Recenti evidenze e nuove prospettive per la terapia del TEV

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Novel oral anticoagulant shop

blood

Prepublished online June 24, 2014;
doi:10.1182/blood-2014-04-571232

Direct oral anticoagulants compared with vitamin K antagonists for acute symptomatic venous thromboembolism: evidence from phase 3 trials

Nick van Es, Michiel Coppens, Sam Schulman, Saskia Middeldorp and Harry R. Büller

First VTE or VTE-related death

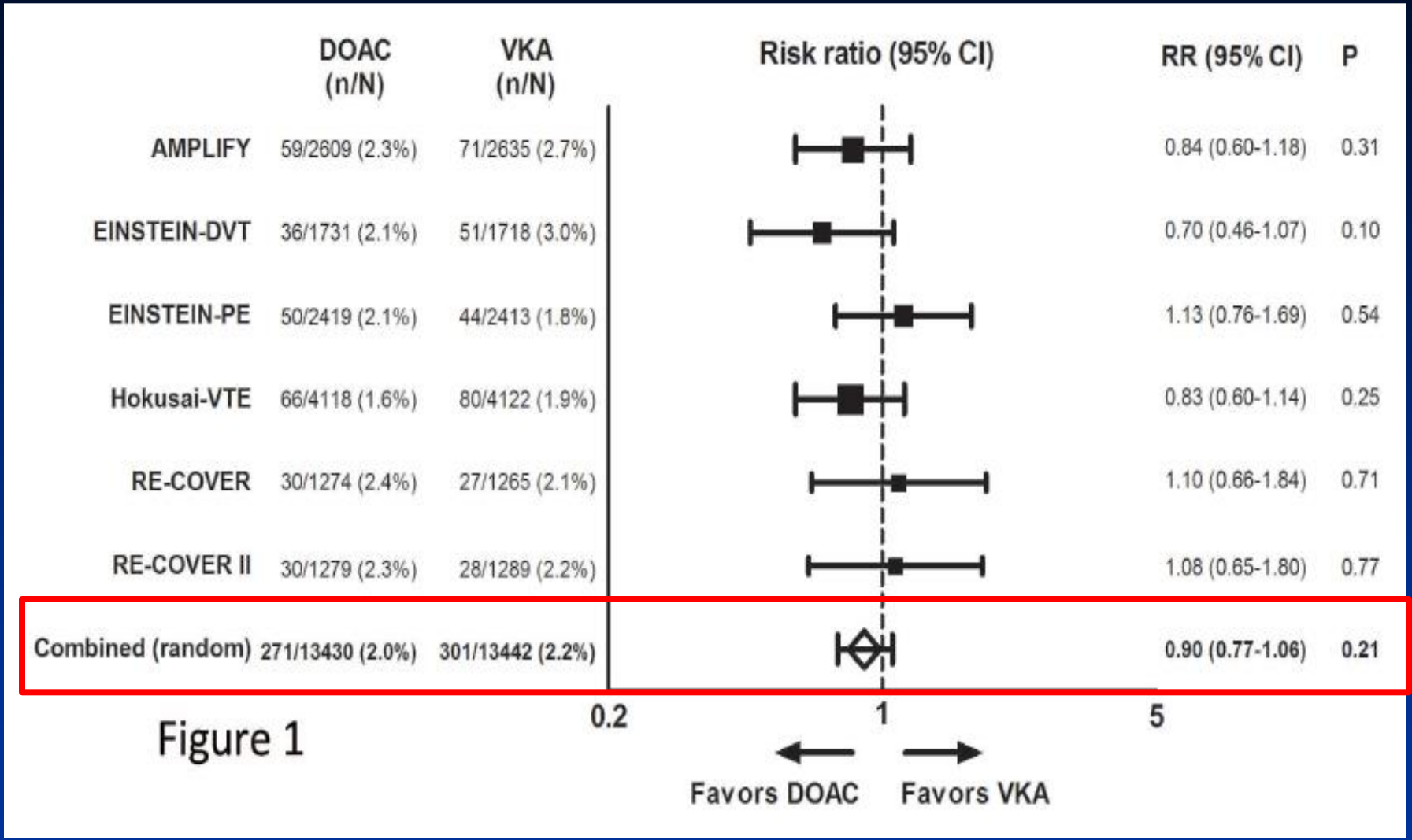


Figure 1

Major bleedings

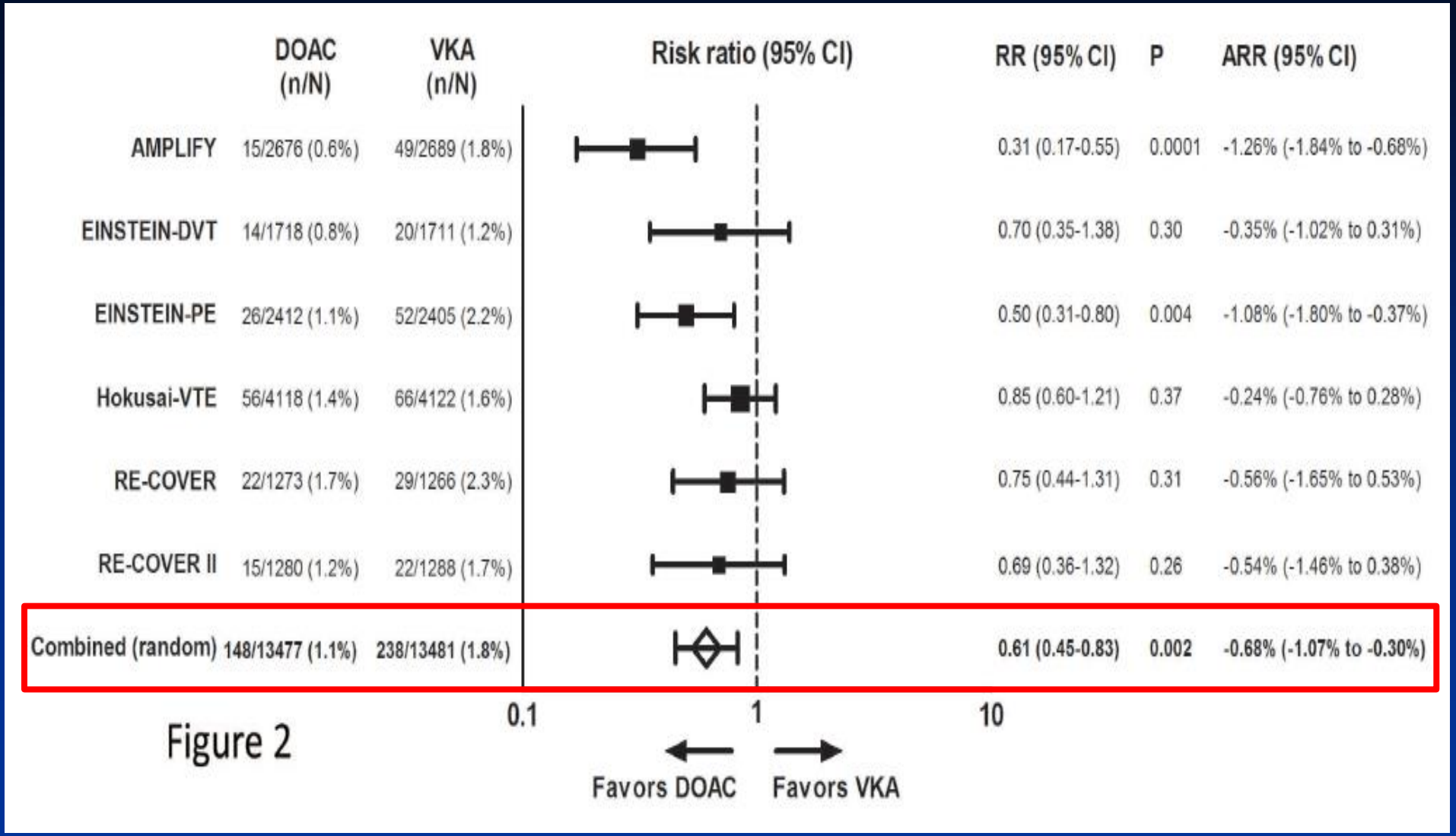


Figure 2

Quale DOAC per la terapia del TEV?

Annals of Internal Medicine

ORIGINAL RESEARCH

Risk for Recurrent Venous Thromboembolism and Bleeding With Apixaban Compared With Rivaroxaban: An Analysis of Real-World Data

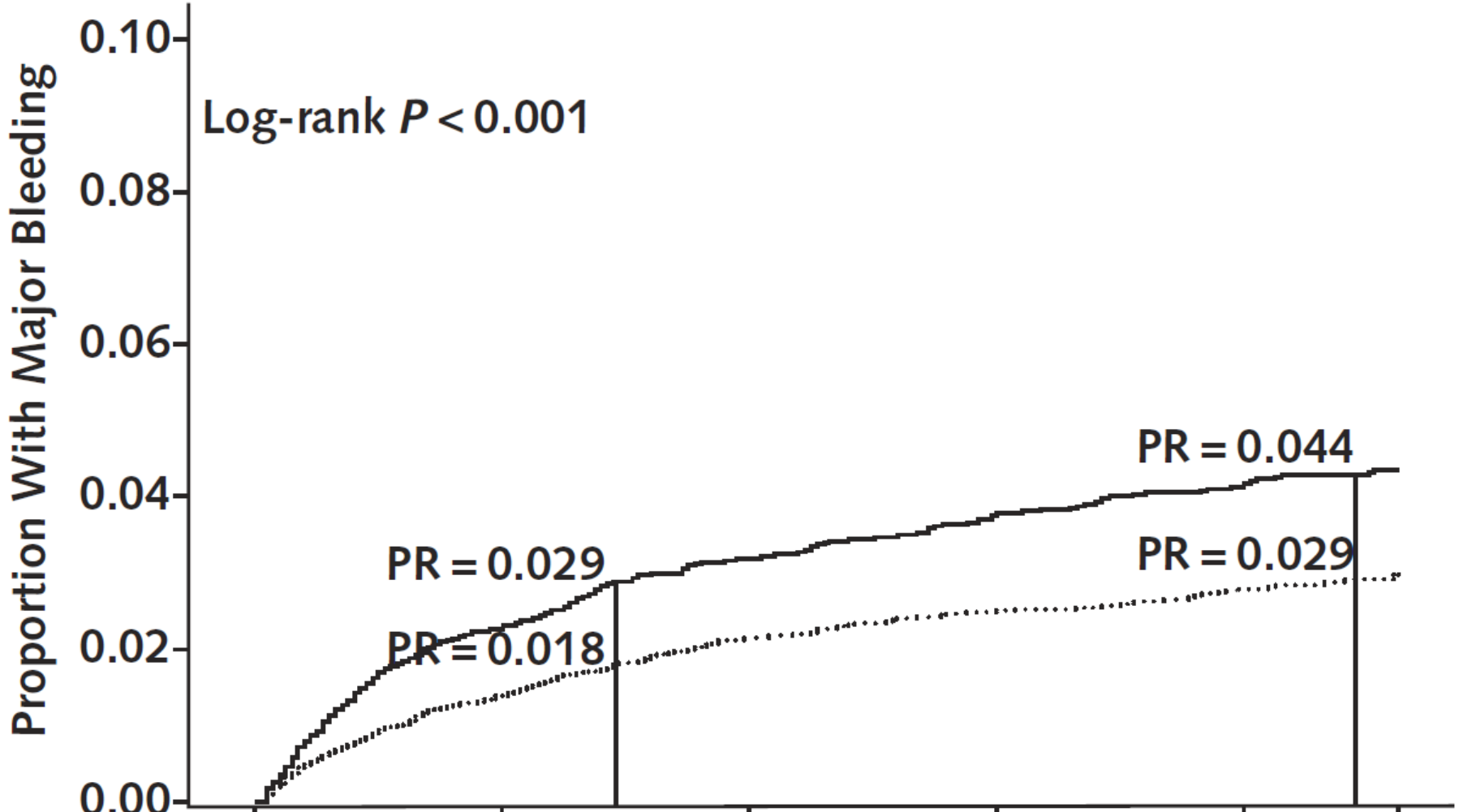
Ghadeer K. Dawwas, MSc, MBA, PhD; Charles E. Leonard, PharmD, MSCE; James D. Lewis, MD, MSCE; and Adam Cuker, MD, MS

Dal colosso assicurativo nordamericano OPTUM (Pennsylvania)

Ann Intern Med 2021

Table 1. Demographic and Clinical Characteristics of New Users of Apixaban and Rivaroxaban Among Patients With VTE

Characteristic	Prematching Cohort			Postmatching Cohort		
	Apixaban (*n* = 28 287)	Rivaroxaban (*n* = 21 613)	Standardized Difference	Apixaban (*n* = 18 618)	Rivaroxaban (*n* = 18 618)	Standardized Difference
Demographic characteristics						
Mean age (SD), *y*	70.3 (14.3)	65.7 (15.6)	0.33	67.4 (15.1)	67.5 (14.8)	0.01
Male sex, *n (%)*	12 729 (45.0)	10 411 (48.2)	0.06	8839 (47.5)	8823 (47.4)	0.00
Baseline comorbid conditions, *n (%)*						
Alcohol use disorder	1222 (4.3)	896 (4.1)	0.01	793 (4.3)	768 (4.1)	0.01
Anemia	4840 (17.1)	3134 (14.5)	0.07	2819 (15.1)	2796 (15.0)	0.00
Angina	782 (2.8)	471 (2.2)	0.04	433 (2.3)	433 (2.3)	0.00
Cancer	6273 (22.2)	4703 (21.8)	0.01	3979 (21.4)	4171 (22.4)	0.03
Chronic kidney disease	11 551 (40.8)	6042 (28.0)	0.26	5681 (30.5)	5765 (31.0)	0.01
Chronic lung disease	10 127 (35.8)	6577 (30.4)	0.11	5906 (31.7)	5941 (31.9)	0.00
Coronary artery disease	372 (1.3)	249 (1.2)	0.01	224 (1.2)	229 (1.2)	0.00
Diabetes	9937 (35.1)	5871 (27.2)	0.17	5491 (29.5)	5478 (29.4)	0.00
Drug misuse disorder	1490 (5.3)	984 (4.6)	0.03	874 (4.7)	877 (4.7)	0.00
End-stage renal disease	614 (2.2)	81 (0.4)	0.12	279 (1.5)	76 (0.4)	0.09
Heart failure	7752 (27.4)	3746 (17.3)	0.23	3619 (19.4)	3623 (19.5)	0.00
Hemophilia	37 (0.1)	82 (0.4)	0.07	37 (0.2)	35 (0.2)	0.00
HIV infection	123 (0.4)	81 (0.4)	0.01	70 (0.4)	76 (0.4)	0.01
Hyperlipidemia	14 756 (52.2)	9438 (43.7)	0.17	8670 (46.6)	8611 (46.3)	0.01
Hypertension	21 538 (76.1)	14 026 (64.9)	0.26	12 783 (68.7)	12 840 (69.0)	0.01
Liver disease	3489 (12.3)	2320 (10.7)	0.05	2078 (11.2)	2101 (11.3)	0.00
Peripheral vascular disease	7602 (26.9)	3922 (18.1)	0.20	3769 (20.2)	3769 (20.2)	0.00
Stroke	7755 (27.4)	3375 (15.6)	0.26	3604 (19.4)	3255 (17.5)	0.05
Tobacco use	54 (0.2)	16 (0.1)	0.03	16 (0.1)	16 (0.1)	0.00
Transient ischemic attack	3981 (14.1)	3215 (14.9)	0.02	2734 (14.7)	2698 (14.5)	0.01
Ulcer	2663 (9.4)	1358 (6.3)	0.11	1264 (6.8)	1292 (6.9)	0.01



At risk, *n*					
Apixaban	18 618	11 715	8623	5592	3886
Rivaroxaban	18 618	10 496	7652	5029	3729

