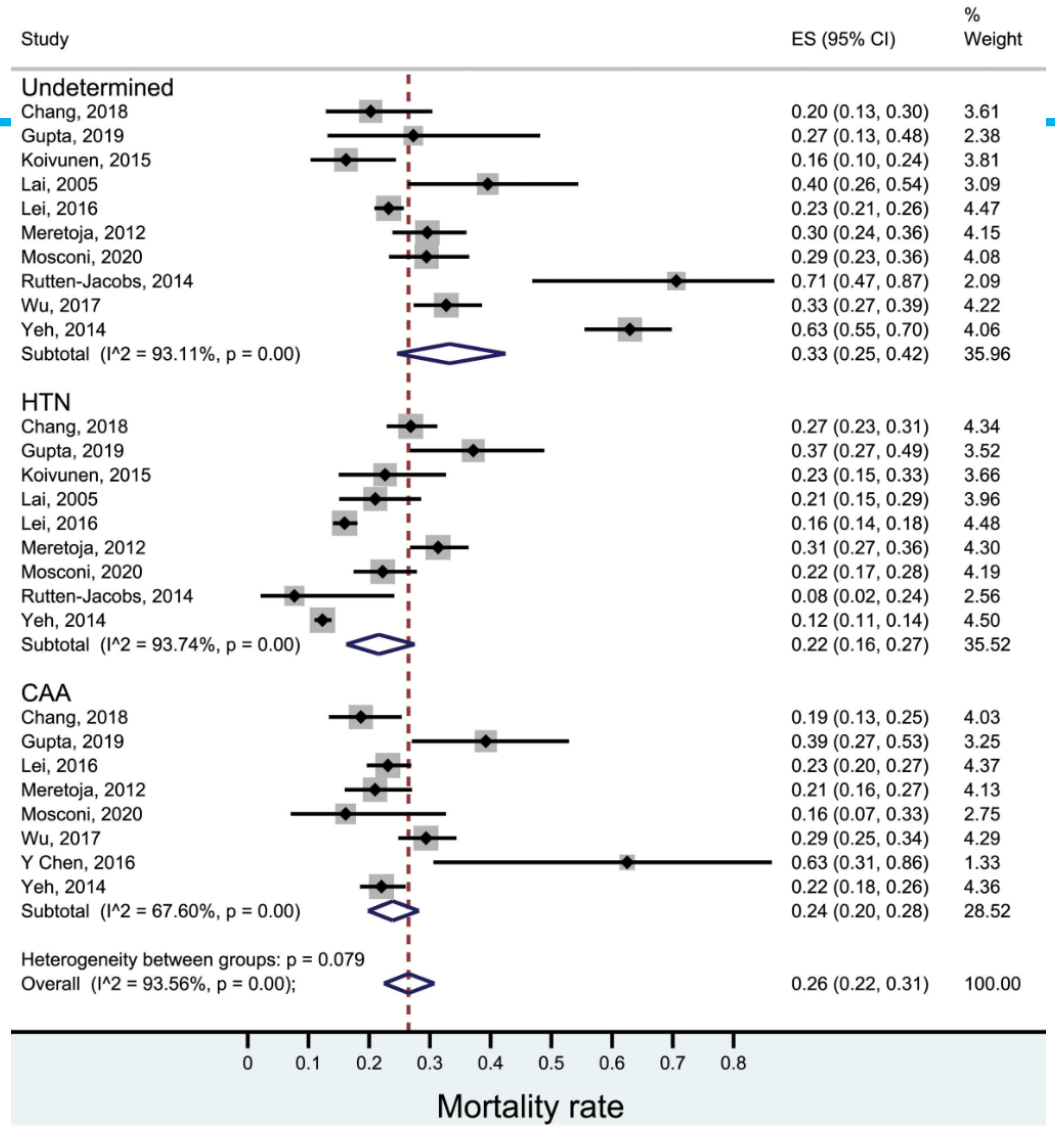
Mortality (2)

Table. Overview of the Primary Analyses

EtiologyRates	Hypertensive arteriopathy (95% CI)	n	I^2, *P* for Cochran Q	CAA (95% CI)	n	I^2, *P* for Cochran Q	Undetermined (95% CI)	n	I^2, *P* for Cochran Q	*P* for subgroup difference
Prevalence	50% (43%–58%)	22	98.7%, *P*<0.001	12% (7%–17%)	15	98.7%, *P*<0.001	18% (13%–23%)	24	98.3%, *P*<0.001	<0.001
Mortality	22% (16%–27%)	9	94.1%, *P*<0.001	24% (20%–28%)	8	67.6%, *P*<0.001	33% (25%–42%)	10	93.1%, *P*<0.001	0.079
IVH	40% (27%–53%)	8	94.1%, *P*<0.001	28% (23%–33%)	7	74.7%, *P*<0.001	38% (28%–48%)	8	94.1%, *P*<0.001	0.084
ICH volume, mL	16.2 (10.9–21.5)	3	95.0%, *P*<0.001	24.7 (19.7–29.8)	3	81.8%, *P*<0.001	15.4 (6.2–24.5)	3	96.7%, *P*<0.001	<0.001

CAA indicates cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; and IVH, intraventricular hemorrhage.

The rates of short-term mortality (Figure 3) were observed to be the highest among patients with undetermined ICH at 33% (10 studies [95% CI, 25%–42%]; *P* for Cochran Q statistic, <0.001; I^2=93.1%) followed by CAA-ICH at 24% (8 studies [95% CI, 20%–28%]; *P* for Cochran Q statistic, <0.001; I^2=67.6%) and HTN-A ICH at 22% (9 studies [95% CI, 16%–27%]; *P* for Cochran Q statistic, <0.001; I^2=94.1%). The difference in the short-term mortality rates among the three ICH subgroups was nonsignificant (*P*=0.079).



Mortality (3)

Predicting mortality in traumatic intracranial hemorrhage

Andrew Y. Powers, BA,[1] Mauricio B. Pinto,[1] Oliver Y. Tang,[1] Jia-Shu Chen,[1] Cody Doberstein, BS,[1] and Wael F. Asaad, MD, PhD[1–5]

[1]Department of Neurosurgery, Warren Alpert Medical School of Brown University; [2]Carney Institute for Brain Science, Brown University; [3]Department of Neuroscience, Brown University; and [4]Norman Prince Neurosciences Institute and [5]Department of Neurosurgery, Rhode Island Hospital, Providence, Rhode Island

J Neurosurg Volume 132 • February 2020

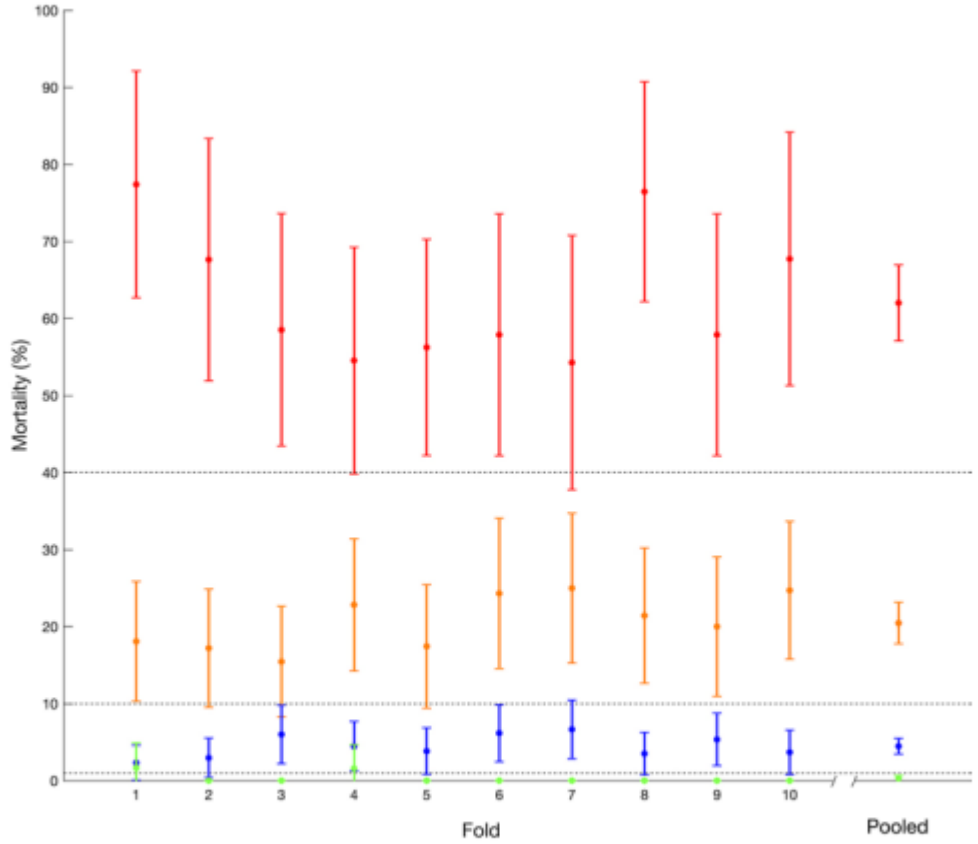


FIG. 2. Calibration plot showing the mortality of grade I (*green*), grade II (*blue*), grade III (*orange*), and grade IV (*red*) hemorrhages in comparison with the predicted mortality ranges (*dotted lines*). *Error bars* represent 95% CIs. Figure is available in color online only.

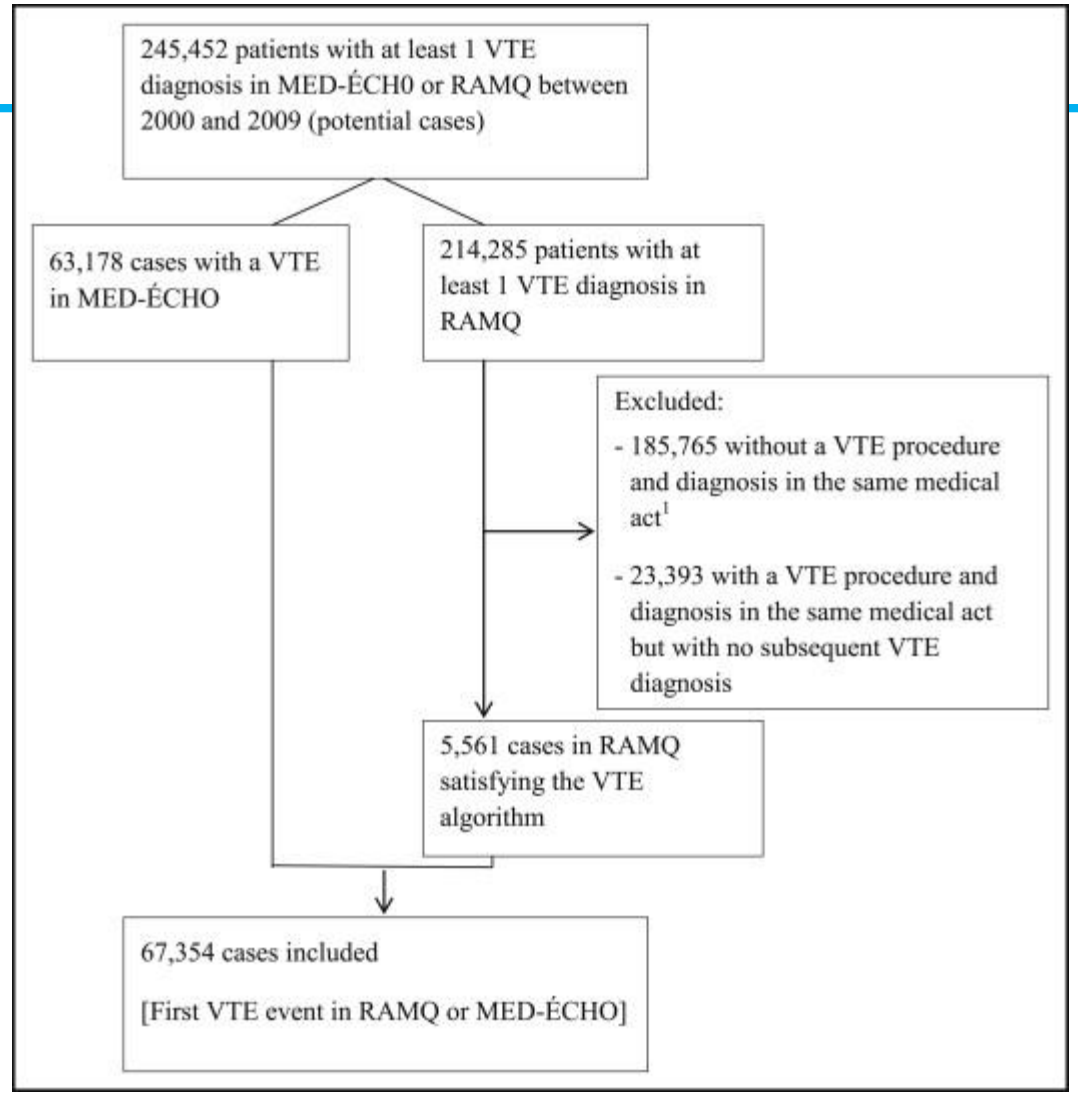
Mortality (4)

AJM online
Clinical research study

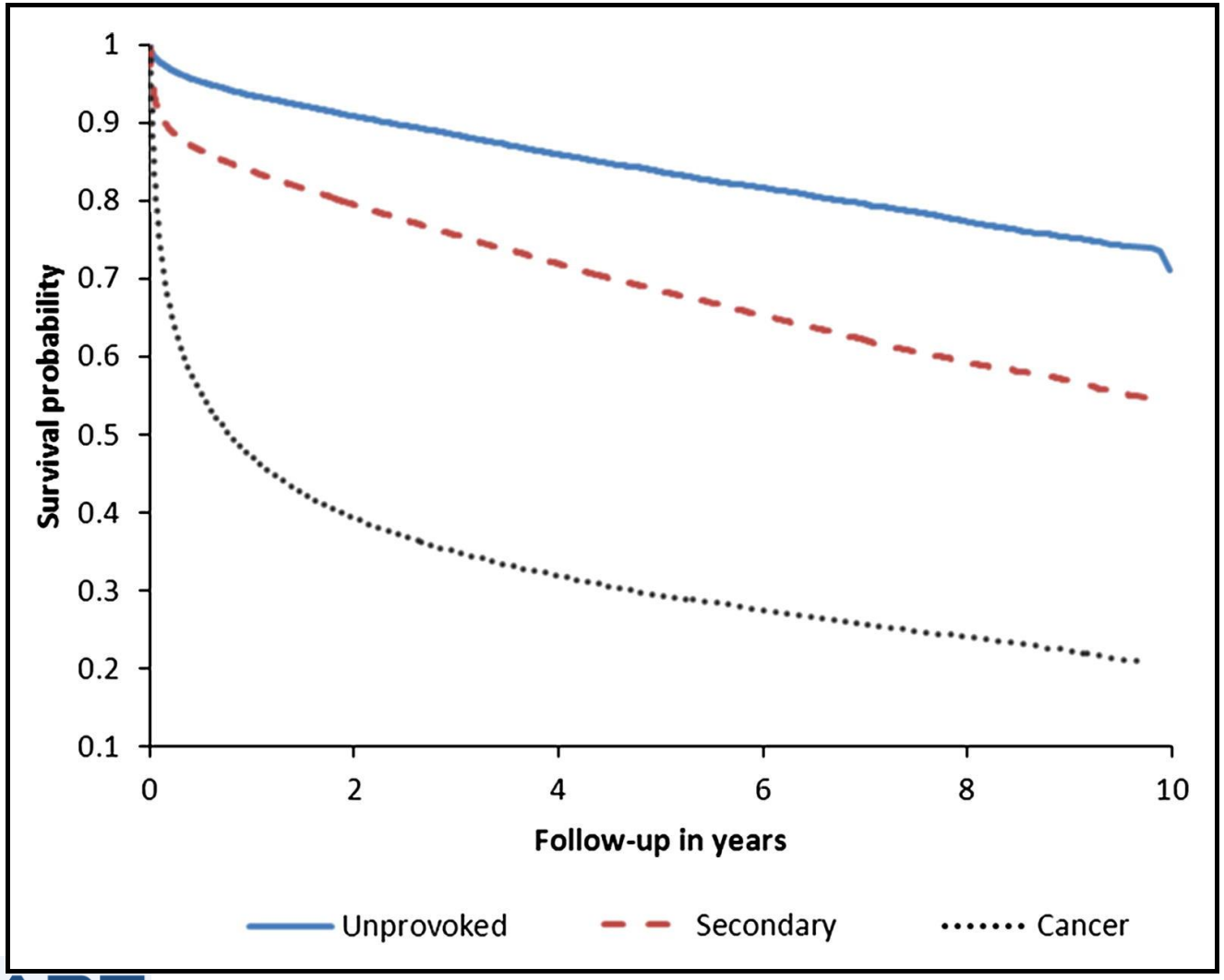
Incidence of and Mortality from Venous Thromboembolism in a Real-world Population: The Q-VTE Study Cohort

Material from this manuscript was presented at the 54th American Society of Hematology Annual Meeting in Atlanta, Georgia on December 8, 2012.

Vicky Tagalakis MD, MSc [a], Valérie Patenaude MSc [a], Susan R. Kahn MD, MSc [a], Samy Suissa PhD [b]



Mortality (5)



- The 30 day and 1 year case fatality rate after VTE were 10.6% (95% CI) and 23.0% (95% CI)

The moment for start anti-coagulation on ICH patient

Management of oral anticoagulation after intracerebral hemorrhage

Joji B Kuramatsu and Hagen B Huttner

International Journal of Stroke
2019, Vol. 14(3) 238–246

DOI: 10.1177/1747493019828555
journals.sagepub.com/home/wso
SAGE

Abstract

Background: The most recent years have significantly expanded knowledge regarding risks an oral anticoagulation (OAC) after intracerebral hemorrhage (ICH). No randomized data is yet av large observational studies and meta-analyses have investigated the impact of resuming OAC on tl hemorrhagic complications in these high-risk patients after ICH.

Aims: The present review will summarize the most important studies conducted over the last y relevant factors help guiding on decision-making on whether to start OAC after ICH.

Summary of review: Several important factors (demographic, co-morbidities, clinical chara considered before individual decision-making for or against OAC is employed. Existing observat patients after ICH with indication for long-term oral anticoagulation benefit from OAC given si thromboembolic events without significantly increasing bleeding complications. Studies even sug clinical outcomes may be improved. Prospective trials currently recruiting patients will clarify whe or left atrial appendage closure as a meaningful alternative – is of clinical net-benefit.