Impiego dei DOAC nella grave insufficienza renale

Thrombosis Research 229 (2023) 77–85

Contents lists available at ScienceDirect

Thrombosis Research

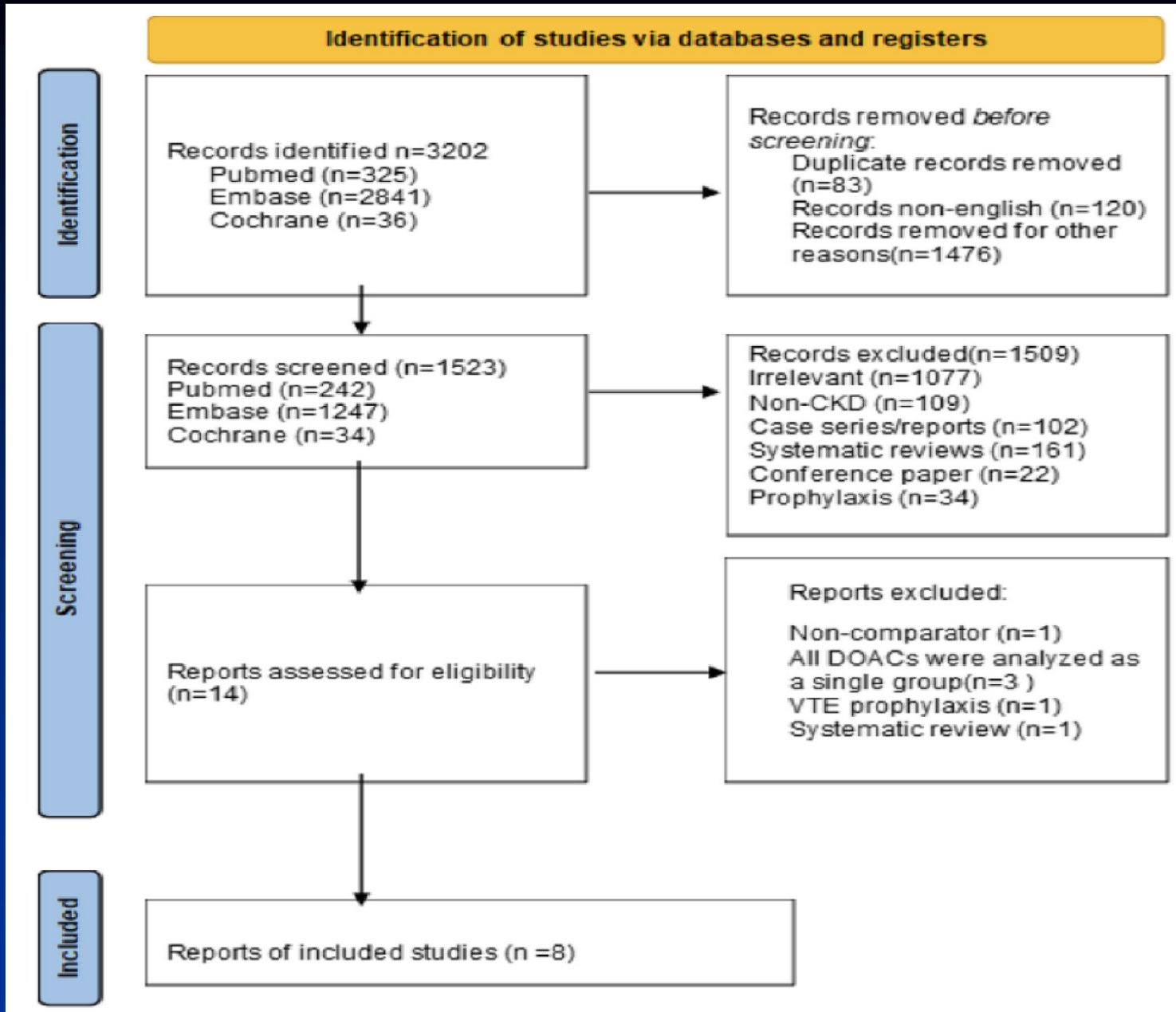
journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Safety and efficacy of apixaban versus low-molecular weight heparin or vitamin-K antagonists for venous thromboembolism treatment in patients with severe renal failure: A systematic review and meta-analysis

Anwar Almajdi [a], Sara Almutairi [a], Maha Alharbi [b,*]

[a] College of Pharmacy, Kuwait University, Kuwait
[b] Department of Pharmacy Practice, College of Pharmacy, Kuwait University, Kuwait



DOACs=direct anticoagulants, CKD= chronic kidney disease, VTE= venous thromboembolism.

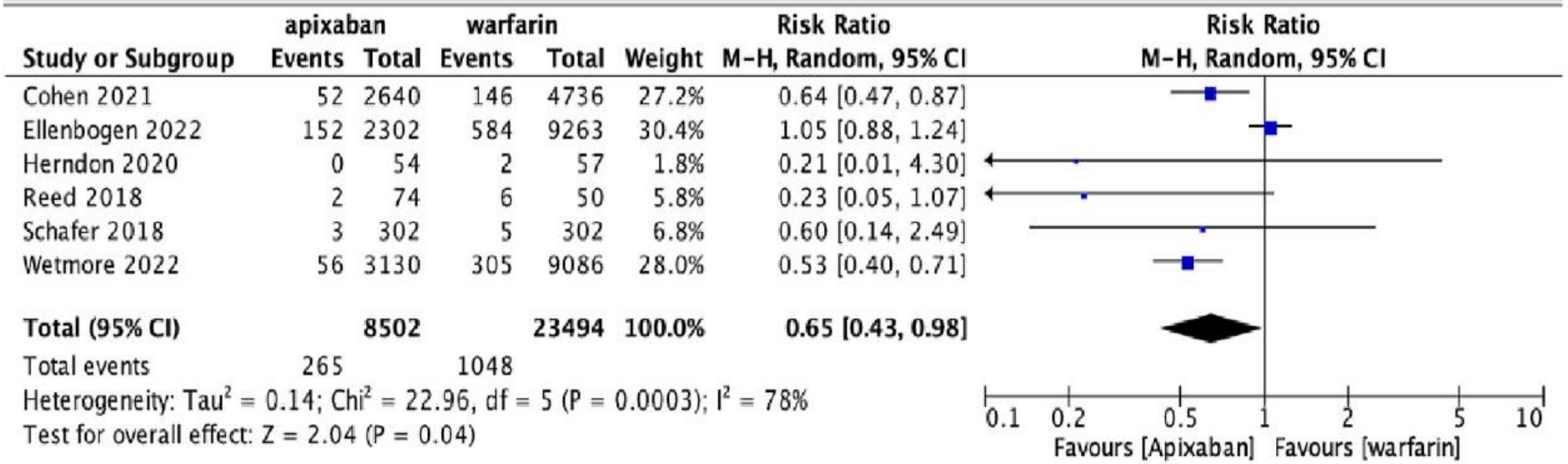


Fig. 2. Recurrent VTE.

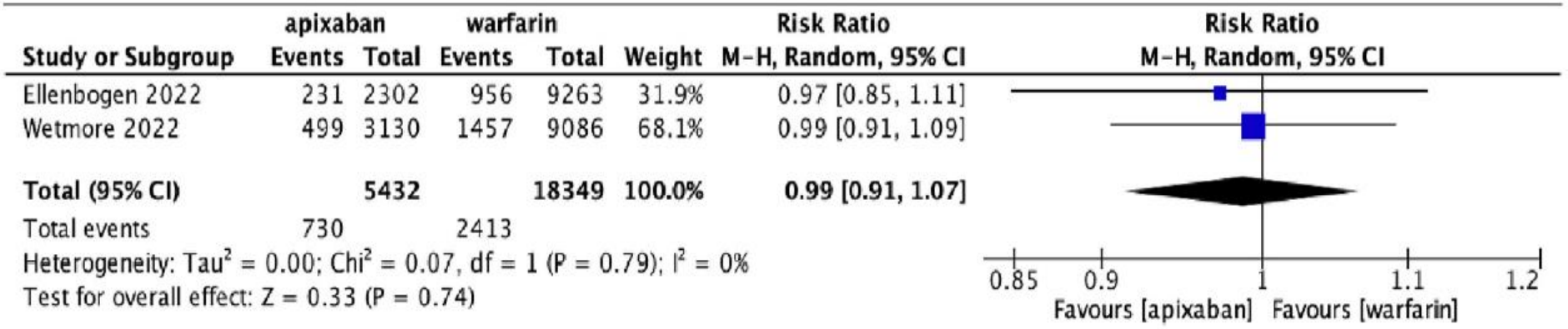


Fig. 3. All-cause mortality.

Study or Subgroup	apixaban Events	Total	warfarin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Sarrat 2017	0	40	7	120	0.3%	0.20 [0.01, 3.37]
Hanni 2020	1	128	12	733	0.6%	0.48 [0.06, 3.64]
Herndon 2020	4	54	8	57	1.8%	0.53 [0.17, 1.65]
Reed 2018	4	74	11	50	1.9%	0.25 [0.08, 0.73]
Schafer 2018	33	302	63	302	11.7%	0.52 [0.35, 0.77]
Cohen 2021	113	2640	232	4736	24.0%	0.87 [0.70, 1.09]
Wetmore 2022	103	3130	402	9086	24.8%	0.74 [0.60, 0.92]
Ellenbogen 2022	238	2302	1269	9263	35.0%	0.75 [0.66, 0.86]
Total (95% CI)		**8670**		**24347**	**100.0%**	**0.72 [0.62, 0.84]**
Total events	496		2004			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 10.58$, df = 7 (P = 0.16); $I^2 = 34\%$
Test for overall effect: Z = 4.16 (P < 0.0001)

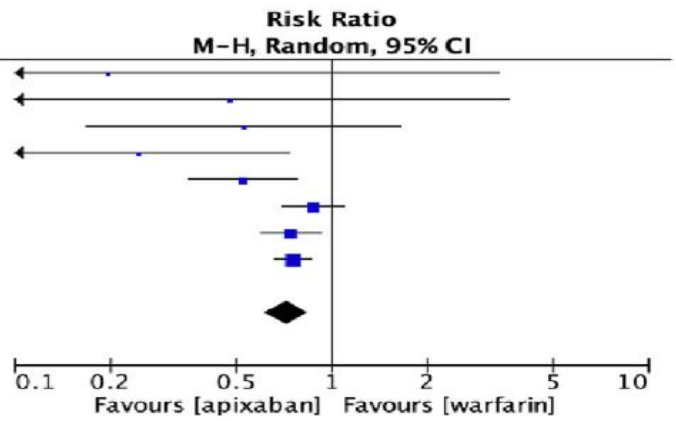


Fig. 4. Major bleeding.

Study or Subgroup	apixaban Events	Total	warfarin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Cohen 2021	253	2640	657	4736	45.3%	0.69 [0.60, 0.79]
Ellenbogen 2022	351	2302	1675	9263	48.8%	0.84 [0.76, 0.94]
Herndon 2020	4	54	3	57	2.2%	1.41 [0.33, 6.00]
Sarrat 2017	5	40	7	120	3.7%	2.14 [0.72, 6.38]
Total (95% CI)		**5036**		**14176**	**100.0%**	**0.81 [0.65, 1.00]**
Total events	613		2342			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 8.98$, df = 3 (P = 0.03); $I^2 = 67\%$
Test for overall effect: Z = 1.92 (P = 0.05)

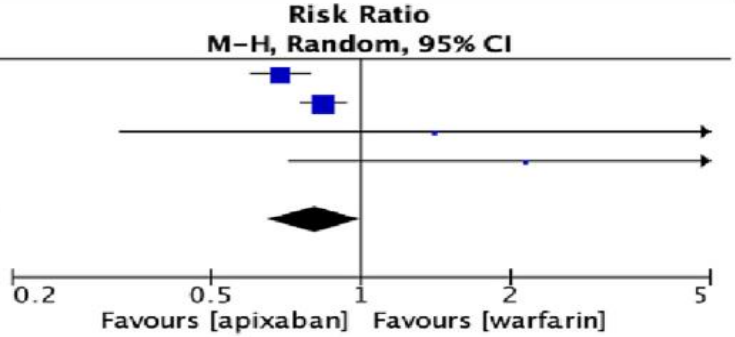


Fig. 5. CRNMB.

Study or Subgroup	apixaban Events	Total	warfarin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Hanni 2020	6	128	64	733	58.9%	0.54 [0.24, 1.21]
Herndon 2020	3	54	15	57	31.5%	0.21 [0.06, 0.69]
Sarrat 2017	1	40	3	120	9.6%	1.00 [0.11, 9.34]
Total (95% CI)		**222**		**910**	**100.0%**	**0.42 [0.21, 0.86]**
Total events	10		82			

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 2.23$, df = 2 (P = 0.33); $I^2 = 10\%$
Test for overall effect: Z = 2.38 (P = 0.02)

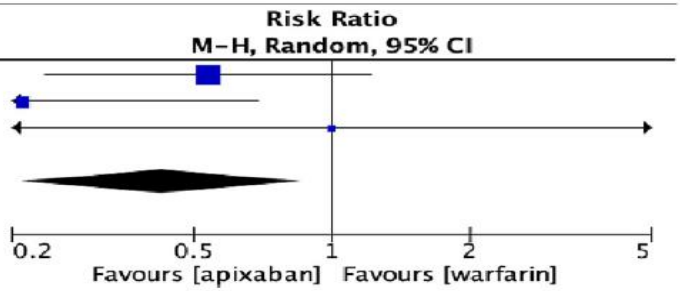
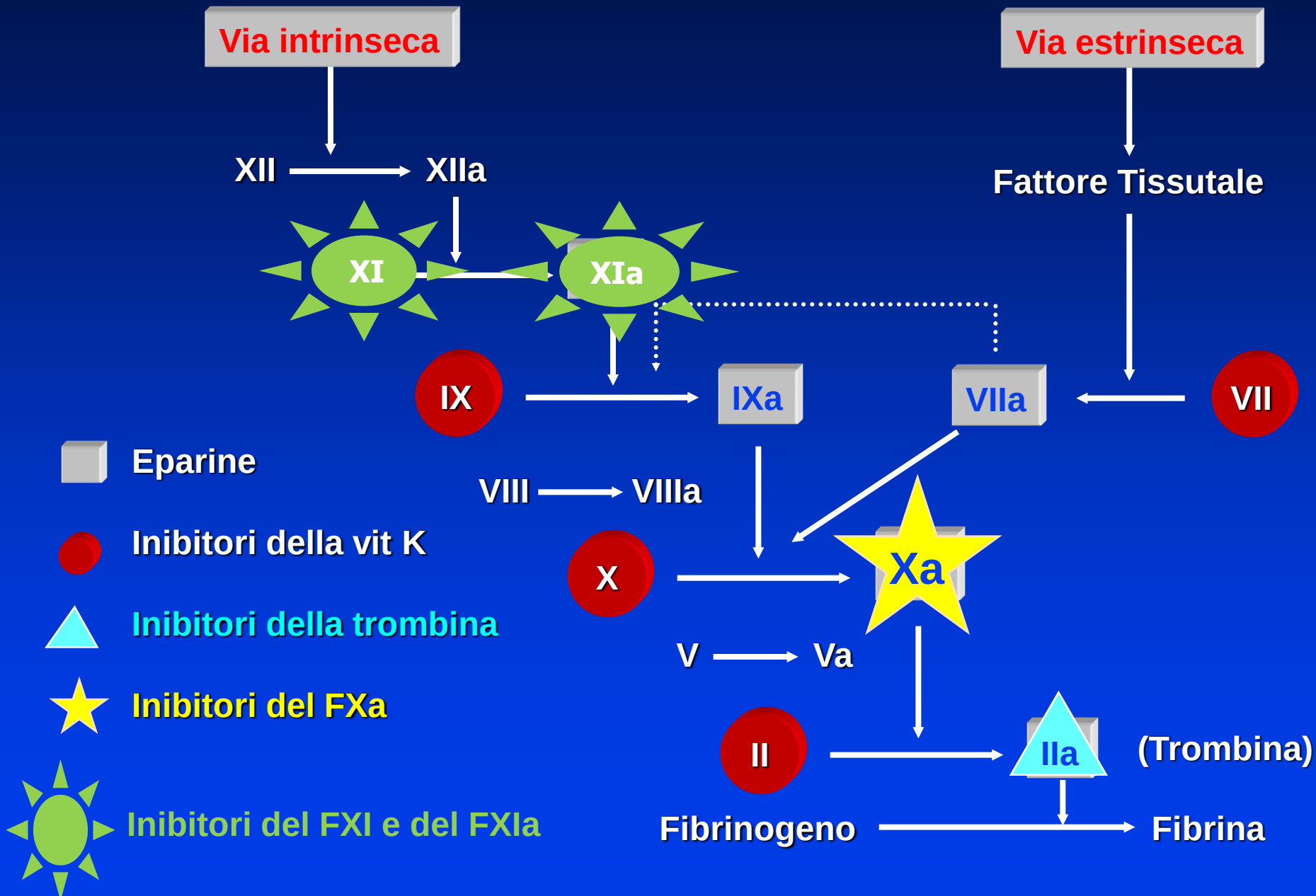
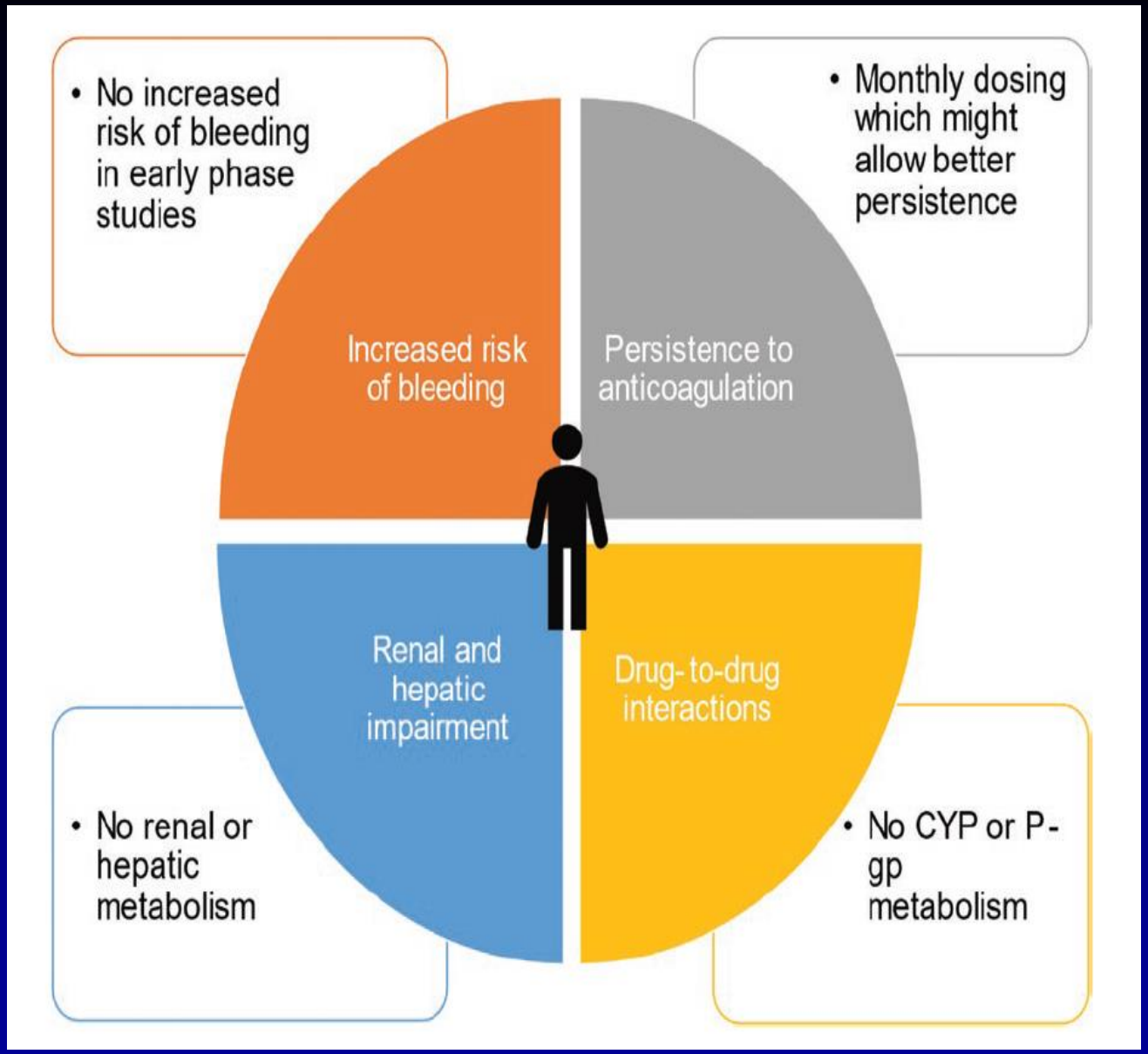


Fig. 6. Minor bleeding.