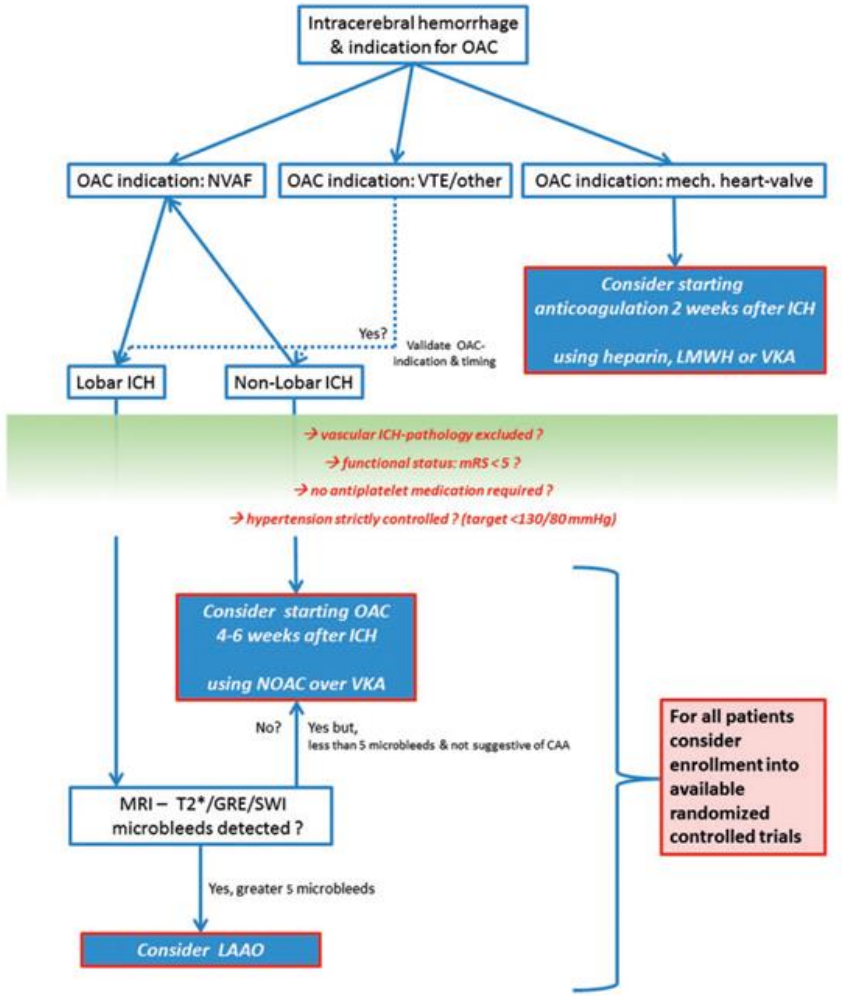
Conclusions: Large sized and well-executed investigations (moderate quality of evidence) a resumption after ICH decreases thromboembolic complications and long-term mortality without bleeding complications. Further, data suggest that resumption may be safer in non-lobar ICH comp overall, thoughtful selection, strict blood pressure control, and precise communication are paran patient on OAC after ICH.

Table 1. Studies reporting ischemic and hemorrhagic event rates according to treatment

Study (pub. year)	Design	Sample size	NVAF, n (%)	Risk of intracranial hemorrhage		Risk of ischemic stroke	
				OAC	No OAC	OAC	No OAC
Kuramatsu (2015)	Retrospective	719	566 (79%)	ICH 3.9 per py	ICH 3.9 per py	3.9 per py	12.7 per py
Nielsen (2015)	Retrospective	1752	1752 (100%)	8.0 per py	8.6 per py	5.3 per py	10.4 per py
Park (2016)	Retrospective	428	304 (71%)	ICH 2.1 per py	0 per py	2.8 per py	8 per py
Chao (2016)	Retrospective	12,917	12,917 (100%)	5.9 per py	4.2 per py	3.4 per py	5.8 per py
Pennlert (2017)	Retrospective	2777	2777 (100%)	ICH 6.9 per 3y	ICH 4.4 per 3y	6.3 per 3y	13.8 per 3y

NVAF: non-valvular atrial fibrillation; OAC: oral anticoagulation.

Figure 1. Suggested flow of diagnostic and therapeutic procedures in OAC-ICH.
OAC: oral anticoagulation; NVAF: non-valvular atrial fibrillation; VTE: venous thromboembolism; Other: including all indications for oral anticoagulation, i.e. by-pass grafting, thrombus formation, structural cardiac diseases, cerebral sinus thrombosis, arterial dissections, thrombophilia; ICH: intracerebral hemorrhage; LMWH: Low-molecular-weight heparin; VKA: vitamin-K-anatagonists; mRS: modified Rankin Scale; NOAC: novel oral anticoagulants; CAA: cerebral amyloid angiopathy; MRI: magnetic resonance imaging; GRE: gradient recalled echo; SWI: susceptibility-weighted imaging.



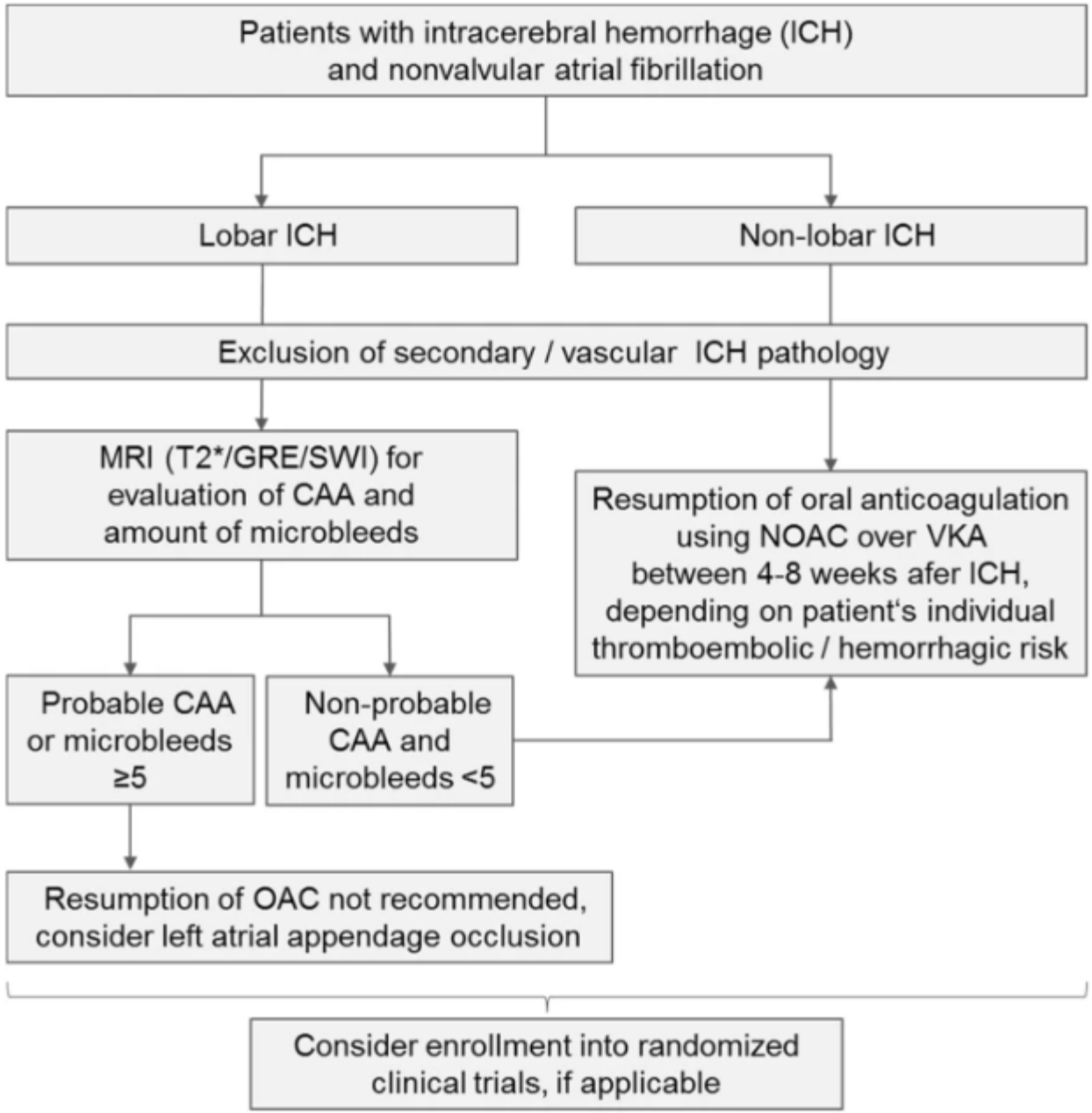
The moment for start anti-coagulation on ICH patient

Table 1 Large randomized controlled trials investigating pharmacological or interventional treatment for stroke prevention after ICH

Trial name (ClinicalTrials.gov)	Design	Allocation ratio	Study population	Est. sample size (n)	Location	Intervention	Est. primary completion date
Pharmacological treatment							
APACHE-AF (NCT02565693)	Open label	1:1	ICH and AF	100	Netherlands	Apixaban vs antiplatelets or none	January 2021
ASPIRE (NCT03907046)	Quadruple-blind	1:1	Non-lobar ICH and AF	700	USA	Apixaban vs ASS 81 mg/d	April 2024
NASPAF-ICH (NCT02998905)	PROBE	1:1	ICH and AF	100	Canada	NOAC vs ASS 81 mg/d	October 2019
PRESTIGE-AF	Open label	1:1	ICH	662	Europe	NOAC vs antiplatelets or none	November 2022
SoSTART (NCT03153150)	PROBE	1:1	ICH and AF	800	United Kingdom	OAC vs antiplatelets or none	July 2021
STATICH (NCT03186729)	PROBE	1:1	ICH and AF or no AF	500	Scandinavia	OAC or antiplatelets vs none	June 2021
Left atrial appendage occlusion (LAAO)							
A_3ICH (NCT03243175)	PROBE	1:1:1	ICH and AF	300	France	Apixaban vs LAAO vs antiplatelets or none	December 2022
Amulet IDE (NCT02879448)	Open label	1:1	High bleeding risk and AF	1878	Worldwide	Amulet LAAO vs WATCHMAN LAAO	February 2020
ASAP-TOO (NCT02928497)	Open label	2:1	High bleeding risk and AF	888	Belgium, Denmark, USA	LAAO vs antiplatelets or none	December 2023
CLOSURE-AF (NCT03463317)	Open label	1:1	High bleeding risk and AF	1512	Germany	LAAO vs active comparator (NOAK or VKA)	February 2021
LAAOS III (NCT01561651)	Quadruple-blind	1:1	Cardiopulmonary bypass surgery and AF	4812	Canada	Surgical LAAO vs best medical treatment	November 2022
PRAGUE-17 (NCT02426944)	Open label	1:1	History of bleeding and AF	400	Czech Republic	LAAO vs NOAK	May 2018
STROKECLOSE (NCT02830152)	PROBE	2:1	ICH and AF	750	Sweden	LAAO vs best medical treatment	May 2022

Information based on data from international (US, Asian, European) registries
Abbreviations: *AF* atrial fibrillation, *Est.* estimated, *ICH* inracranial hemorrhage, *LAAO* left atrial appendage occlusion, *PROBE* prospective randomized open blinded end-point

Fig. 2



Which anticoagulation ag

Cardiovascular Disease and Stroke (S. Prabhakaran, Section Editor) | Open Acce
Published: 21 May 2018

Anticoagulation Resumption After Intracer Hemorrhage

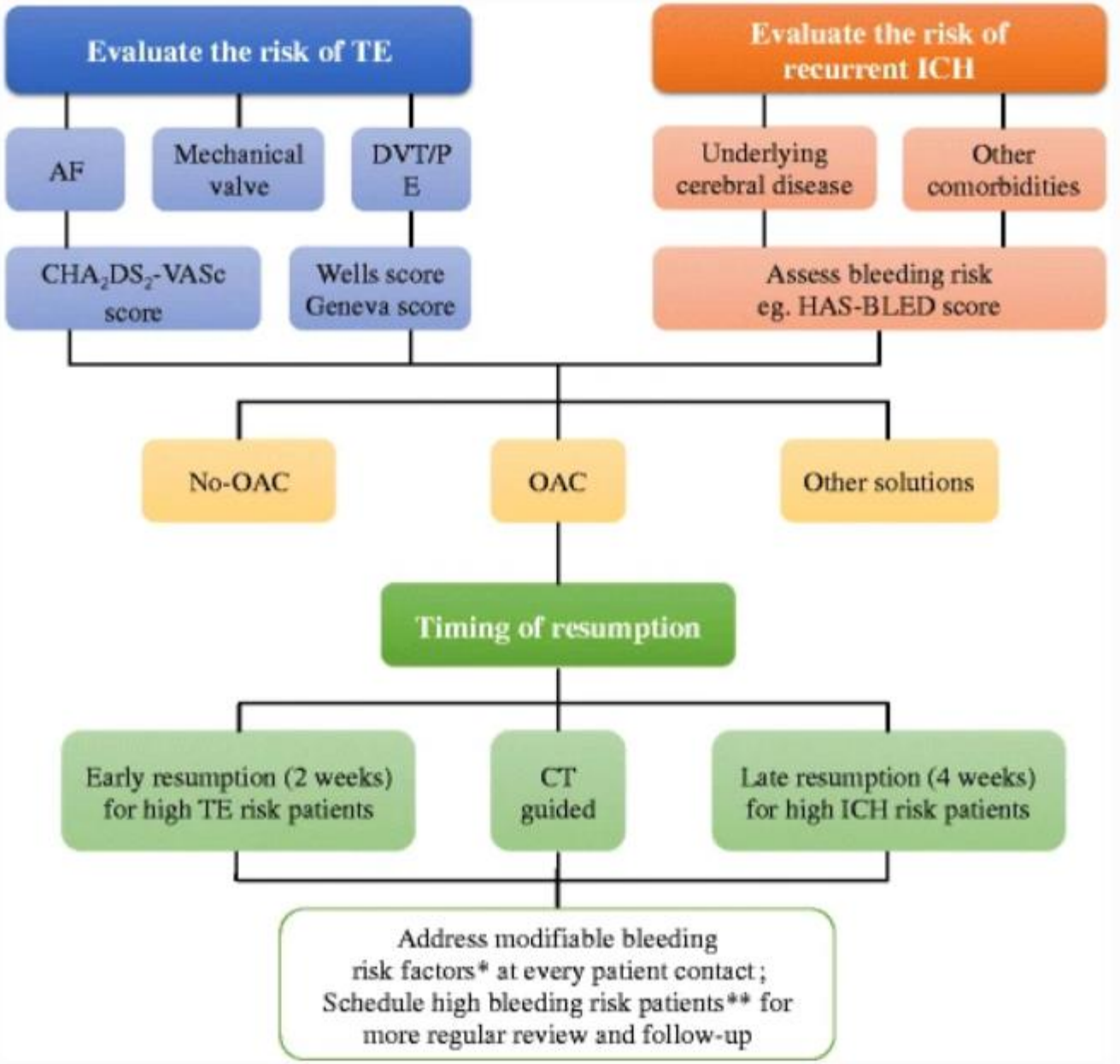
Yan-guang Li & Gregory Y. H. Lip

Current Atherosclerosis Reports **20**, Article number: 32 (2018) | Cite this article

Abstract

Purpose of review

Decision-making on resuming oral anticoagulant (OAC) after intracere evokes significant debate among clinicians. Such patients have been ex randomized clinical trials. This review article provides a comprehensiv evidence on anticoagulation resumption after ICH.



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SOON CHUN HYANG UNIVERSITY HOSPITAL CHEONAN

First Author	Design	No.	Patients with OAC resumption				Patients without OAC resumption			HR (95% CI) of OAC resumption		
			Time of OAC restarting (days)	Incidence of recurrent ICH*	Incidence of TE*	Incidence all-cause mortality*	Incidence of recurrent ICH*	Incidence of TE*	Incidence all-cause mortality*	ICH	TE	All-cause mortality
Ottosen [1•]	Population-based cohort	6369	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.90 (0.44–1.82)	0.58 (0.35–0.97)	0.59 (0.43–0.82)
Witt [14]	Retrospective cohort	160	14	7.6	3.7	18.5	3.7	12.3	31.1	0.47 (0.10–2.30)	0.28 (0.06–1.27)	0.76 (0.30–1.89)
Nielsen [15••]	Nationwide cohort	1752	34	8.0	5.3	9.7	8.6	10.4	19.1	0.91 (0.56–1.49)	0.59 (0.33–1.03)	0.55 (0.37–0.82)
Kuramatsu [16]	Nationwide cohort	719	31	3.9	5.2	8.2	3.9	15.0	37.5	N/A	N/A	0.26 (0.13–0.53)
Nielsen [17••]	Nationwide cohort	2415	31	5.8	3.3	19.6	5.3	8. 9	35.5	1.31 (0.68–2.50)	0.43 (0.21–0.86)	0.51 (0.37–0.71)
Santosh [18]	Meta-analysis	5306	N/A	N/A	N/A	N/A	7.8	N/A	N/A	1.01 (0.58–1.77)	0.34 (0.25–0.45)	N/A
Poli [19]	Nationwide cohort	244	N/A	N/A	2.0	3.0	N/A	6.0	8.0	N/A	0.19 (0.06–0.60)	0.17 (0.06–0.45)
Park [20]	Retrospective	528	117	1.4	2.4	1.4	0	8.3	4.8	N/A	0.19 (0.08–0.47)	N/A

HR hazard ratio, *CI* confidence interval, *ICH* intracerebral hemorrhage, *OAC* oral anticoagulants, *TE* thromboembolism