Prospettive legate agli inibitori del fattore XI

Bersaglio di vecchi e nuovi farmaci anticoagulanti





Abelacimab per la terapia del TEV in soggetti con K

- ASTER (vs apixaban)
- MAGNOLIA (vs dalteparina in pazienti con neoplasie GI o GU)

Prospettive legate alla trombolisi

Review › Circulation. 2024 Sep 10;150(11):884-898. doi: 10.1161/CIRCULATIONAHA.124.069728. Epub 2024 Sep 9.

Targeting Fibrinolytic Inhibition for Venous Thromboembolism Treatment: Overview of an Emerging Therapeutic Approach

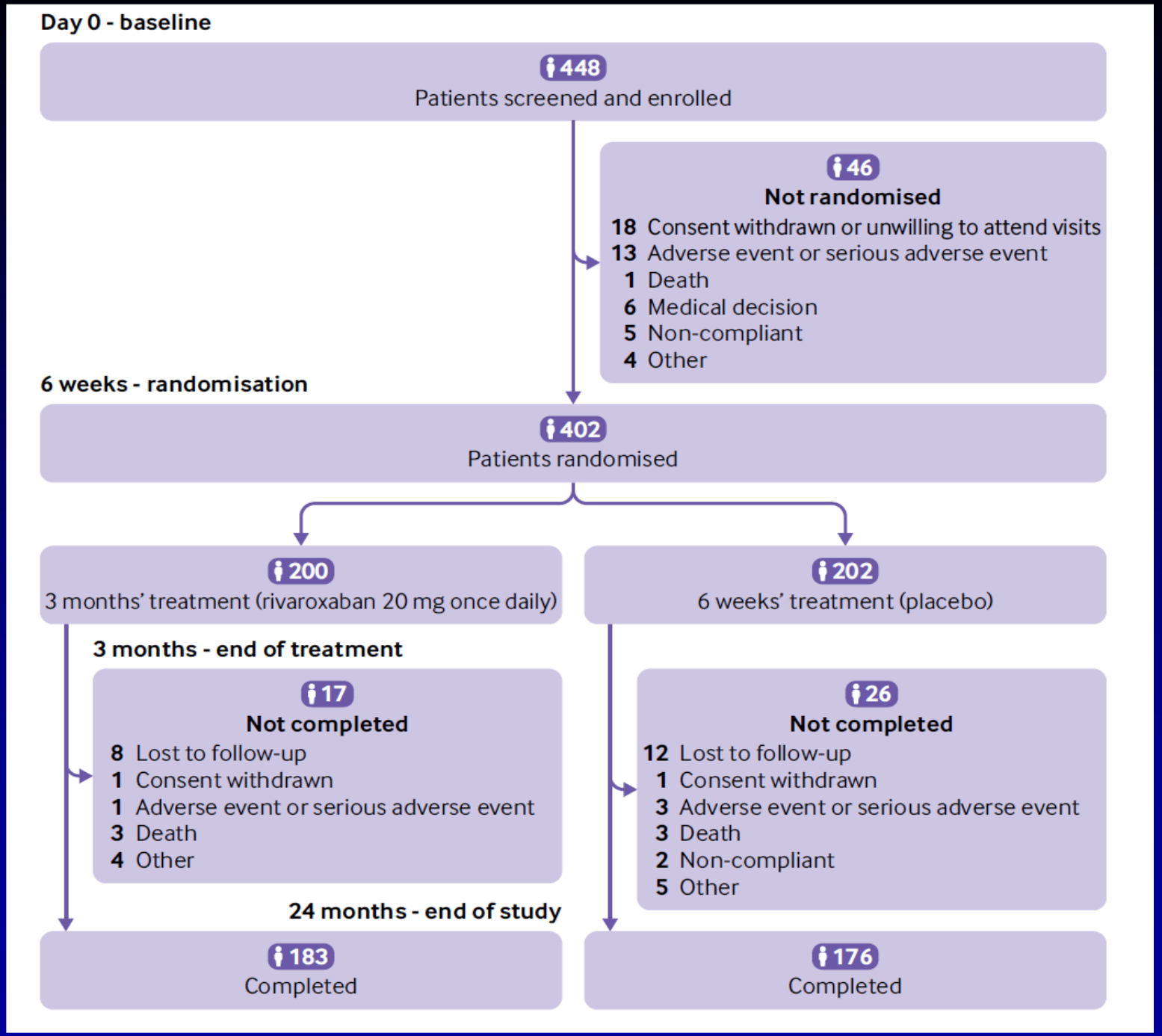
Satish Singh [1 2], Pardeep Kumar [1 3], Yogendra S Padwad [1 3], Farouc A Jaffer [4], Guy L Reed [2]

Rivalutazione della TVP distale isolata

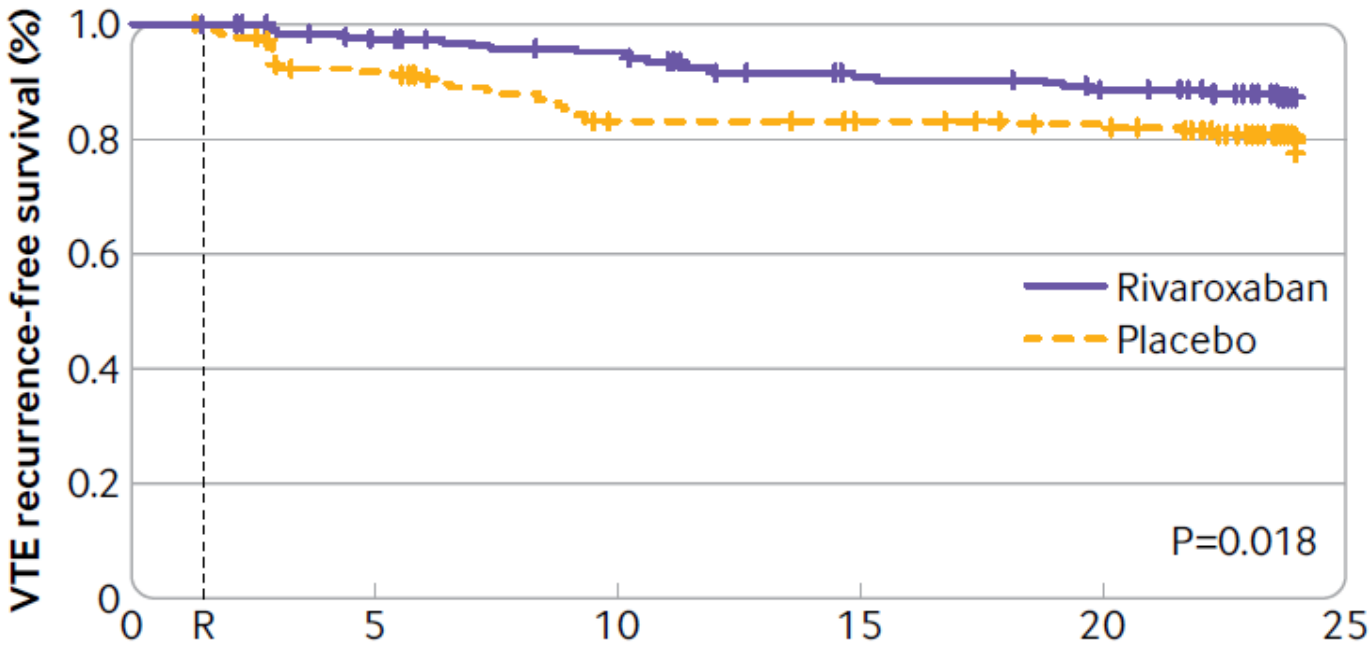
Rivaroxaban treatment for six weeks versus three months in patients with symptomatic isolated distal deep vein thrombosis: randomised controlled trial

Walter Ageno,[1] Lorenza Bertù,[1] Eugenio Bucherini,[2] Giuseppe Camporese,[3] Francesco Dentali,[1] Matteo Iotti,[4] Gianfranco Lessiani,[5] Roberto Parisi,[6] Paolo Prandoni,[7] Michelangelo Sartori,[8] Adriana Visonà,[9] Elisabetta Bigagli,[10] Gualtiero Palareti,7 on behalf of the RIDTS study group

BMJ 2022; 379: e072623


Day 0 - baseline
448
Patients screened and enrolled
46
Not randomised
18 Consent withdrawn or unwilling to attend visits
13 Adverse event or serious adverse event
1 Death
6 Medical decision
5 Non-compliant
4 Other
6 weeks - randomisation
402
Patients randomised
200
3 months' treatment (rivaroxaban 20 mg once daily)
202
6 weeks' treatment (placebo)
3 months - end of treatment
17
Not completed
8 Lost to follow-up
1 Consent withdrawn
1 Adverse event or serious adverse event
3 Death
4 Other
26
Not completed
12 Lost to follow-up
1 Consent withdrawn
3 Adverse event or serious adverse event
3 Death
2 Non-compliant
5 Other
24 months - end of study
183
Completed
176
Completed

Characteristics	Rivaroxaban group (n=200)	Placebo group (n=202)
Sex:		
Women	116 (58)	119 (59)
Men	84 (42)	83 (41)
Mean (SD) age (years)	65.0 (16.0)	65.3 (15.4)
Mean (SD) body mass index	26.5 (4.4)	26.9 (4.5)
Site of thrombosis:		
Axial vein	69 (34)	71 (35)
Muscular vein	131 (65)	131 (65)
Symptoms at baseline:		
Swelling	114 (57)	109 (54)
Erythema	8 (4)	14 (7)
Pain	160 (80)	156 (77)
Other	9 (4)	10 (5)
Time from symptom onset to enrolment (days):		
1-5	151 (75)	144 (71)
6-10	20 (10)	36 (18)
>10	29 (14)	22 (11)
Risk factors for venous thromboembolism:		
None	81 (40)	86 (43)
Surgery	30 (15)	17 (8)
Injury	35 (17)	41 (20)
Prolonged bed rest	29 (14)	25 (12)
Oral contraception	8 (4)	7 (3)
Pregnancy	0 (0)	0 (0)
Obesity	12 (6)	18 (9)
Acute condition	5 (2)	2 (1)
Other	30 (15)	33 (16)
High risk patients	187 (93)	191 (94)
Family history of venous thromboembolism	25 (12)	33 (16)
Previous venous thromboembolism	33 (16)	26 (13)
Comorbidities:		

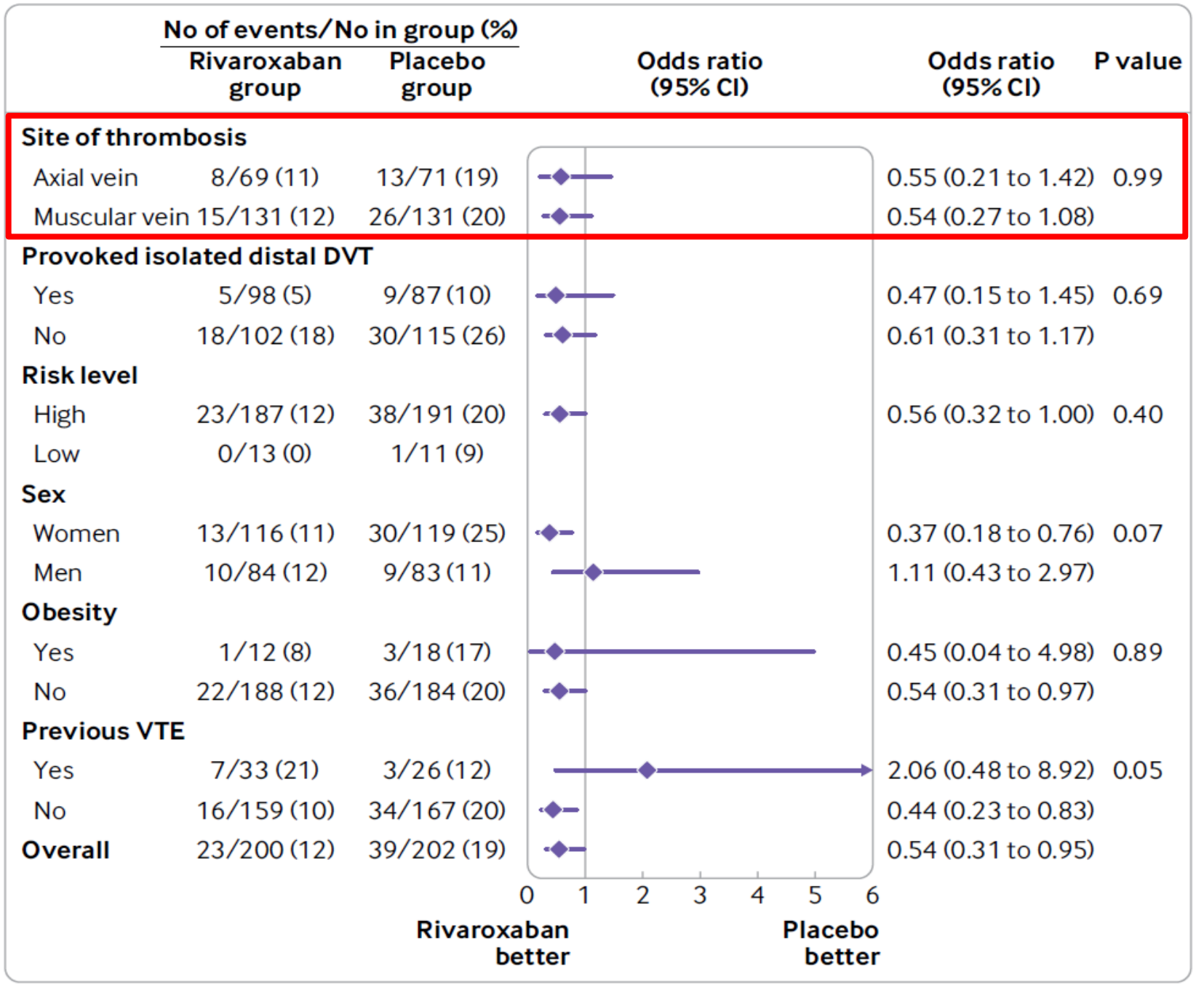


No at risk

Placebo					
202	178	153	150	143	0
Rivaroxaban					
200	188	180	164	157	0

Fig 2 | Kaplan-Meier curve showing recurrence-free survival in patients with symptomatic isolated distal deep vein thrombosis. VTE=venous thromboembolism

No major bleedings from prolonging rivaroxaban


No of events/No in group (%)
Rivaroxaban group
Placebo group
Odds ratio (95% CI)
Odds ratio (95% CI)
P value
Site of thrombosis
Axial vein 8/69 (11) 13/71 (19) 0.55 (0.21 to 1.42) 0.99
Muscular vein 15/131 (12) 26/131 (20) 0.54 (0.27 to 1.08)
Provoked isolated distal DVT
Yes 5/98 (5) 9/87 (10) 0.47 (0.15 to 1.45) 0.69
No 18/102 (18) 30/115 (26) 0.61 (0.31 to 1.17)
Risk level
High 23/187 (12) 38/191 (20) 0.56 (0.32 to 1.00) 0.40
Low 0/13 (0) 1/11 (9)
Sex
Women 13/116 (11) 30/119 (25) 0.37 (0.18 to 0.76) 0.07
Men 10/84 (12) 9/83 (11) 1.11 (0.43 to 2.97)
Obesity
Yes 1/12 (8) 3/18 (17) 0.45 (0.04 to 4.98) 0.89
No 22/188 (12) 36/184 (20) 0.54 (0.31 to 0.97)
Previous VTE
Yes 7/33 (21) 3/26 (12) 2.06 (0.48 to 8.92) 0.05
No 16/159 (10) 34/167 (20) 0.44 (0.23 to 0.83)
Overall 23/200 (12) 39/202 (19) 0.54 (0.31 to 0.95)
0 1 2 3 4 5 6
Rivaroxaban better
Placebo better