*Per 100 person-years

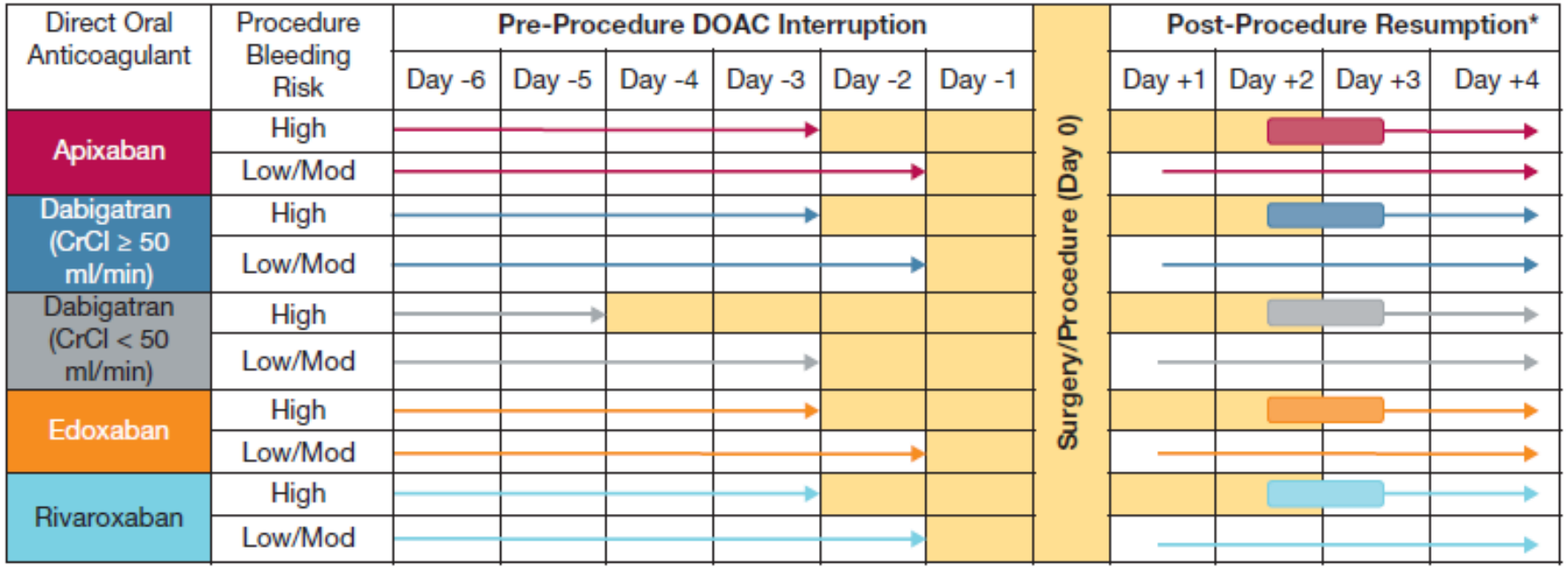
Table : Studies evaluating risk of hemorrhage and thromboembolism after ICH

Risk factor category	Risk factors	Modifiable risk factors
Risk factors for recurrent ICH	Large area ICH, ICH history, lobar ICH location, cerebral microbleeds, amyloid angiopathy, arteriovenous malformation, cerebral aneurysm, lacunar infarcts, leukoaraiosis, Asian population	Alcohol, tobacco, anemia, hepatic disease, high risk of fall
Risk factors for both ICH and thromboembolism	Elderly, coagulopathy, previous IS, malignancy	Hypertension, diabetes, kidney dysfunction, labile INR
Risk factors of thromboembolism	AF, HF, vascular disease, mechanical heart valve, VTE history, female sex, recent surgery	Decreased ambulation

AF atrial fibrillation, *HF* heart failure, *INR* international normalized ratio, *IS* ischemic stroke, *VTE* venous thromboembolism; other abbreviations see Table 1

Table : Clinical risk factors of recurrent ICH and thromboembolism

Which OAC is best



No DOAC administered that day

*DOAC can be resumed ~24 hours after low/moderate-bleed-risk procedures, and 48-72 hours after high-bleed-risk procedures. In selected patients at high risk for VTE, low-dose anticoagulants (i.e., enoxaparin, 40 mg daily or dalteparin, 5,000 IU daily) can be given for the first 48-72 hours post-procedure.

Figure 2 – *Perioperative management of direct oral anticoagulants (DOACs). CrCl = creatinine clearance.*

Which OAC is best?

- Re-bleeding 을 줄이면서 cardiovascular event 는 감소 시키는 것이 중요

- Short half-life , DOAC vs LWMHs

- Low dose vs standard dose

Thrombosis Research 173 (

Contents lists available a

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Full Length Article

Direct oral anticoagulant (DOAC) versus low-m (LMWH) for treatment of cancer associated thr review and meta-analysis

Ang Li[a,*], David A. Garcia[a], Gary H. Lyman[b,c], Marc Carrier

[a] Division of Hematology, University of Washington School of Medicine, Seattle, WA, United States
[b] Divisions of Public Health Sciences and Clinical Research, Fred Hutchinson Cancer Research Center, S
[c] Division of Medical Oncology, University of Washington School of Medicine, Seattle, WA, United State
[d] Clinical Epidemiology, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

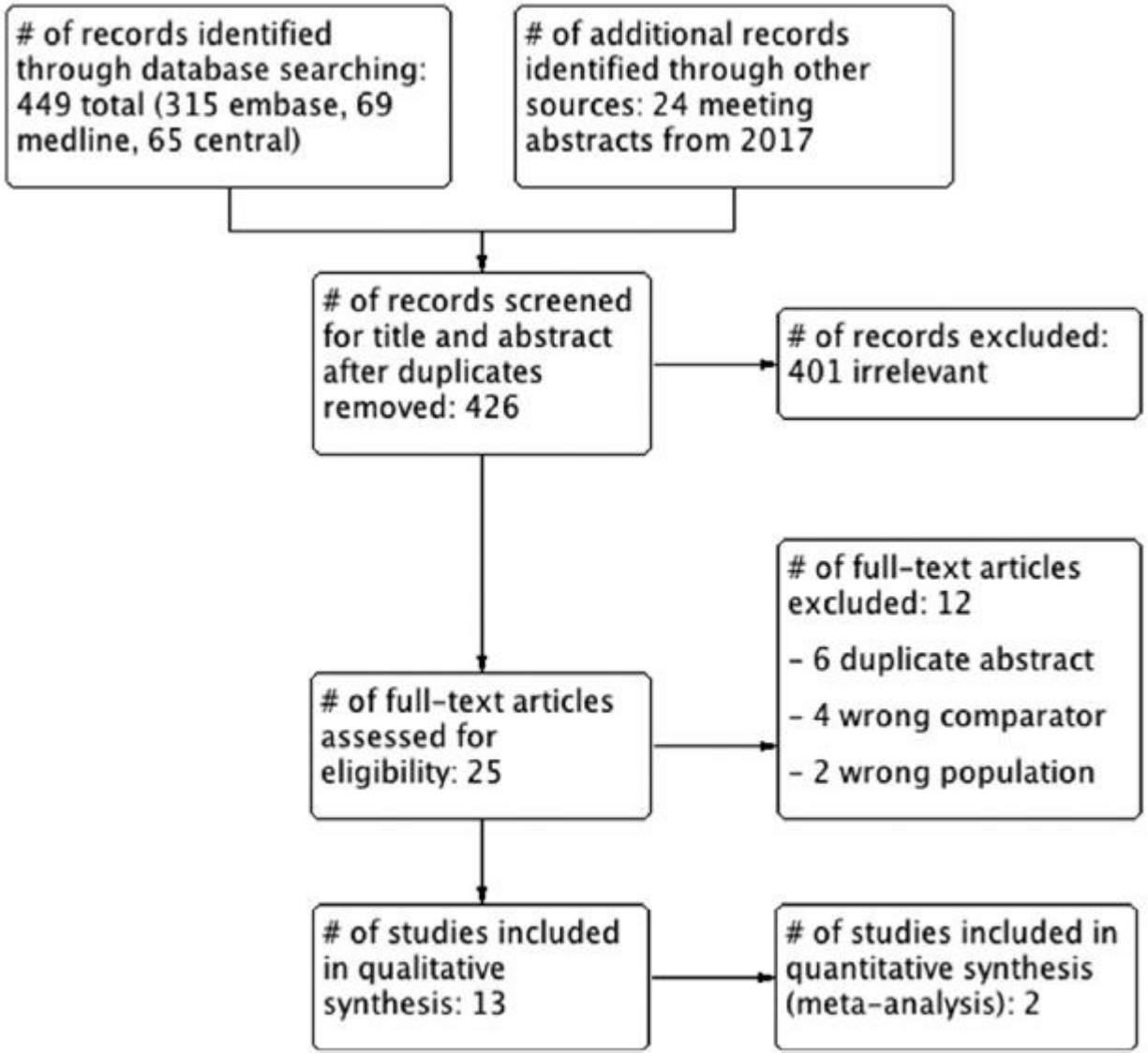
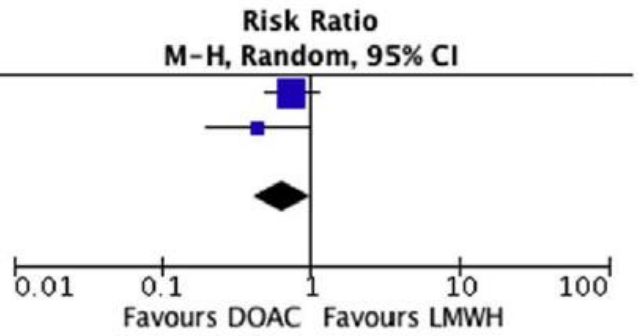


Fig. 1. PRISMA flow diagram for study inclusion and exclusion.

(A)

Study or Subgroup	DOAC Events	DOAC Total	LMWH Events	LMWH Total	Weight	Risk Ratio M-H, Random, 95% CI
Raskob 2017	34	522	46	524	73.4%	0.74 [0.48, 1.14]
Young 2017	8	203	18	203	26.6%	0.44 [0.20, 1.00]
Total (95% CI)		**725**		**727**	**100.0%**	**0.65 [0.42, 1.01]**
Total events	42		64			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 1.21$, df = 1 (P = 0.27); $I^2 = 17\%$
Test for overall effect: Z = 1.92 (P = 0.06)

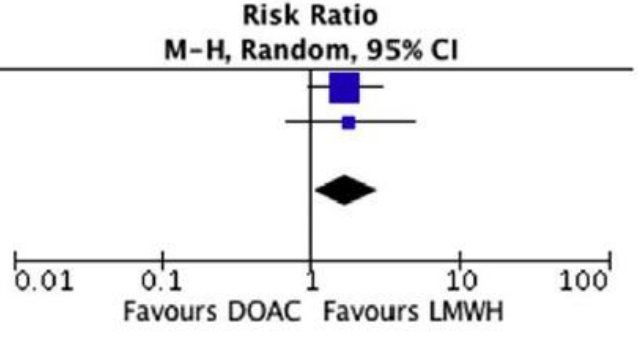


A) VTE recurrence by 6 months

(B)

Study or Subgroup	DOAC Events	DOAC Total	LMWH Events	LMWH Total	Weight	Risk Ratio M-H, Random, 95% CI
Raskob 2017	29	522	17	524	73.5%	1.71 [0.95, 3.08]
Young 2017	11	203	6	203	26.5%	1.83 [0.69, 4.86]
Total (95% CI)		**725**		**727**	**100.0%**	**1.74 [1.05, 2.88]**
Total events	40		23			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.01$, df = 1 (P = 0.91); $I^2 = 0\%$
Test for overall effect: Z = 2.17 (P = 0.03)

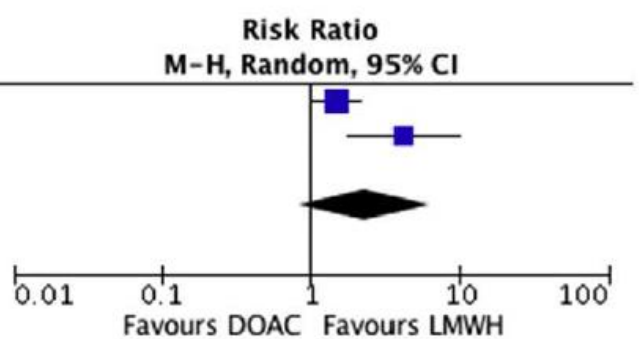


B) Major bleeding by 6 months

(C)

Study or Subgroup	DOAC Events	DOAC Total	LMWH Events	LMWH Total	Weight	Risk Ratio M-H, Random, 95% CI
Raskob 2017	64	522	43	524	57.6%	1.49 [1.04, 2.16]
Young 2017	25	203	6	203	42.4%	4.17 [1.75, 9.94]
Total (95% CI)		**725**		**727**	**100.0%**	**2.31 [0.85, 6.28]**
Total events	89		49			

Heterogeneity: $Tau^2 = 0.42$; $Chi^2 = 4.60$, df = 1 (P = 0.03); $I^2 = 78\%$
Test for overall effect: Z = 1.64 (P = 0.10)

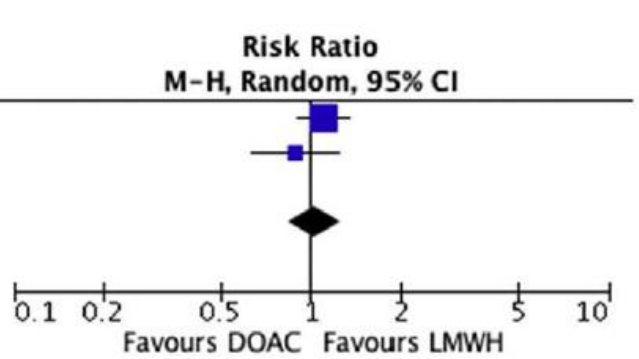


C) Clinically relevant non-major bleeding by 6 months

(D)

Study or Subgroup	DOAC Events	DOAC Total	LMWH Events	LMWH Total	Weight	Risk Ratio M-H, Random, 95% CI
.Raskob 2017	140	522	127	524	69.1%	1.11 [0.90, 1.36]
.Young 2017	48	203	54	203	30.9%	0.89 [0.63, 1.24]
Total (95% CI)		**725**		**727**	**100.0%**	**1.03 [0.85, 1.26]**
Total events	188		181			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.18$, df = 1 (P = 0.28); $I^2 = 15\%$
Test for overall effect: Z = 0.33 (P = 0.74)



D) Overall mortality by 6 months

Which OAC is best?

- Re-bleeding 을 줄이면서 cardiovascular event 는 감소 시키는 것이 중요
- Short half-life , DOAC vs LWMHs
- Low dose vs standard dose

Hindawi
Cardiology Research and Practice
Volume 2022, Article ID 4713826, 10 pages
https://doi.org/10.1155/2022/4713826

Research Article

Real-World Comparisons of Low-Dose NOACs versus Standard-Dose NOACs or Warfarin on Efficacy and Sa Patients with AF: A Meta-Analysis

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Received 29 November 2021; Accepted 9 February 2022; Published 7 March 2022

Academic Editor: Domenico Della Rocca

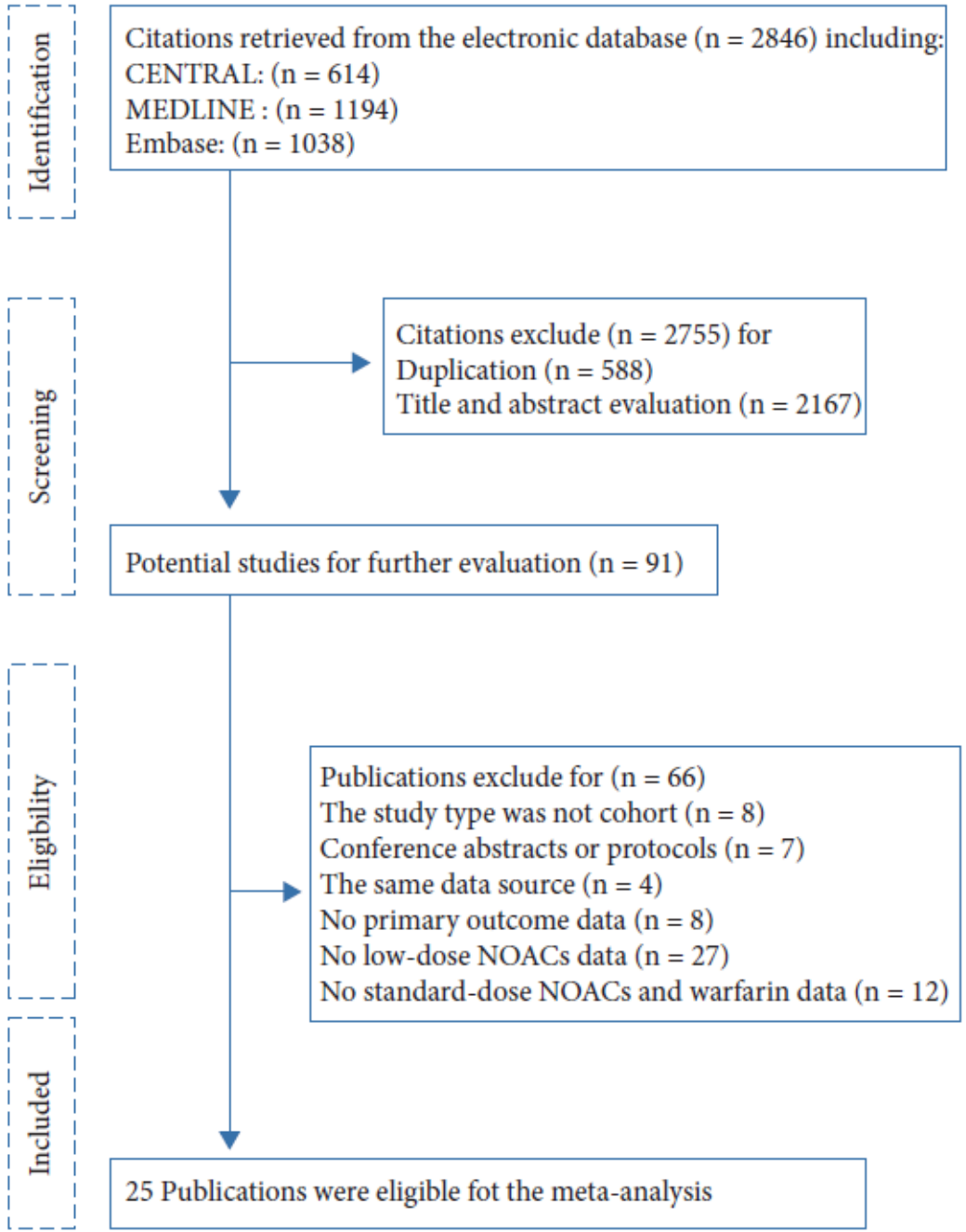


FIGURE 1: Flow-chart for the selection of included studies.