Six-week low-molecular-weight heparin versus 12-week warfarin for calf deep vein thrombosis: A randomized, prospective, open-label study

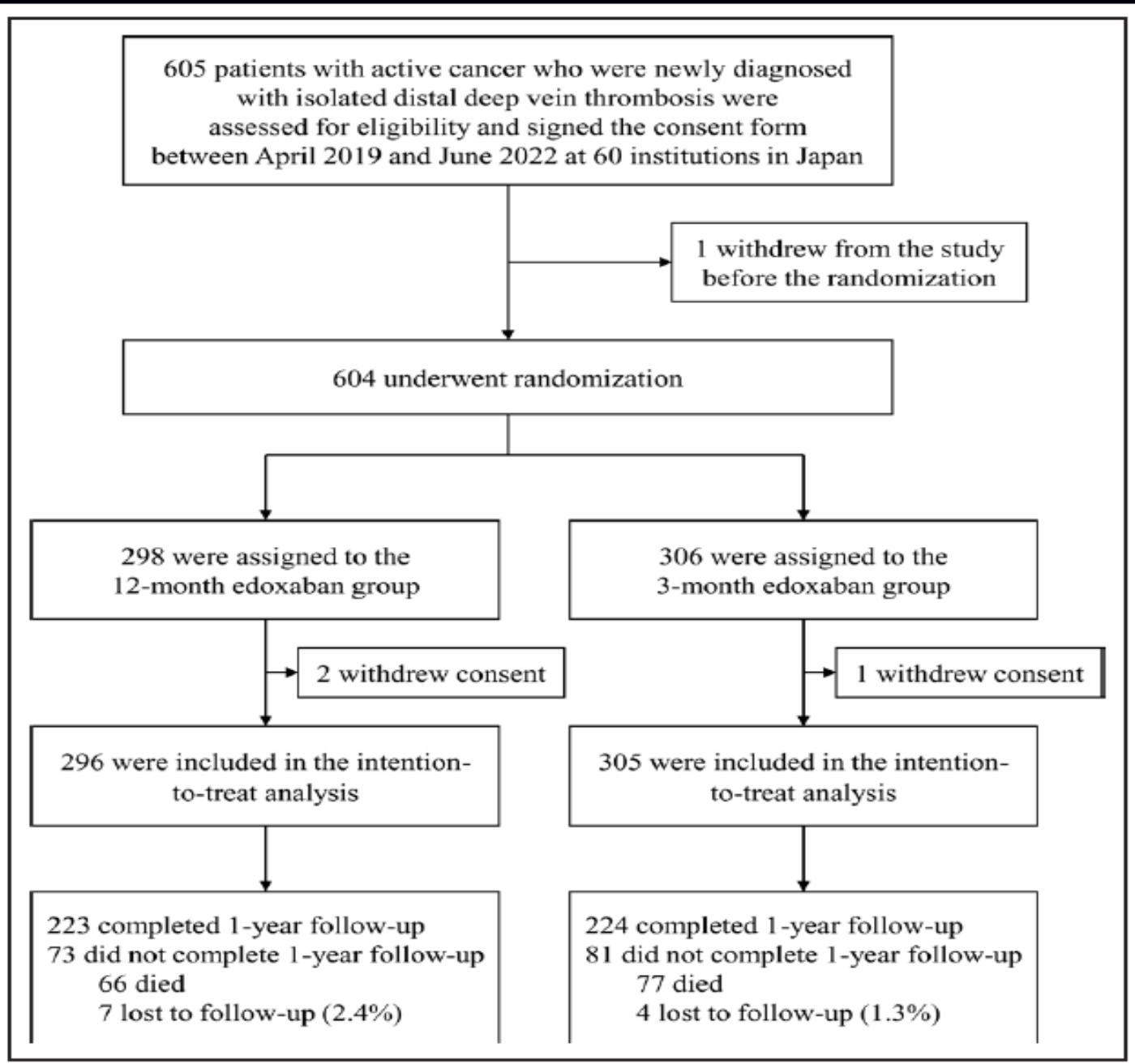
Michelangelo Sartori[1] | Matteo Iotti[2] | Giuseppe Camporese[3] | Sergio Siragusa[4] | Davide Imberti[5] | Eugenio Bucherini[6] | Sara Corradini[2] | Walter Ageno[7] | Paolo Prandoni[8] | Angelo Ghirarduzzi[2]

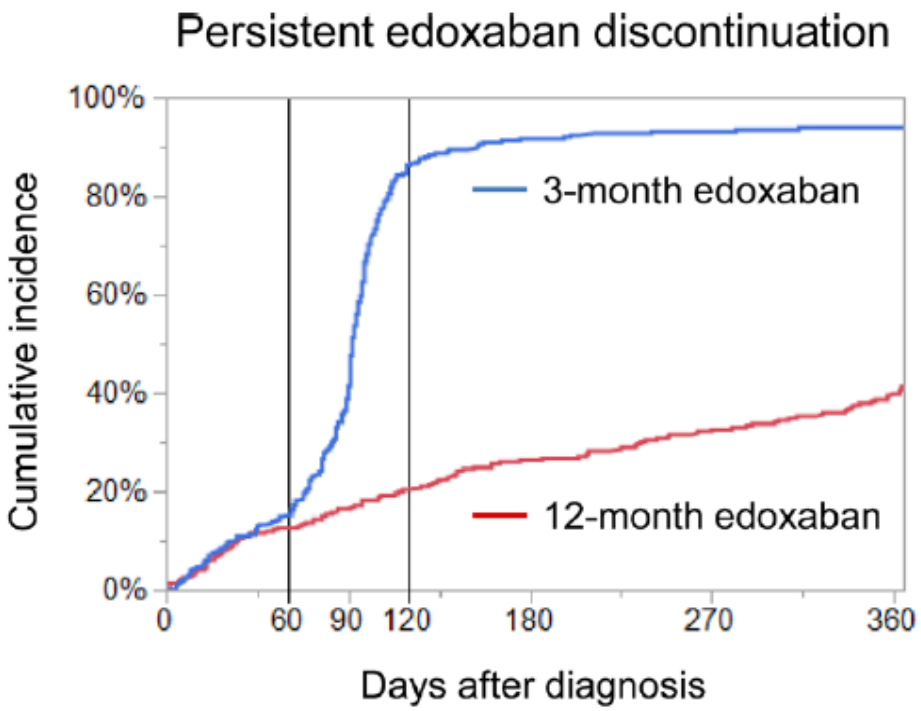
Amer J Hematol 2024

Edoxaban for 12 Months Versus 3 Months in Patients With Cancer With Isolated Distal Deep Vein Thrombosis (ONCO DVT Study): An Open-Label, Multicenter, Randomized Clinical Trial

Yugo Yamashita, MD; Takeshi Morimoto, MPH, MD; Nao Muraoka, MD; Takuya Oyakawa, MD; Michihisa Umetsu, MD; Daijirou Akamatsu, MD; Yuji Nishimoto, MD; Yukihito Sato, MD; Takuma Takada, MD; Kentaro Jujo, MD; Yuichiro Minami, MD; Yoshito Ogihara, MD; Kaoru Dohi, MD; Masashi Fujita, MD; Tatsuya Nishikawa, MD; Nobutaka Ikeda, MD; Go Hashimoto, MD; Kazunori Otsui, MD; Kenta Mori, MD; Daisuke Sueta, MD; Yukari Tsubata, MD; Masaaki Shoji, MD; Ayumi Shikama, MD; Yutaka Hosoi, MD; Yasuhiro Tanabe, MD; Ryuki Chatani, MD; Kengo Tsukahara, MD; Naohiko Nakanishi, MD; Kitae Kim, MD; Satoshi Ikeda, MD; Makoto Mo, MD; Yusuke Yoshikawa, MD; Takeshi Kimura, MD; on behalf of the ONCO DVT Study Investigators

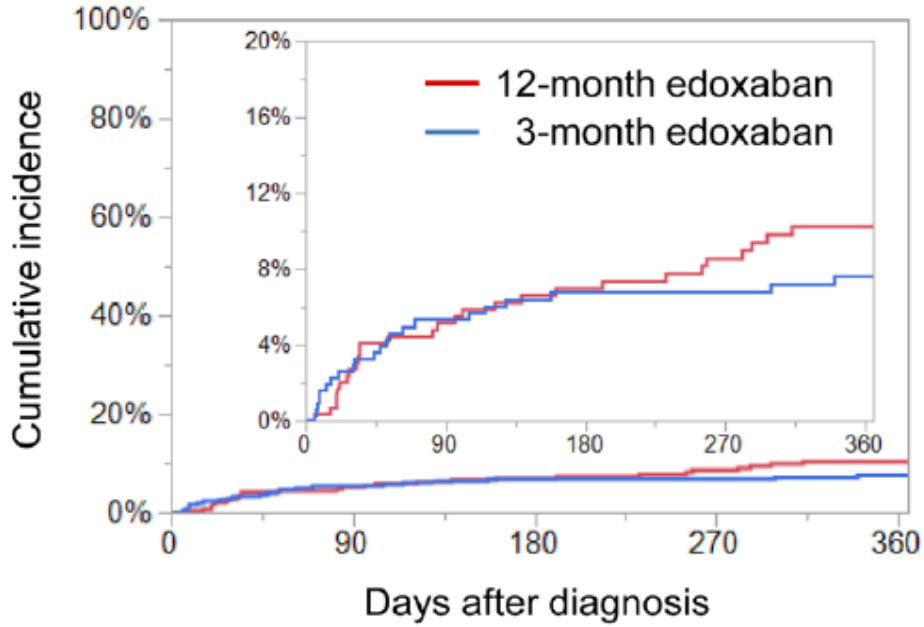
Circulation 2023


605 patients with active cancer who were newly diagnosed with isolated distal deep vein thrombosis were assessed for eligibility and signed the consent form between April 2019 and June 2022 at 60 institutions in Japan
1 withdrew from the study before the randomization
604 underwent randomization
298 were assigned to the 12-month edoxaban group
306 were assigned to the 3-month edoxaban group
2 withdrew consent
1 withdrew consent
296 were included in the intention-to-treat analysis
305 were included in the intention-to-treat analysis
223 completed 1-year follow-up
73 did not complete 1-year follow-up
66 died
7 lost to follow-up (2.4%)
224 completed 1-year follow-up
81 did not complete 1-year follow-up
77 died
4 lost to follow-up (1.3%)



	0-day	60-day	90-day	120-day	180-day	365-day
12-month edoxaban						
N of patients with discontinuation		37	48	60	76	116
N of patients on edoxaban	296	253	240	224	202	151
Cumulative incidence		12.6%	16.4%	20.6%	26.3%	41.3%
3-month edoxaban						
N of patients with discontinuation		46	124	256	271	277
N of patients on edoxaban	305	255	173	40	23	15
Cumulative incidence		15.2%	41.4%	86.3%	91.6%	93.9%

Major secondary endpoint (Major bleeding)



	0-day	60-day	90-day	120-day	180-day	365-day
12-month edoxaban						
N of patients with event		13	15	17	20	28
N of patients at risk	296	273	267	261	245	210
Cumulative incidence		4.4%	5.2%	5.9%	7.0%	10.2%
3-month edoxaban						
N of patients with event		14	16	18	20	22
N of patients at risk	305	279	271	264	250	217
Cumulative incidence		4.7%	5.3%	6.1%	6.8%	7.6%

Thrombosis Research 235 (2024) 75–78

Contents lists available at ScienceDirect

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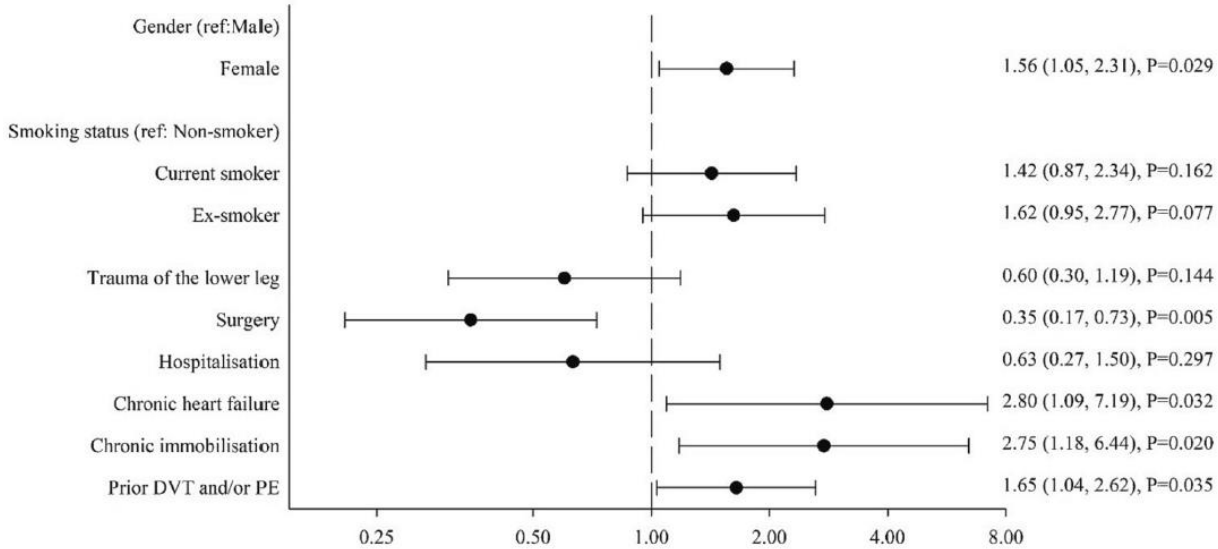
Letter to the Editors-in-Chief

Incidence and risk factors of post-thrombotic syndrome in patients with isolated calf vein thrombosis. Findings from the GARFIELD-VTE registry

Paolo Prandoni[a,*], Sylvia Haas[b], Meg Fluharty[c], Sebastian Schellong[d], Shinya Goto[e], Peter MacCallum[f], Eric Tse[g], Karen Pieper[c], Gloria Kayani[c], Ajay Kakkar[c], on behalf of the GARFIELD-VTE investigators[1]

www.garfieldregistry.org

The GARFIELD-VTE registry is funded by an unrestricted research grant from Bayer AG



Odds Ratios (ORs) with 95% Confidence Intervals for stepwise logistic regression of risk factors predicting post thrombotic (PTS) syndrome in patients proximal deep vein thrombosis. List of risk factors for inclusion in initial model were gender, ethnicity, diagnosis, acute medical illness, hospitalisation, long haul travel, trauma of the lower leg, surgery, acute cancer, chronic heart failure, immobilisation, family history of VTE, history of cancer, prior DVT and/or PE, and renal insufficiency.

CALF DVT 754 patients (3-year f-up) **OVERALL PTS 21.2%** **SEVERE PTS 1.3%**

The GARFIELD-VTE registry is funded by an unrestricted research grant from Bayer AG

Aspetti di terapia dell'EP primaria

Classification of PE based on early mortality risk

Early mortality risk		Indicators of risk			
		Haemo-dynamic instability	Clinical parameters of PE severity/ comorbidity: PESI III–V or sPESI ≥1	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		+	(+)	+	(+)
Interme-diate	**Intermediate–high**	-	+	+	+
	Intermediate–low	-	+	One (or none) positive	
Low		-	-	-	Assessment optional; if assessed, negative

©ESC

CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; TTE = transthoracic echocardiography.

Contemporary Management and Clinical Course of Acute Pulmonary Embolism: The COPE Study

Cecilia Becattini[1] Giancarlo Agnelli[1] Aldo P. Maggioni[2] Francesco Dentali[3] Andrea Fabbri[4] Iolanda Enea[5] Fulvio Pomero[6] Maria Pia Ruggieri[7] Andrea di Lenarda[8] Ludovica Anna Cimini[1] Giuseppe Pepe[9] Susanna Cozzio[10] Donata Lucci[2] Michele M. Gulizia[2,11] on behalf of COPE Investigators*

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[2] ANMCO Research Center, Heart Care Foundation, Florence, Italy
[3] Department of Clinical and Experimental Medicine, Insubria University, Varese, Italy
[4] Emergency Department, "Presidio Ospedaliero Morgagni-Pierantoni," Forlì, Italy
[5] U.O.C. Medicina e Chirurgia d'Urgenza, A.O.R.N. "S. Anna e S. Sebastiano," Caserta, Italy
[6] Division of Internal Medicine, Michele and Pietro Ferrero Hospital, Verduno, Italy
[7] U.O.C. Medicina d'Urgenza e Pronto Soccorso, AO San Giovanni Addolorata, Roma, Italy
[8] Cardiovascular Center, University Hospital and Health Services of Trieste, Italy
[9] PS e Medicina d'Urgenza, Nuovo Ospedale Versilia, Lido di Camaiore, Italy
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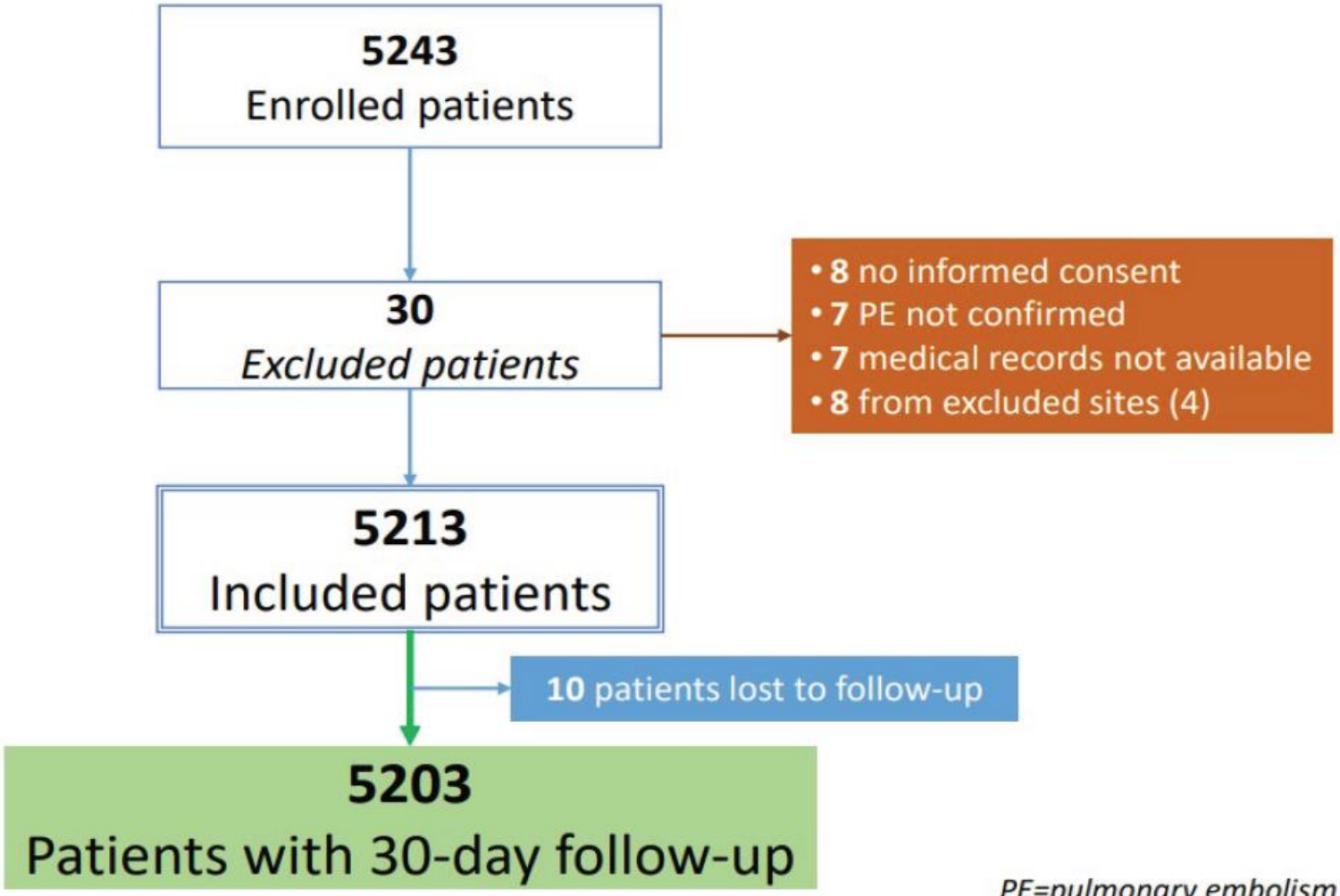
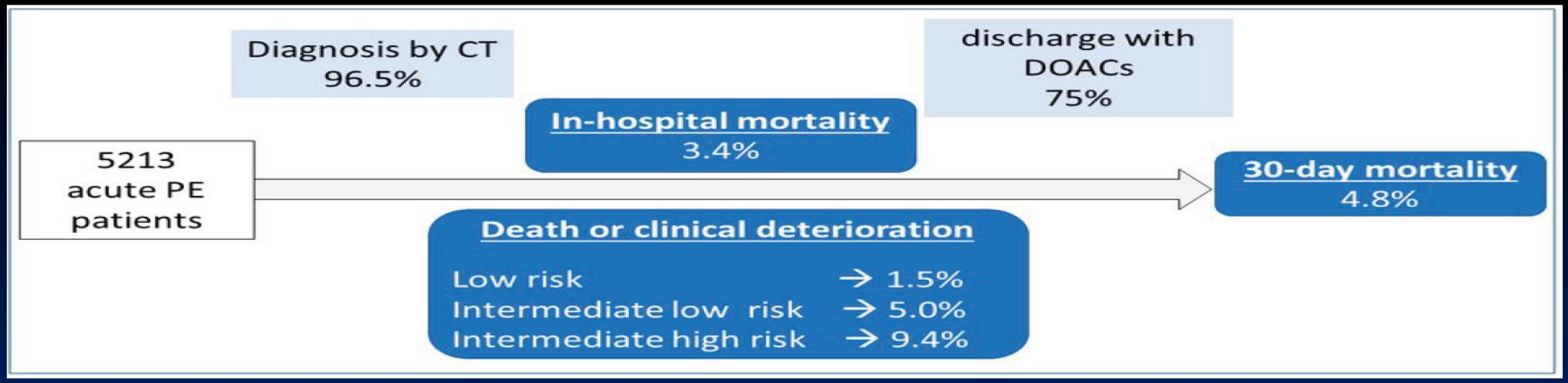
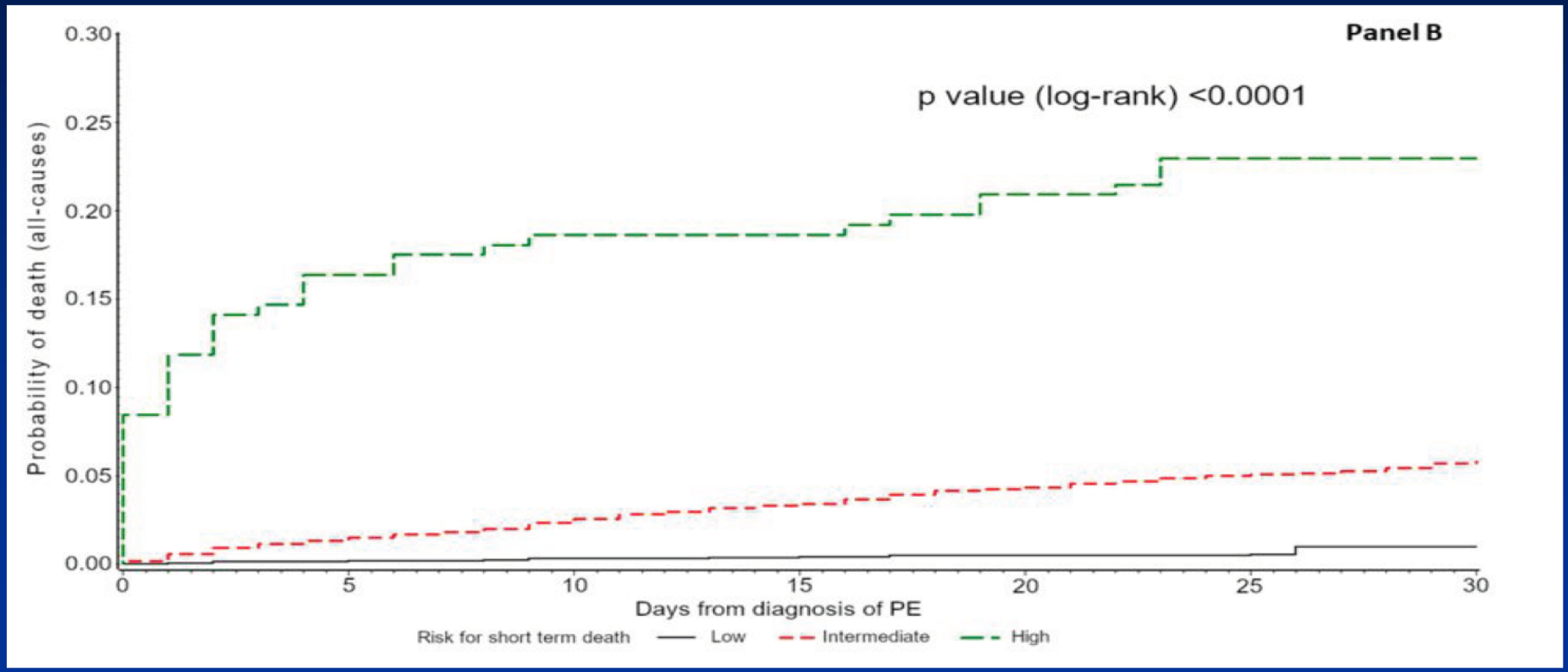
Thromb Haemost 2023;123:613–626.

Patients disposition



PE=pulmonary embolism


Diagnosis by CT
96.5%
discharge with
DOACs
75%
In-hospital mortality
3.4%
5213
acute PE
patients
30-day mortality
4.8%
Death or clinical deterioration
Low risk → 1.5%
Intermediate low risk → 5.0%
Intermediate high risk → 9.4%


Panel B
p value (log-rank) <0.0001
Probability of death (all-causes)
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0
5
10
15
20
25
30
Days from diagnosis of PE
Risk for short term death
Low
Intermediate
High

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 83, NO. 1, 2024
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Contemporary Management and Outcomes of Patients With High-Risk Pulmonary Embolism

Taisei Kobayashi, MD,[a,b] Steven Pugliese, MD,[c] Sanjum S. Sethi, MD, MPH,[d] Sahil A. Parikh, MD,[d] Joshua Goldberg, MD,[e] Fahad Alkhafan, MD, MPH,[f] Clara Vitarello, MPH,[f] Kenneth Rosenfield, MD,[g] Robert Lookstein, MD,[h] Brent Keeling, MD,[i] Andrew Klein, MD,[j] C. Michael Gibson, MS, MD,[f,k] Lauren Glassmoyer, MD,[a] Sameer Khandhar, MD,[a] Eric Secemsky, MD,[k] Jay Giri, MD, MPH[a,b]

Reduced-Dose Intravenous Thrombolysis for Acute Intermediate–High-risk Pulmonary Embolism: Rationale and Design of the Pulmonary Embolism International THrOmbolysis (PEITHO)-3 trial

Olivier Sanchez[1,2,3,4] Anaïs Charles-Nelson[5,6] Walter Ageno[7] Stefano Barco[8,9] Harald Binder[10] Gilles Chatellier[3,5,6] Daniel Duerschmied[11] Klaus Empen[12] Melanie Ferreira[13] Philippe Girard[4,14] Menno V. Huisman[15] David Jiménez[16] Sandrine Katsahian[3,5,6,17] Matija Kozak[18] Mareike Lankeit[8,19,20] Nicolas Meneveau[4,21,22] Piotr Pruszczyk[23] Antoniu Petris[24] Marc Righini[25] Stephan Rosenkranz[26] Sebastian Schellong[27] Branislav Stefanovic[28] Peter Verhamme[29] Kerstin de Wit[30] Eric Vicaut[31] Andreas Zirlik[32] Stavros V. Konstantinides[8,33] Guy Meyer[1,3,4,†] for the PEITHO-3 Investigators

Thromb Haemost 2022

Large-bore Mechanical Thrombectomy Versus Catheter-directed Thrombolysis in the Management of Intermediate-risk Pulmonary Embolism: Primary Results of the PEERLESS Randomized Controlled Trial

Jaber WA, Gonsalves CF, Stortecky S, Horr S, Pappas O, Gandhi RT, Pereira K, Giri J, Khandhar SJ, Ammar KA, Lasorda DM, Stegman B, Busch L, Dexter Ii DJ, Azene EM, Daga N, Elmasri F, Kunavarapu CR, Rea ME, Rossi JS, Campbell J, et al.

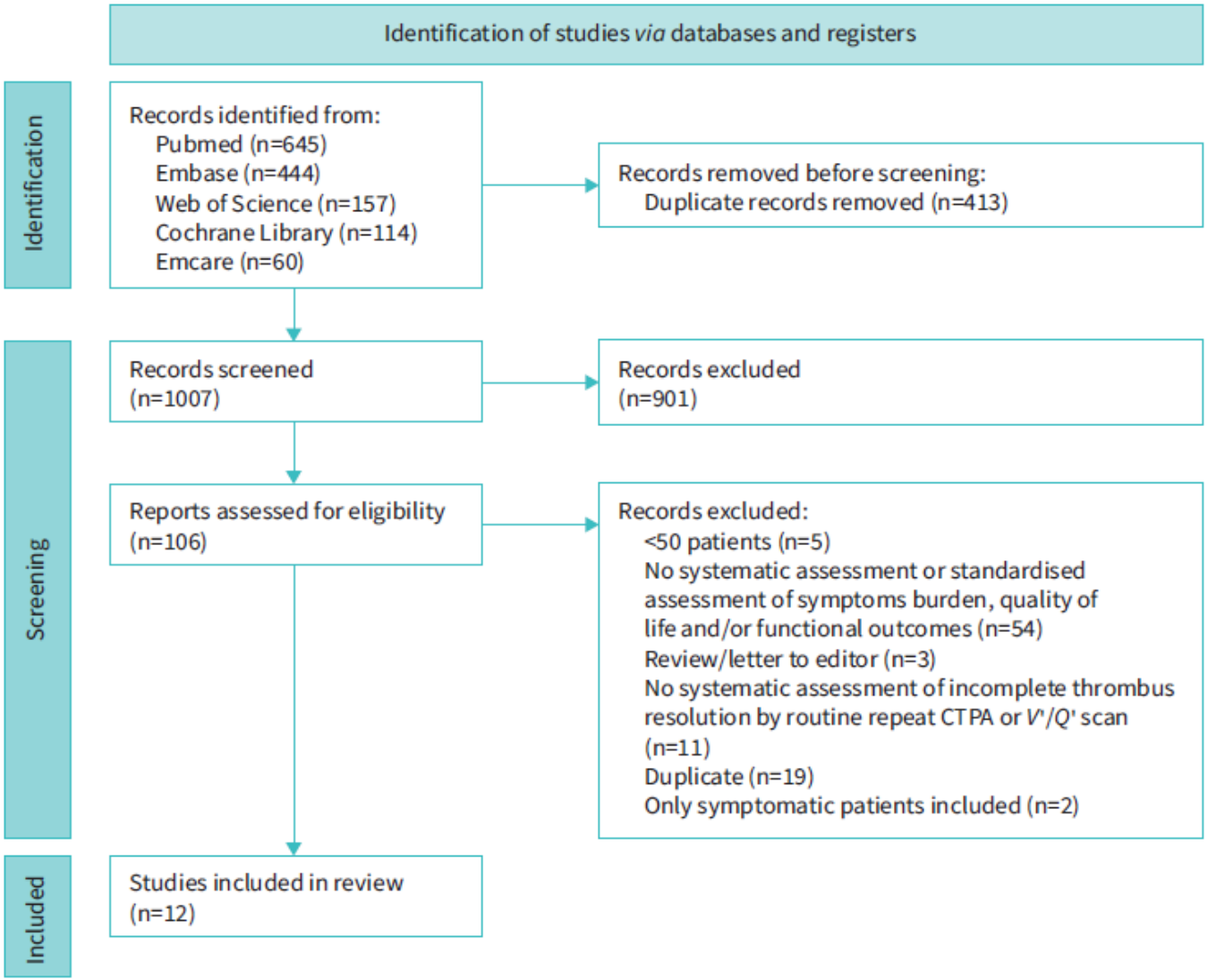
Circulation 2024

ERJ OPEN RESEARCH
ORIGINAL RESEARCH ARTICLE
L.A. CIMINI ET AL.