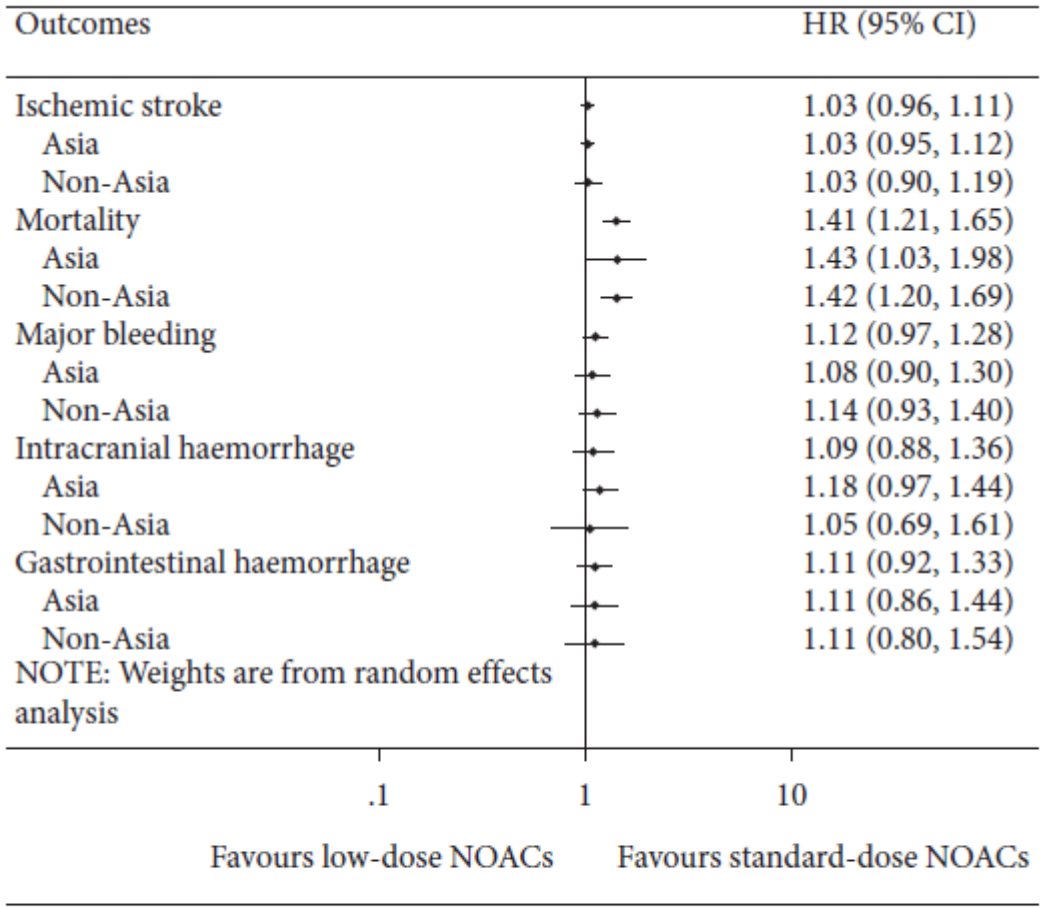


FIGURE 2: Meta-analyses of the efficacy and safety for low-dose NOACs versus standard-dose NOACs. HR = hazard ratio and CI = confidence interval.

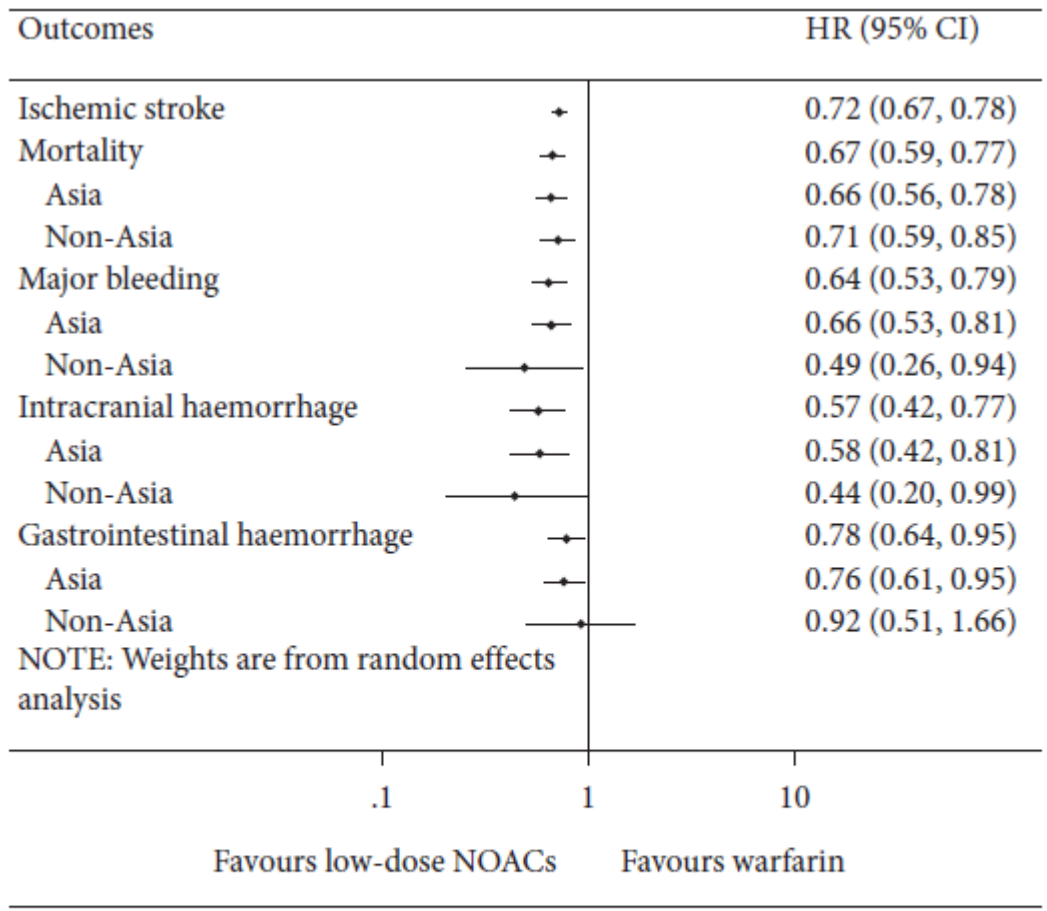


FIGURE 3: Meta-analyses of the efficacy and safety for low-dose NOACs versus warfarin. HR = hazard ratio and CI = confidence interval.

Anti-coagulation with bleeding control? (1)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tranexamic Acid in Patients Undergoing Noncardiac Surgery

P.J. Devereaux, M. Marcucci, T.W. Painter, D. Conen, V. Lomivorotov, D.I. Sessler, M.T.V. Chan, F.K. Borges, M.J. Martínez-Zapata, C.Y. Wang, D. Xavier, S.N. Ofori, M.K. Wang, S. Efremov, G. Landoni, Y.V. Kleinlugtenbelt, W. Szczeklik, D. Schmartz, A.X. Garg, T.G. Short, M. Wittmann, C.S. Meyhoff, M. Amir, D. Torres, A. Patel, E. Duceppe, K. Ruetzler, J.L. Parlow, V. Tandon, E. Fleischmann, C.A. Polanczyk, A. Lamy, S.V. Astrakov, M. Rao, W.K.K. Wu, K. Bhatt, M. de Nadal, V.V. Likhvantsev, P. Paniagua, H.J. Aguado, R.P. Whitlock, M.H. McGillion, M. Prystajecky, J. Vincent, J. Eikelboom, I. Copland, K. Balasubramanian, A. Turan, S.I. Bangdiwala, D. Stillo, P.L. Gross, T. Cafaro, P. Alfonsi, P.S. Roshanov, E.P. Belley-Côté, J. Spence, T. Richards, T. VanHelder, W. McIntyre, G. Guyatt, S. Yusuf, and K. Leslie, for the POISE-3 Investigators*

Devereaux, P. J., et al. "Tranexamic acid in patients undergoing noncardiac surgery." *New England Journal of Medicine* 386.21 (2022): 1986-1997.

Anti-coagulation with bleeding control? (2)

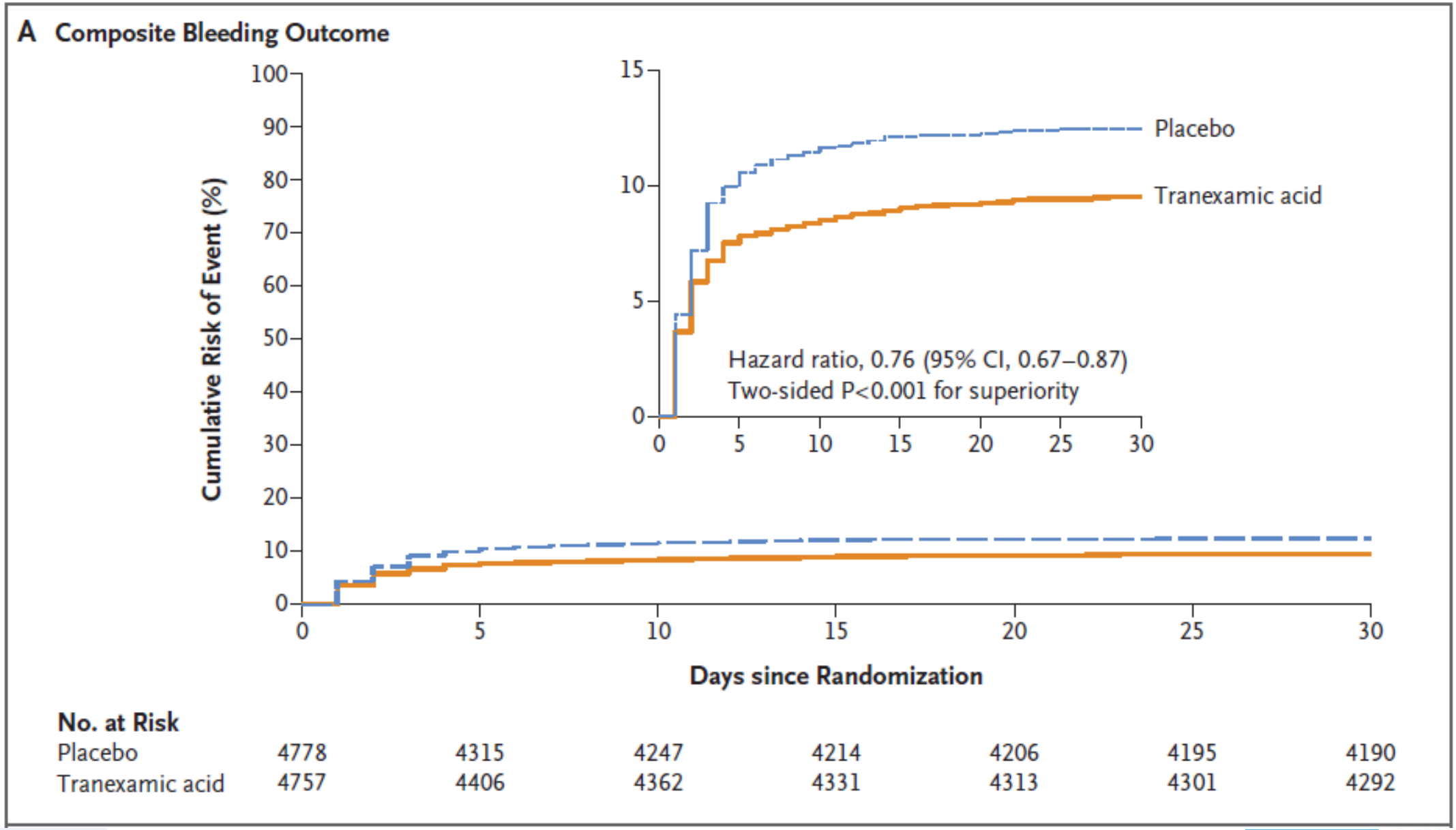
- Method
  - randomly assigned to receive tranexamic acid 1g or placebo at the start and end of surgery