Pulmonary perfusion defects or residual vascular obstruction and persistent symptoms after pulmonary embolism: a systematic review and meta-analysis

Ludovica Anna Cimini, Dieuwke Luijten, Stefano Barco, Waleed Ghanima, Øyvind Jervan, Susan R. Kahn, Stavros Konstantinides, Daniel Lachant, Yoshihisa Nakano, Maarten Ninaber, Josien van Es, Thijs van Mens, Anton Vonk Noordegraaf, Cecilia Becattini and Frederikus A. Klok

ERJ 2024


Identification of studies *via* databases and registers
Identification
Records identified from:
Pubmed (n=645)
Embase (n=444)
Web of Science (n=157)
Cochrane Library (n=114)
Emcare (n=60)
Records removed before screening:
Duplicate records removed (n=413)
Screening
Records screened
(n=1007)
Records excluded
(n=901)
Reports assessed for eligibility
(n=106)
Records excluded:
<50 patients (n=5)
No systematic assessment or standardised assessment of symptoms burden, quality of life and/or functional outcomes (n=54)
Review/letter to editor (n=3)
No systematic assessment of incomplete thrombus resolution by routine repeat CTPA or *V'*/*Q'* scan (n=11)
Duplicate (n=19)
Only symptomatic patients included (n=2)
Included
Studies included in review
(n=12)

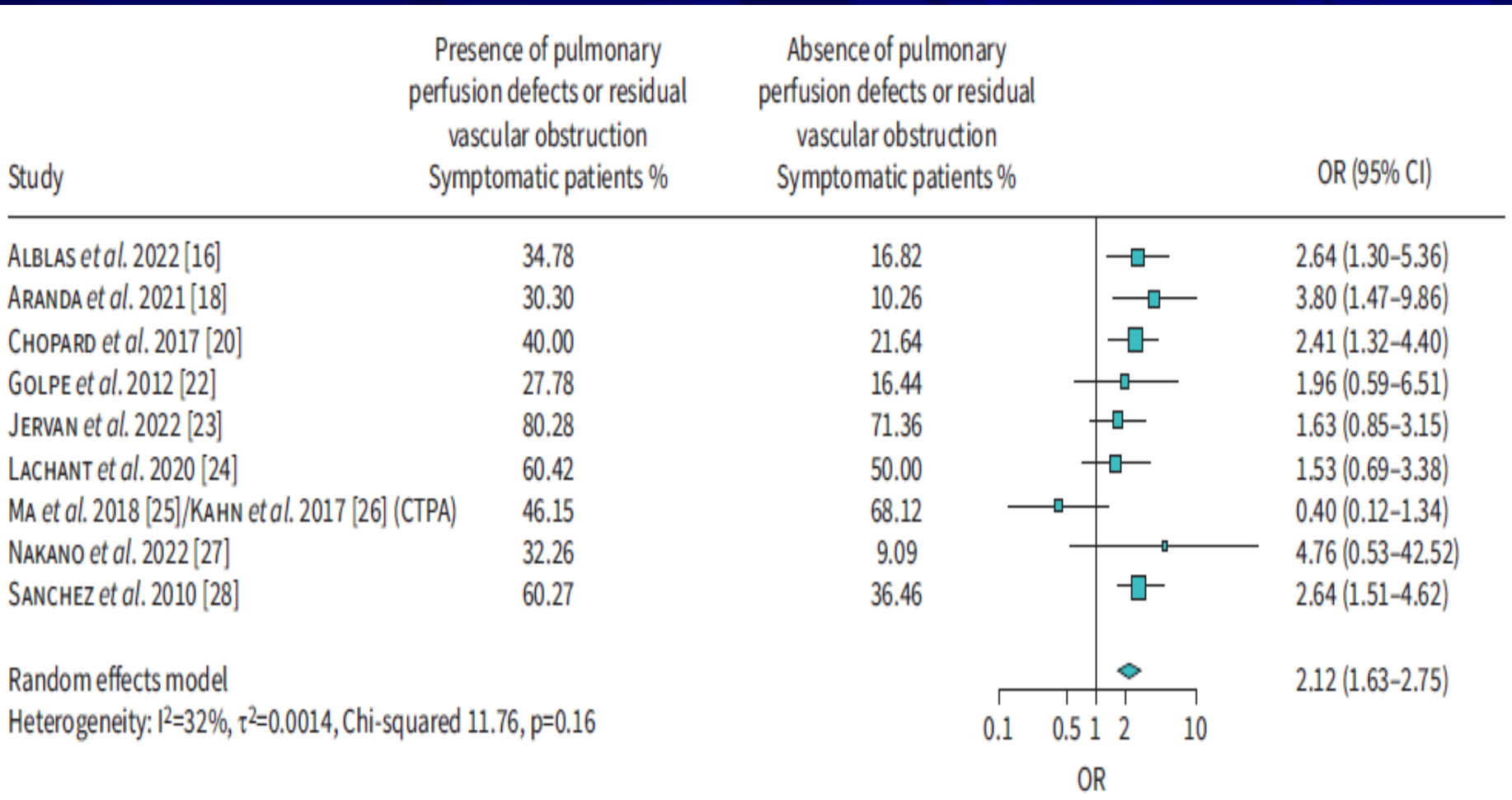


FIGURE 2 Presence of pulmonary perfusion defects or residual vascular obstruction and persistent symptoms during follow-up. CTPA: computed tomography pulmonary angiogram.

Received: 4 January 2019 | Accepted: 1 May 2019

DOI: 10.1111/jth.14477

REVIEW ARTICLE

Risk of recurrent venous thromboembolism after acute pulmonary embolism: Role of residual pulmonary obstruction and persistent right ventricular dysfunction. A meta-analysis

Cecilia Becattini[1] | Michela Giustozzi[1] | Pau Cerdà[2] | Ludovica A. Cimini[1] | Antoni Riera-Mestre[3] | Giancarlo Agnelli[1]

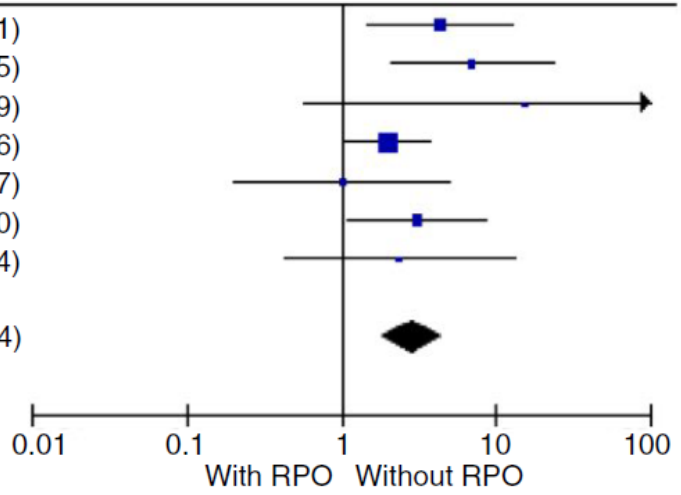
JTH 2019

(A)

Study or subgroup	With RPO Events	With RPO Total	Without RPO Events	Without RPO Total	Weight	Odds ratio M-H, Random, 95% CI
Meneveau 2012	8	102	6	314	15.8%	4.37 (1.48, 12.91)
Alhadad 2012	34	151	3	75	12.8%	7.07 (2.10, 23.85)
Begic 2014	1	11	0	53	1.9%	15.29 (0.58, 401.49)
Planquette 2016	19	60	47	250	37.6%	2.00 (1.07, 3.76)
Pesavento 2016	2	16	11	89	7.6%	1.01 (0.20, 5.07)
Pesavento 2017	15	324	5	323	17.4%	3.09 (1.11, 8.60)
Meysman 2017	4	13	3	19	6.9%	2.37 (0.43, 13.04)
Total (95% CI)		677		1124	100.0%	2.87 (1.81, 4.54)
Total events	83		75			

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 6.71$, $df = 6$ ($P = 0.35$); $I^2 = 11\%$

Test for overall effect: $Z = 4.50$ ($P < 0.00001$)



(B)

Study or subgroup	With RPO Events	With RPO Total	Without RPO Events	Without RPO Total	Weight	Odds ratio M-H, Random, 95% CI
Golpe 2012	1	18	7	73	13.5%	0.55 (0.06, 4.82)
Meneveau 2012	7	102	5	314	30.0%	4.55 (1.41, 14.68)
Begic 2014	0	11	0	48		Not estimable
Pesavento 2016	1	16	11	89	13.9%	0.47 (0.06, 3.94)
Chopard 2017	13	70	21	171	42.5%	1.63 (0.76, 3.47)
Total (95% CI)		217		695	100.0%	1.61 (0.65, 3.98)
Total events	22		44			

Heterogeneity: $\tau^2 = 0.35$; $\chi^2 = 5.21$, $df = 3$ ($P = 0.16$); $I^2 = 42\%$

Test for overall effect: $Z = 1.04$ ($P = 0.30$)

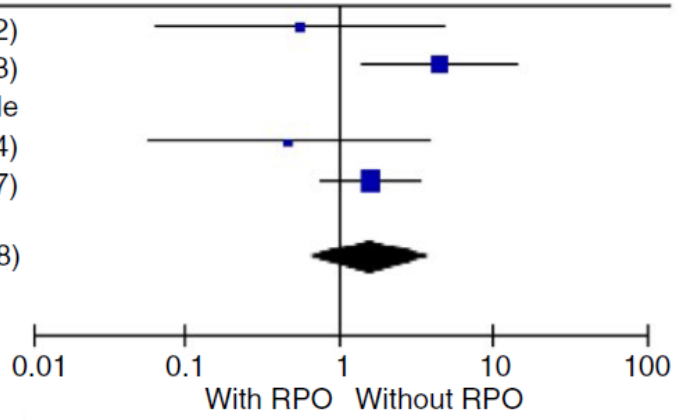


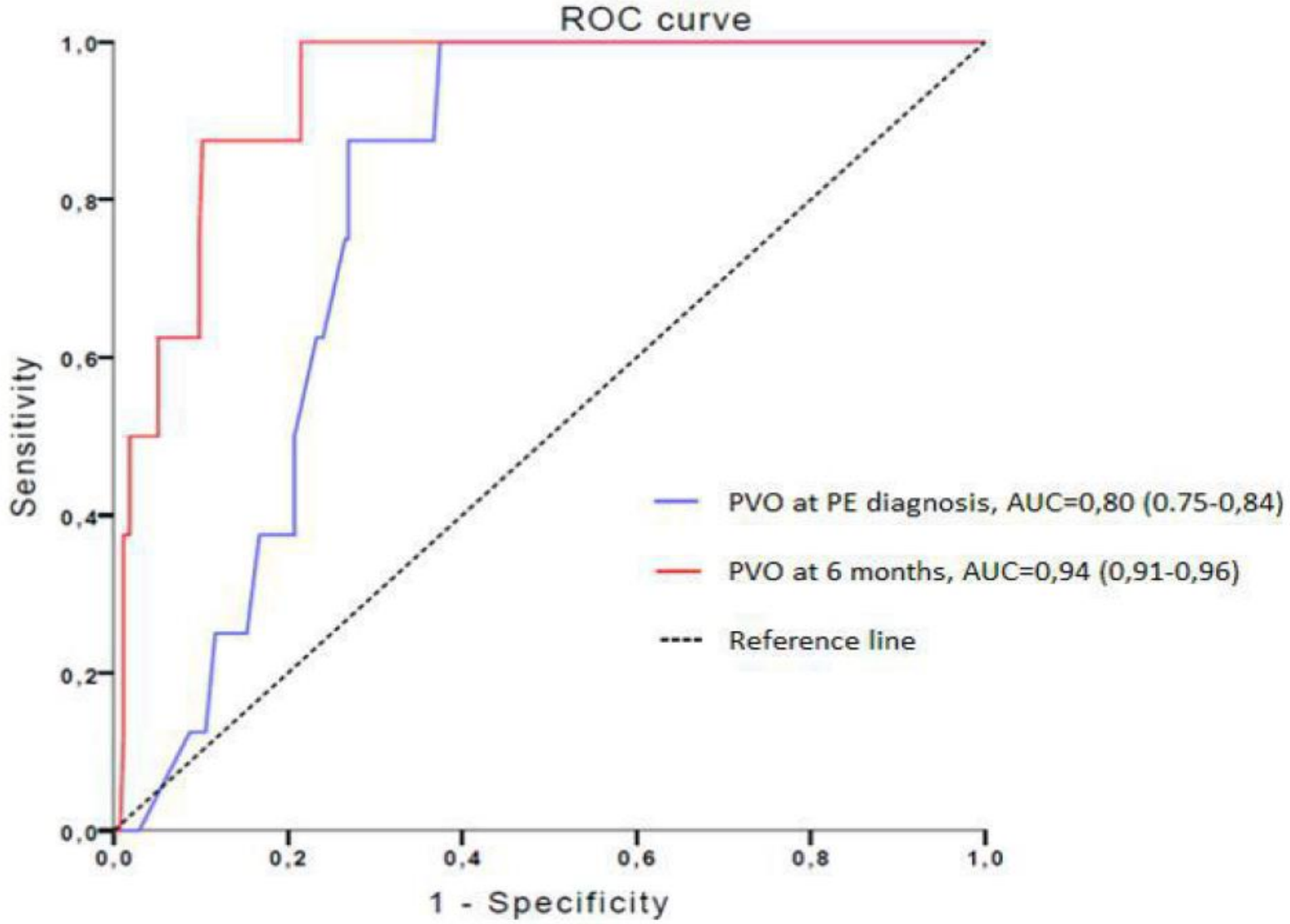
FIGURE 2 Forest plot for the incidence of recurrent pulmonary embolism (A) and all-cause death (B) based on the presence or absence of residual pulmonary obstruction RPO. CI, confidence interval

Frequency and predictors for chronic thromboembolic pulmonary hypertension after a first unprovoked pulmonary embolism: Results from PADIS studies

Alexandre Fauché[1] | Emilie Presles[2,3] | Olivier Sanchez[3,4] | Xavier Jaïs[5] | Raphael Le Mao[1,3] | Philippe Robin[3,6] | Gilles Pernod[3,7] | Laurent Bertoletti[3,8] | Patrick Jego[3,9] | Florence Parent[3,5] | Catherine A. Lemarié[1,3] | Florent Leven[10] | Pierre-Yves Le Roux[3,6] | Pierre-Yves Salaun[3,6] | Michel Nonent[11] | Philippe Girard[3,12] | Karine Lacut[1,3] | Laurent Savale[5] | Solen Mélac[1,3] | Marie Guégan[1,3] | Patrick Mismetti[3,8] | Silvy Laporte[2,3] | Christophe Leroyer[1,3] | David Montani[5] | Francis Couturaud[1,3] | Cécile Tromeur[1,3] | for the PADIS-PE Investigators

JTH 2022;12: 2850-59

Characteristics	CTEPH n=9	No CTEPH n=328	Hazard Ratio (95% CI)	p-value
Clinical Characteristics				
Age, mean (SD), y	73.9 (9.7)	57.7 (17.8)	**1.07 (1.02-1.14)**	**0.0112**
> 65 years, no (%)	8 (88.9)	125 (38.1)	**8.78 (1.41-54.6)**	**0.020**
Women, no (%)	6 (66.7)	168 (51.2)	1.52 (0.39-6.04)	0.548
Body-mass index, mean (SD), Kg/m²	25.2 (6.5)	27.4 (5.5)	0.91 (0.80-1.05)	0.202
CTEPH-associated risk factors				
Associated conditions and diseases				
History of splenectomy, no. (%)	0 (0.0)	2 (0.6)	*	-
Thyroid substitution therapy, no. (%)	2 (22.2)	25 (7.6)	3.21 (0.70-14.8)	0.135
Chronic inflammatory disease, no. (%)	0 (0.0)	5 (1.5)	*	-
Ventriculo-atrial shunt, no. (%)	0 (0.0)	0 (0.0)	*	-
Non-O blood groups, no. (%)	3 (37.5)	209 (71.6)	**0.24 (0.06-0.99)**	**0.0477**
Thrombophilic disorders†				
Minor thrombophilia	2 (25)	75 (24)	1.10 (0.23-5.19)	0.908
Heterozygous factor V Leiden	0 (0.0)	32 (10.0)	0.45 (0.02-9.06)	0.600
Heterozygous G20210A prothrombin gene variant	1 (11.1)	19 (6.0)	2.06 (0.33-13.1)	0.442
Elevated factor VIII (99th percentile)	1 (12.5)	33 (10.2)	1.89 (0.30-12.1)	0.500
Major thrombophilia	3 (37.5)	42 (13.5)	**5.33 (1.25-22.8)**	**0.024**
Antithrombin deficiency	1 (12.5)	3 (0.9)	*	-
Protein C deficiency	0 (0.0)	4 (1.2)	*	-
Protein S deficiency	0 (0.0)	1 (0.3)	*	-
Homozygous factor V Leiden	0 (0.0)	0 (0.0)	*	-
Heterozygous factor V Leiden and heterozygous factor G20210A prothrombin gene variant	0 (0.0)	1 (0.4)	*	-
Antiphospholipid antibodies	2 (25.0)	34 (10.7)	4.36 (0.89-21.3)	0.068
Anticardiolipin antibodies (99th percentile)	0 (0.0)	5 (1.60)	*	-
Lupus anticoagulant	2 (25.0)	30 (9.3)	**5.22 (1.07-25.5)**	**0.041**
Index pulmonary embolism description				
Associated deep vein thrombosis, no. (%)	3 (42.9)	99 (31.2)	1.52 (0.340-6.81)	0.582
Echocardiographic at PE diagnosis				
Echocardiographic signs of PH / RVD, no. (%)	4 (66.7)	38 (38.4)	3.46 (0.65-18.5)	0.147
sPAP, mean (SD)	51.6 (19.0)	40.9 (14.6)	1.05 (1.00-1.10)	0.053
sPAP at diagnosis > 60 mmHg, no. (%)	3 (60.0)	9 (10.3)	**12.5 (2.10-74.8)**	**0.005**
Initial PVO (as continuous variable), mean (SD)	60.5 (9.2)	34.8 (23.9)	**1.06 (1.02-1.09)**	**0.004**



	PVO (%)	HR (95% CI) for CTEPH	p-value
PVO at PE diagnosis	45.0	33.0 (1.64-667)	0.023
PVO at 6 months	14.0	63.9 (3.11-1310)	0.007

Implicazioni cliniche (1)

- La necessità di un pronto ed efficace ripristino della canalizzazione vascolare sia in soggetti ad alto rischio che in quelli a rischio intermedio è ineludibile

- Si tratta di individuare provvedimenti efficaci gravati da un minor rischio emorragico

Implicazioni cliniche (2)

- Una scintigrafia polmonare (non la ripetizione dell'angioTC!) a distanza di sei mesi dall'episodio acuto può aiutare a riconoscere i candidati al prolungamento dell'anticoagulazione, prescindendo dalla severità e dalla natura dell'episodio

Prevenzione estesa a tutti nel TEV idiopatico?

Overview of extended treatment studies with NOACs/ ASA

Study	Study treatment duration (planned)	Experimental high		Experimental low		Placebo/Aspirin	
		RVTE	MB	RVTE	MB	RVTE	MB
RESONATE[1]	6 months	0.4%	0.3%			5.6%	0%
AMPLIFY EXT[2]	12 months	1.7%	0.1%	1.7%	0.2%	8.8%	0.5%
EINSTEIN Extension[3]	6 or 12 months	1.3%	0.7%			7.1%	0%
EINSTEIN Choice	Up to 12 months	1.5%	0.5%	1.2%	0.4%	4.4%**	0.3%**
WARFASA/ ASPIRE pool[4]*	Up to 48 months	5.1%	0.5%			7.1%	0.4%

Caveat: Incidences as reported and not annualized (Except ASA Studies), mean Tx duration may differ from planned

**Comparison with ASA

RVTE: recurrent VTE, MB: Major Bleeding according to ISTH,
Experimental high/ low refer to dose of NOAC used for AMPLIFY Ext and Einstein Choice

1. Schulman *et al. N Engl J Med* 2013; 2. Agnelli *et al. N Engl J Med* 2013; 3. The EINSTEIN Investigators. *N Engl J Med* 2010; 4. Simes et al. Circulation 2014

REGULAR ARTICLE

blood advances

Check for updates

D-dimer and reduced-dose apixaban for extended treatment after unprovoked venous thromboembolism: the Apidulcis study

Gualtiero Palareti,[1] Daniela Poli,[2] Walter Ageno,[3] Cristina Legnani,[1] Emilia Antonucci,[1] Eugenio Bucherini,[4] Sophie Testa,[5] Oriana Paoletti,[5] Antonio Chistolini,[6] Alessandra Serrao,[6] Ida Martinelli,[7] Paolo Bucciarelli,[7] Anna Falanga,[8] Alberto Tosetto,[9] Luca Sarti,[10] Daniela Mastroiacovo,[11] Benilde Cosmi,[12] Adriana Visonà,[13] Rita Carlotta Santoro,[14] Nello Zanatta,[15] Elvira Grandone,[16] Lorenza Bertù,[3] Vittorio Pengo,[17] Lucia Caiano,[3] and Paolo Prandoni,[1] for the Apidulcis study group

[1]Fondazione Arianna Anticoagulazione, Bologna, Italy; [2]Malattie Aterotrombotiche, AOU Careggi, Florence, Italy; [3]UOC Pronto Soccorso, Medicina d'Urgenza e Centro Trombosi ed Emostasi, ASST dei Sette Laghi, Varese, Italy; [4]SS Medicina Vascolare e Angiologia, Medicina 2, AUSL Romagna, Ravenna, Italy; [5]Centro Emostasi e Trombosi, UUOO Laboratorio Analisi chimico-cliniche e microbiologiche, ASST Cremona, Cremona, Italy; [6]Dipartimento di Medicina Traslazionale e di Precisione Sapienza Università di Roma, Rome, Italy; [7]Centro Emofilia e Trombosi A. Bianchi Bonomi, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy; [8]Divisione di Immunoematologia e Medicina Trasfusionale & Centro Emostasi e Trombosi, ASST Papa Giovanni XXIII, Bergamo, Università Milano, Bicocca, Italy; [9]UOC Ematologia, Centro Malattie Emorragiche e Trombotiche (CMET), AULSS 8 Berica Ospedale S. Bortolo, Vicenza, Italy; [10]Centro per la diagnosi e la sorveglianza della malattia tromboembolica, UO Medicina interna d'urgenza, Azienda Ospedaliero Universitaria Policlinico di Modena, Ospedale Civile Baggiovara, Modena, Italy; [11]UOSD Angiologia e Diagnostica Vascolare, Dipartimento Medico, Ospedale Civile SS Filippo e Nicola, Avezzano (AQ), Italy; [12]UO di Angiologia e Malattie della Coagulazione, Dipartimento Medicina Specialistica, Diagnostica e Sperimentale, Università di Bologna; Azienda Ospedaliero Universitaria S. Orsola-Malpighi, IRCCS, Bologna, Italy; [13]UOC Angiologia, Dipatimento di Medicina Clinica, Azienda ULSS 2 Marca Trevigiana, Ospedale San Giacomo Apostolo, Castelfranco Veneto (TV), Italy; [14]Centro Emostasi e Trombosi, Dipartimento Emato-Oncologico, Presidio Ospedaliero deLellis, Az. Osp. "Pugliese-Ciaccio", Catanzaro, Italy; [15]UOSD di Angiologia, Ospedale di Conegliano, Conegliano (TV), Italy; [16]IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo; Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy; Ob/Gyn I.M. First Moscow State Medical University, Moscow, Russia; and [17]Clinica Cardiologica, Azienda Ospedaliera di Padova, Padova, Italy

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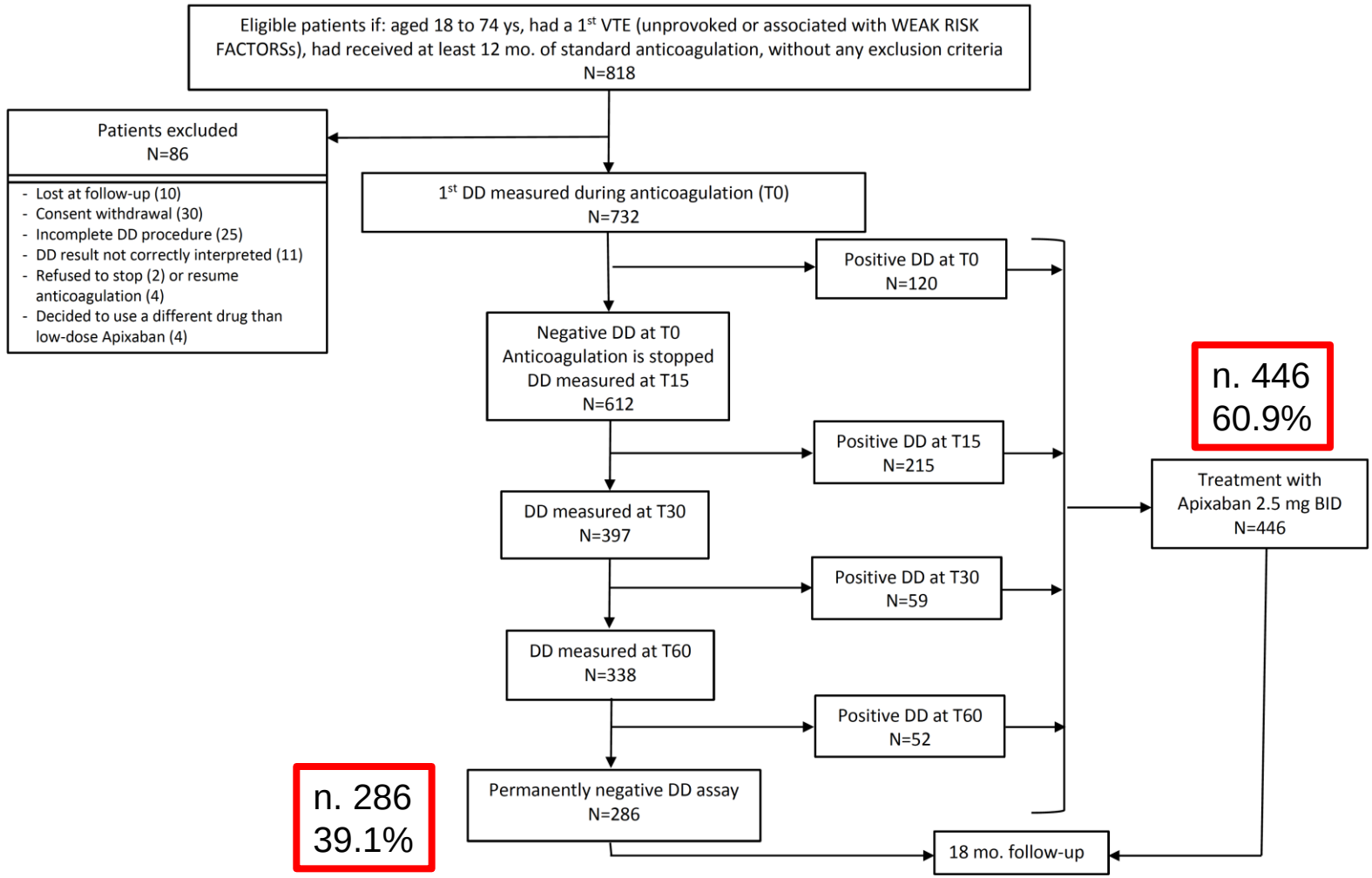
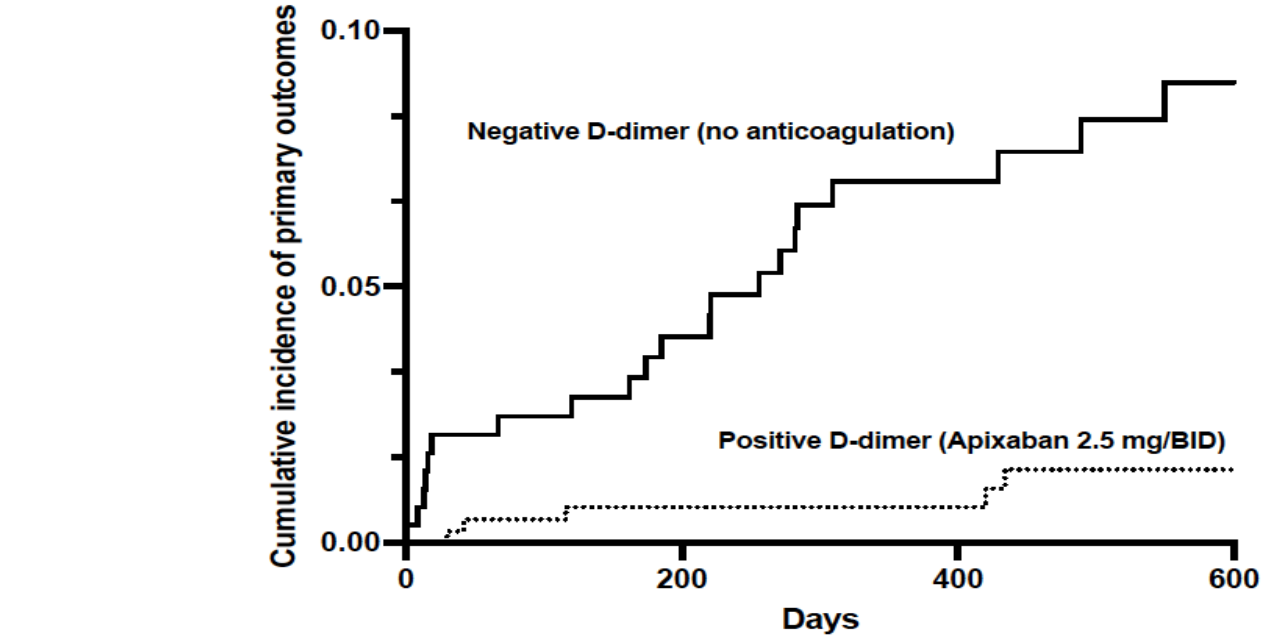
Flow-chart


Eligible patients if: aged 18 to 74 ys, had a 1st VTE (unprovoked or associated with WEAK RISK FACTORSs), had received at least 12 mo. of standard anticoagulation, without any exclusion criteria
N=818
Patients excluded
N=86
- Lost at follow-up (10)
- Consent withdrawal (30)
- Incomplete DD procedure (25)
- DD result not correctly interpreted (11)
- Refused to stop (2) or resume anticoagulation (4)
- Decided to use a different drug than low-dose Apixaban (4)
1st DD measured during anticoagulation (T0)
N=732
Positive DD at T0
N=120
Negative DD at T0
Anticoagulation is stopped
DD measured at T15
N=612
Positive DD at T15
N=215
DD measured at T30
N=397
Positive DD at T30
N=59
DD measured at T60
N=338
Positive DD at T60
N=52
Permanently negative DD assay
N=286
n. 286
39.1%
n. 446
60.9%
Treatment with
Apixaban 2.5 mg BID
N=446
18 mo. follow-up

Palareti G et al, Blood Adv 2022



Khan F et al, Ann Intern Med 2021

Annals of Internal Medicine

REVIEW

Long-Term Risk for Major Bleeding During Extended Oral Anticoagulant Therapy for First Unprovoked Venous Thromboembolism

A Systematic Review and Meta-analysis

Faizan Khan, MSc; Tobias Tritschler, MD; Miriam Kimpton, MD; Philip S. Wells, MD; Clive Kearon, MD, PhD†; Jeffrey I. Weitz, MD; Harry R. Büller, MD, PhD; Gary E. Raskob, PhD; Walter Ageno, MD; Francis Couturaud, MD, PhD; Paolo Prandoni, MD, PhD; Gualtiero Palareti, MD; Cristina Legnani, PhD; Paul A. Kyrle, MD; Sabine Eichinger, MD; Lisbeth Eischer, MD; Cecilia Becattini, MD, PhD; Giancarlo Agnelli, MD, PhD; Maria Cristina Vedovati, MD; Geert-Jan Geersing, MD, PhD; Toshihiko Takada, MD, PhD; Benilde Cosmi, MD, PhD; Drahomir Aujesky, MD; Letizia Marconi, MD, PhD; Antonio Palla, MD; Sergio Siragusa, MD; Charlotte A. Bradbury, MD, PhD; Sameer Parpia, PhD; Ranjeeta Mallick, PhD; Anthonie W.A. Lensing, MD, PhD; Martin Gebel, PhD; Michael A. Grosso, MD; Kednapa Thavorn, PhD; Brian Hutton, PhD; Gregoire Le Gal, MD, PhD; Dean A. Fergusson, PhD; and Marc A. Rodger, MD; and the MAJESTIC Collaborators*

Khan F et al, Ann Intern Med 2021

Table 1. Incidence of Major Bleeding*

Interval of Follow-up During Extended Anticoagulation	Study Cohorts, *n*	Events, *n*			Person-Years, *n*	Incidence Rate per 100 Person-Years (95% CI)		
		Major Bleeding	Intracranial Bleeding	Fatal Bleeding		Major Bleeding	Intracranial Bleeding	Fatal Bleeding
Overall								
VKA	24	207	37	15	12 251	1.74 (1.34-2.20)	0.39 (0.25-0.57)	0.16 (0.10-0.24)
DOAC	11	40	9	2	3934	1.12 (0.72-1.62)	0.29 (0.14-0.50)	0.10 (0.03-0.23)
Year 1								
VKA	24	128	26	9	6989	2.00 (1.56-2.50)	0.53 (0.35-0.74)	0.18 (0.10-0.30)
DOAC	11	40	9	2	3768	1.20 (0.74-1.77)	0.31 (0.15-0.53)	0.11 (0.03-0.24)
Year 2†								
VKA	18	48	7	2	2707	1.65 (0.99-2.48)	0.42 (0.20-0.72)	0.21 (0.07-0.41)
Years 3-5†								
VKA	5	31	4	4	2555	0.95 (0.35-1.83)	0.22 (0.08-0.44)	0.20 (0.07-0.42)

Table 2. Case-Fatality Rate of Major Bleeding*

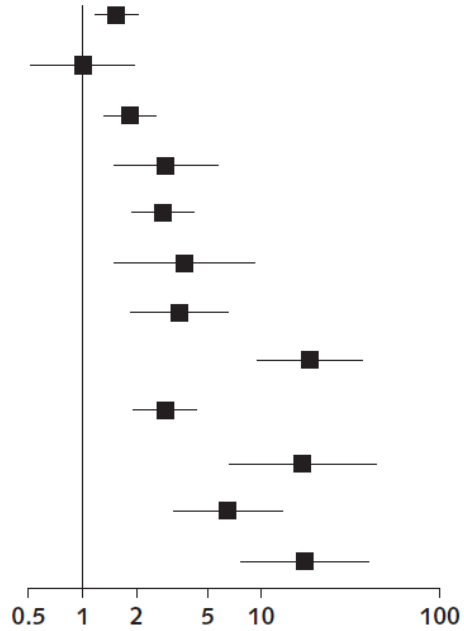
Type of Anticoagulant	Study Cohorts, *n*	Fatal Bleeding Events, *n*	Major Bleeding Events, *n*	Case-Fatality Rate (95% CI), %
Any	33	17	247	8.4 (5.4–12.1)
Vitamin K antagonists	22	15	207	8.3 (5.1–12.2)
Direct oral anticoagulants	11	2	40	9.7 (3.2–19.2)

* I^2 = 0% for all case-fatality rates.

Khan F et al, Ann Intern Med 2021

Figure 2. Incidence of major bleeding, according to presence and absence of risk factors for major bleeding.