- Results
  - A total of 9535 patients underwent randomization
  - 4757 tranexamic acid vs 4778 patients in the placebo

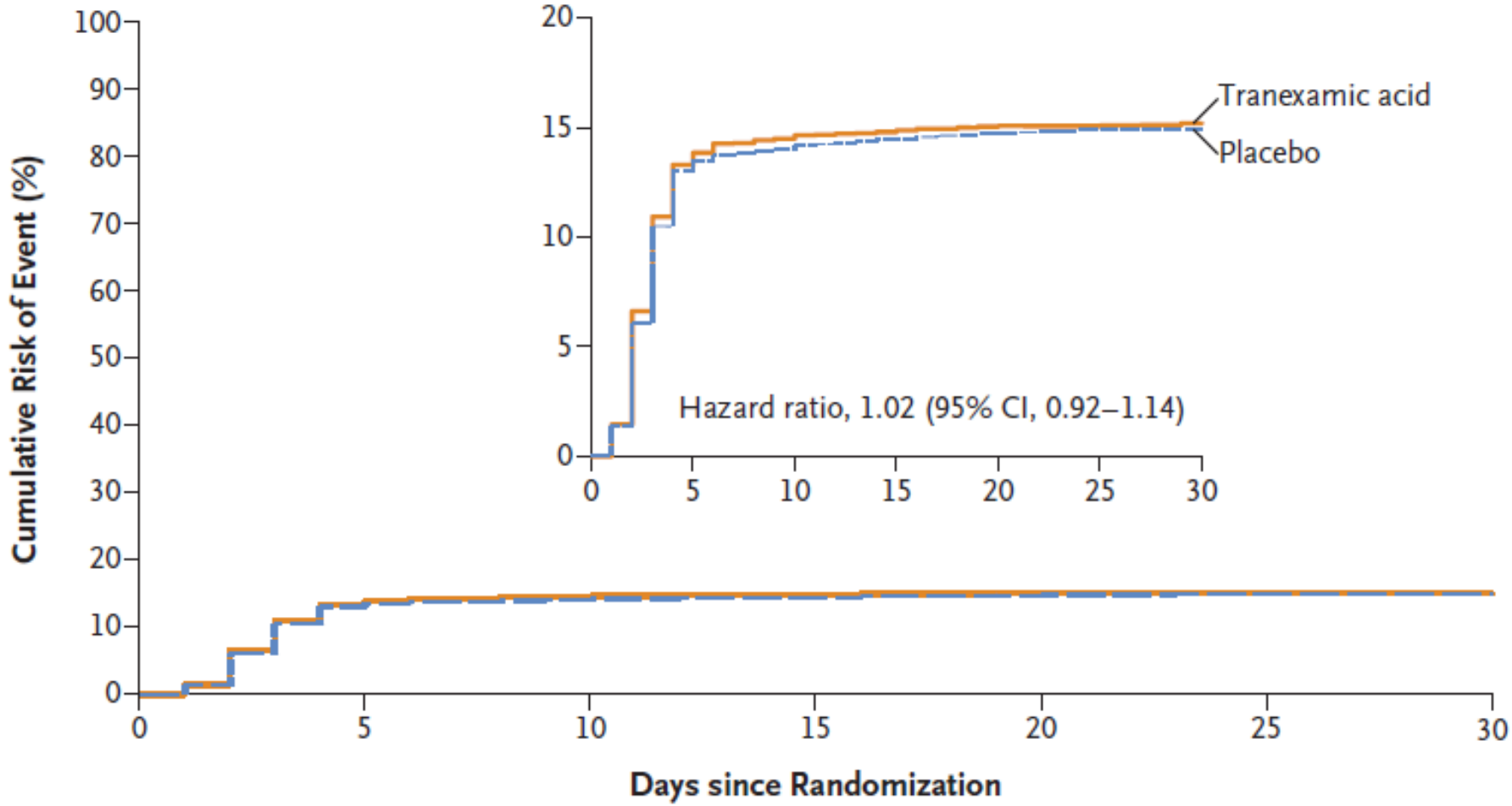
- Conclusions
  - bleeding outcome was significantly lower with tranexamic acid than with placebo
  - Difference in the composite cardiovascular outcome was small

Table 2. Effects of Tranexamic Acid on 30-Day Outcomes.*

Outcome	Tranexamic Acid (N=4757)	Placebo (N=4778)	Hazard Ratio (95% CI)†	P Value
Primary efficacy outcome: composite bleeding outcome — no. (%)‡	433 (9.1)	561 (11.7)	0.76 (0.67–0.87)	<0.001§
Individual components of composite bleeding outcome — no. (%)				
Life-threatening bleeding¶	78 (1.6)	79 (1.7)	0.99 (0.73–1.36)	
Major bleeding¶	363 (7.6)	496 (10.4)	0.72 (0.63–0.83)	
Bleeding into a critical organ¶	12 (0.3)	21 (0.4)	0.57 (0.28–1.16)	
Primary safety outcome: composite cardiovascular outcome — no./total no. (%)‖	649/4581 (14.2)	639/4601 (13.9)	1.02 (0.92–1.14)	0.04**
Individual components of composite cardiovascular outcome — no. (%)				
MINS¶	608 (12.8)	602 (12.6)	1.02 (0.91–1.14)	
Nonhemorrhagic stroke††	24 (0.5)	16 (0.3)	1.51 (0.80–2.84)	
Peripheral arterial thrombosis‡‡	22 (0.5)	23 (0.5)	0.96 (0.53–1.72)	
Symptomatic proximal venous thromboembolism††	32 (0.7)	28 (0.6)	1.15 (0.69–1.91)	
Other secondary outcomes — no. (%)				
Bleeding independently associated with death after noncardiac surgery	416 (8.7)	541 (11.3)	0.76 (0.67–0.87)	
MINS not fulfilling the universal definition of myocardial infarction	549 (11.5)	549 (11.5)	1.01 (0.89–1.13)	
Myocardial infarction	67 (1.4)	53 (1.1)	1.27 (0.89–1.82)	
Net risk–benefit outcome‡‡	983 (20.7)	1046 (21.9)	0.94 (0.86–1.02)	



B Composite Cardiovascular Outcome



No. at Risk

Placebo	4601	4031	3987	3963	3949	3940	3935
Tranexamic acid	4581	4010	3959	3941	3923	3921	3910

Summary

- Bleeding control 은 TXA 를 통해서 조기에 하더라도 VTE 발생을 증가 시키지 않는다
- anti-coagulation 을 하지 않는 것 보다는 OAC 를 통한 anti-coagulation 을 하는 것이 좋다
- 다만 시작 시기는 TE vs recurrence ICH 에 대한 환자의 risk factor 따라 다를 수 있다.
- 아직까지 대규모 연구가 부족 하기는 하지만 LWMH vs warfarin vs low dose DOAC vs standard dose DOAC 에서 선택을 해야 한다면 low dose DOACs vs standard dose DOAC 에서 고민 하는 것이 좋겠다.

What is your treatment choice?

1) Anti-coagulation without bleeding control

2) Bleeding control without anti-coagulation

3) Anti-coagulation with bleeding control

4) No treatment

My choice

- Early use TXA and low dose or normal dose OAC use as soon as.

- After 2 weeks onset ICH
  1) start LWMH 1mg per kg q12h SC
  2) after LWMH start 5 days after change Low dose DOAC with EN
  3) Apixaban 2.5mg bid for 3 month
  4) And f/u pulmonary angio CT with enhanced
  5) Decision stop the medication or use more duration.

Question

감사합니다.