Risk Factor	Study Cohorts, *n*	Major Bleeding Events/Person-Years, *n*/*N*		Incidence Rate per 100 Person-Years (95% CI)		IRR (95% CI)
		Risk Factor Present	Risk Factor Absent	Risk Factor Present	Risk Factor Absent	
Female sex						
VKA	23	94/4476	109/7685	2.02 (1.38–2.78)	1.55 (1.20–1.94)	1.55 (1.17–2.06)
DOAC	11	15/1483	26/2450	1.22 (0.67–1.93)	1.16 (0.70–1.72)	1.00 (0.51–1.95)
Age >65 y						
VKA	22	105/4964	74/6664	1.98 (1.41–2.64)	1.22 (0.87–1.63)	1.84 (1.32–2.57)
DOAC	11	25/1332	15/2606	2.01 (1.26–2.94)	0.66 (0.38–1.02)	2.92 (1.50–5.70)
Creatinine clearance <50 mL/min						
VKA	12	28/816	119/7853	2.89 (1.53–4.67)	1.58 (1.12–2.12)	2.83 (1.90–4.22)
DOAC	7	2/227	27/2642	1.41 (0.30–3.32)	1.13 (0.57–1.87)	3.71 (1.51–9.13)
History of bleeding						
VKA	10	8/230	119/6546	4.08 (1.97–6.91)	1.75 (1.23–2.35)	3.47 (1.86–6.50)
DOAC	10	9/102	27/3497	9.19 (4.13–16.0)	0.85 (0.55–1.21)	18.81 (9.54–37.07)
Concomitant antiplatelet therapy						
VKA	15	31/806	145/8689	3.98 (2.52–5.76)	1.61 (1.19–2.08)	2.89 (1.93–4.34)
DOAC	10	3/144	33/3385	3.45 (1.16–6.90)	1.05 (0.56–1.70)	17.18 (6.68–44.18)
Hemoglobin level <100 g/L						
VKA	12	7/333	139/8578	2.73 (1.13–4.98)	1.45 (0.92–2.10)	6.51 (3.23–13.13)
DOAC	9	2/80	29/3235	4.03 (0.96–9.07)	1.00 (0.59–1.52)	17.41 (7.67–39.55)



Predicting major bleeding during extended anticoagulation for unprovoked or weakly provoked venous thromboembolism

Philip S. Wells,[1] Tobias Tritschler,[2] Faizan Khan,[1,3] David R. Anderson,[4] Susan R. Kahn,[5,6] Alejandro Lazo-Langner,[7] Marc Carrier,[1] Grégoire Le Gal,[1] Lana A. Castellucci,[1] Vinay Shah,[8] Scott Kaatz,[8] Clive Kearon,[9] Susan Solymoss,[5] Russell Zide,[10] Sam Schulman,[9,11] Isabelle Chagnon,[12] Ranjeeta Mallick,[1] Marc A. Rodger,[1,5,*] and Michael J. Kovacs[7,*]

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Blood Adv 2022; 6: 4605-16

Wells PS et al, Blood Adv 2022

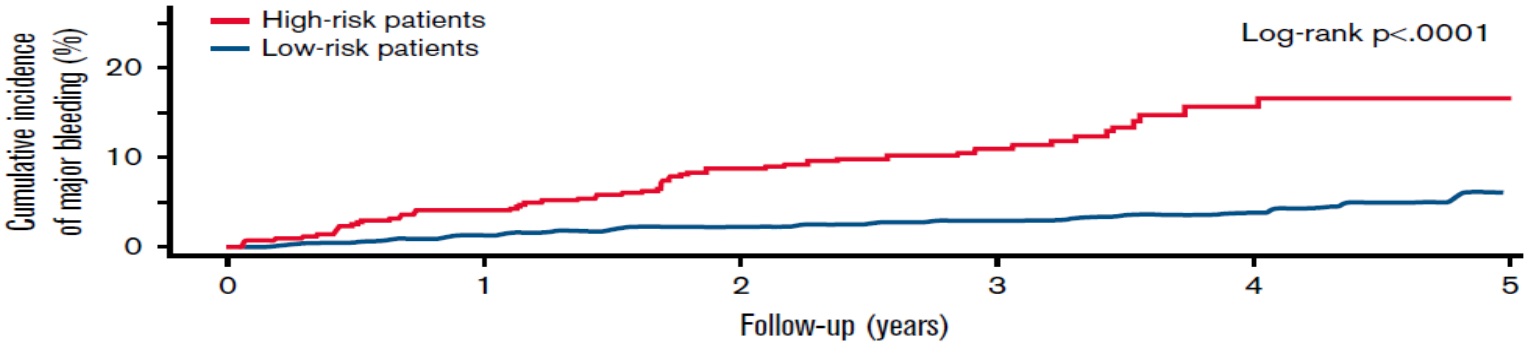
Table 3. New multivariable prediction model (CHAP).

	Original dataset		Imputation dataset	
	Beta-coefficient	Hazard ratio (95% CI)	Beta-coefficient	Hazard ratio (95% CI)
Creatinine (per µmol/L increase)	0.0017	1.002 (0.999-1.004)	0.0017	1.002 (0.999-1.004)
Hemoglobin (per g/L increase)	-0.0127	0.987 (0.980-0.994)	-0.0125	0.987 (0.981-0.994)
Age (per year increase)	0.0251	1.025 (1.011-1.04)	0.0237	1.024 (1.01-1.038)
Antiplatelet agent	0.8995	2.458 (1.47-4.112)	0.8871	2.428 (1.457-4.047)

Abbreviation: CI, confidence interval.

Baseline hazard at 1 year = 0.02.

Sample calculation: 65-year-old patient on concomitant antiplatelet agent with a creatinine level of 115 µmol/L and a hemoglobin of 110 g/L: 0.02 * exp(115*0.0017 + 110*(-0.0127) + 65*0.0251 + 1*0.8995) = 7.6% predicted risk of major bleeding at 1 year of extended anticoagulation.



Follow-up (years)	No. of major bleeds	No. remaining in cohort	Cumulative incidence, % (95% CI)
Low-risk patients			
1	23	1535	1.4 (0.9–2.1)
2	13	1177	2.3 (1.7–3.2)
3	7	815	3.0 (2.2–4.1)
4	5	404	3.8 (2.8–5.1)
5	5	173	5.5 (3.9–7.6)
High-risk patients			
1	24	492	4.4 (2.9–6.4)
2	19	345	8.6 (6.4–11.4)
3	7	232	10.8 (8.2–14.1)
4	8	106	14.9 (11.4–19.3)
5	1	45	16.0 (12.1–21.1)

[high risk = annual rate ≥ 2.5%]

ESC European Society of Cardiology

European Heart Journal (2023) **00**, 1–14
https://doi.org/10.1093/eurheartj/ehac776

CLINICAL RESEARCH
Thrombosis and antithrombotic treatment

Recurrent venous thromboembolism and bleeding with extended anticoagulation: the VTE-PREDICT risk score

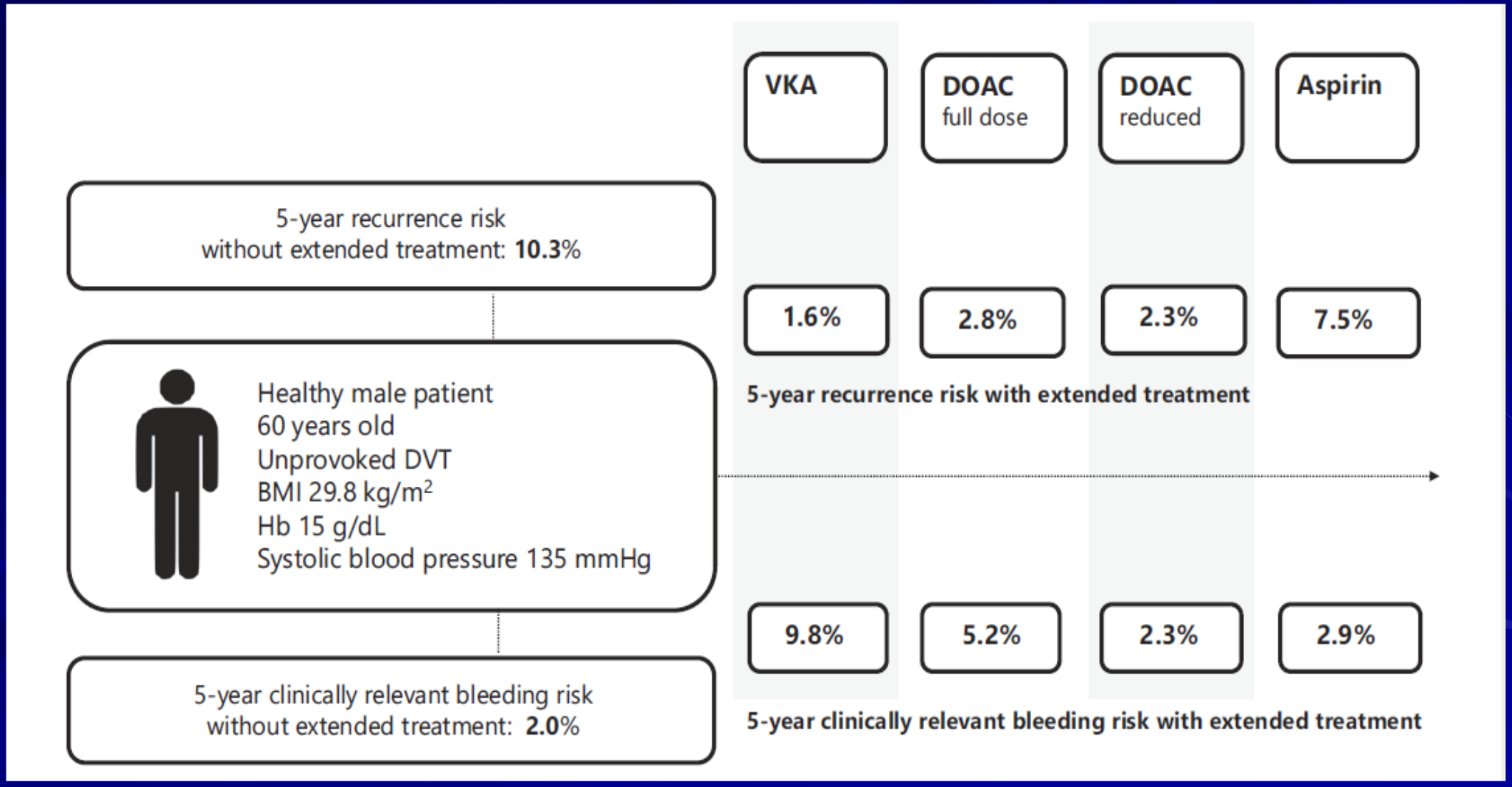
Maria A. de Winter [1], Harry R. Büller[2], Marc Carrier[3], Alexander T. Cohen[4], John-Bjarne Hansen[5], Karin A.H. Kaasjager[1], Ajay K. Kakkar[6], Saskia Middeldorp[7], Gary E. Raskob[8], Henrik T. Sørensen[9], Frank L.J. Visseren[10], Philip S. Wells[3], Jannick A.N. Dorresteijn [10†], Mathilde Nijkeuter [1*†], and the VTE-PREDICT study group

EHJ 2023

Table 2 Prediction models for recurrent VTE and bleeding

	Predictor	Recurrent VTE		Bleeding	
		sHR (95% CI)	$\chi 2$ statistic	sHR (95% CI)	$\chi 2$ statistic
Demographics and physical examination	Age (per decade)	1.01 (0.97–1.06)	0.20	1.05 (1.03–1.08)	7.95
	Female sex	0.86 (0.75–0.98)	2.38	1.14 (1.05–1.24)	4.87
	BMI (kg/m^2; per 1 unit increase)	1.00 (0.99–1.02)	0.21		
	Systolic blood pressure (per 10 mmHg)			1.07 (1.03–1.10)	14.36
Index event	PE	1.02 (0.89–1.18)	0.05	1.07 (0.98–1.17)	1.47
	Provoked by surgery, trauma or immobilization	0.81 (0.68–0.98)	3.16		
	Provoked by oestrogen therapy	0.68 (0.47–1.00)	2.53		
Medical history	History of cancer	1.53 (1.14–2.06)	6.44	2.48 (2.00–3.07)	128.44
	History of VTE	1.13 (0.97–1.32)	1.10		
	History of bleeding			1.26 (1.11–1.44)	4.57
	Stroke			1.26 (1.08–1.46)	3.72
Lab values	Hb (g/dL; per 1 unit increase)			0.95 (0.93–0.97)	9.69
Co-medication	NSAIDs			1.22 (1.08–1.38)	5.92

https://vtepredict.com



DOAC score per le predizione del rischio emorragico in soggetti con fibrillazione atriale candidati a terapia con DOAC

Clinical risk prediction tool	Points
Age, y	
65–69	2
70–74	3
75–79	4
≥80	5
Creatinine clearance/estimated glomerular filtration rate (mL/min)	
30–60	1
<30	2
Underweight (body mass index <18.5 kg/m^2)	1
Stroke/transient ischemic attack/embolism history	1
Diabetes	1
Hypertension	1
Antiplatelet use	
Aspirin	2
Dual-antiplatelet	3
Nonsteroidal anti-inflammatory (NSAID) use	1
Bleeding history	3
Liver disease*	2

0-3 rischio molto basso; 4-5 basso; 6-7 intermedio
8-9 alto; ≥10 molto alto

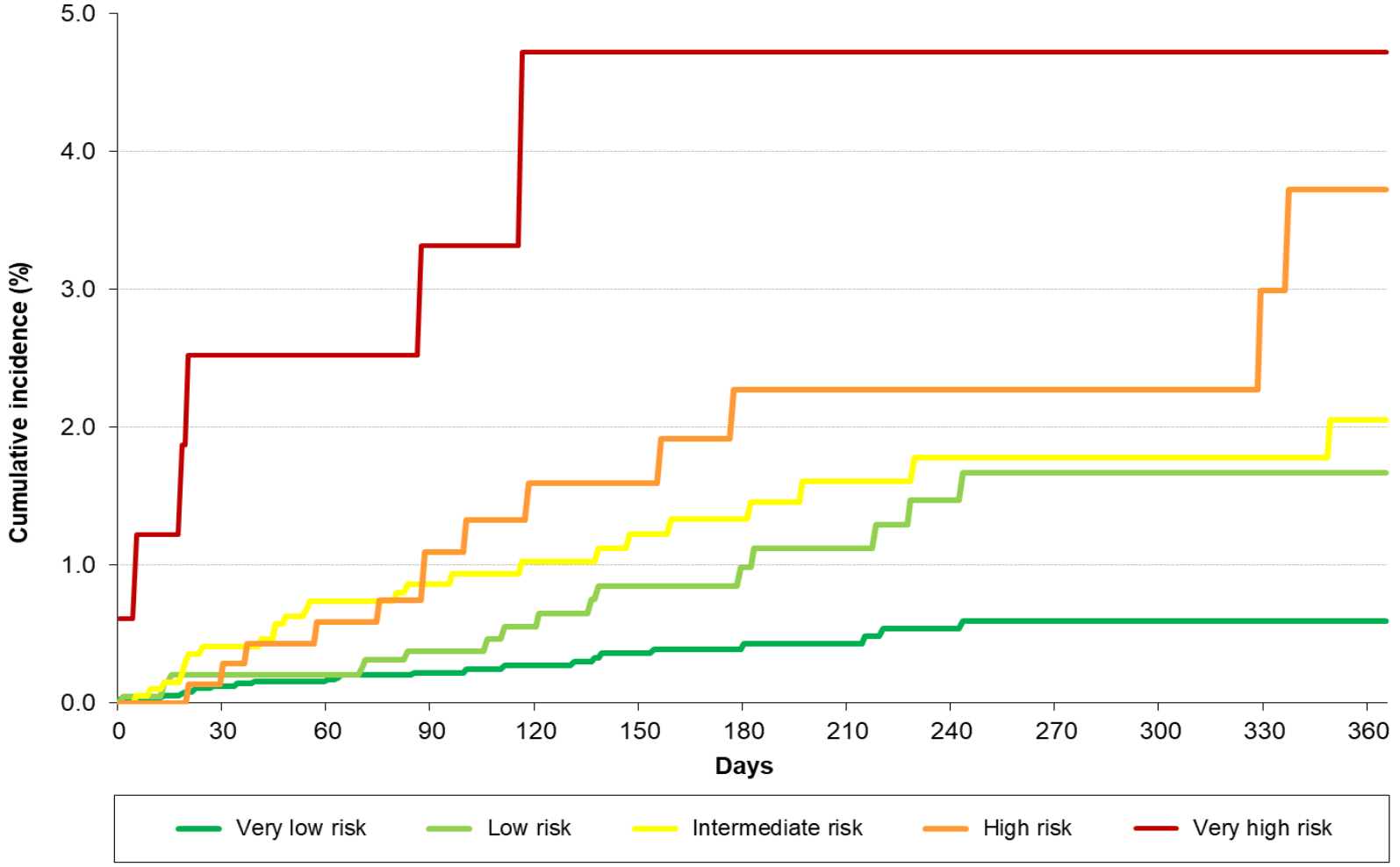
DOAC Score for prediction of major bleeding in patients with venous thromboembolism Findings from the RIETE registry

Prandoni P, Bilora F, Pesavento R, Pedrajas JM, Fernández-Reyes JL, Gómez-Cuervo C, Villalobos A, Alda-Lozano A, Simioni P, Monreal M

Thromb Res 2025 [in press]

Features	Patients on DOAC treatment (N = 12 835)
Age (mean years ±SD)	62±18
Males	6,727 (52.4)
Previous VTE	2,159 (16.8)
Initial VTE presentation	
- PE (with/without DVT)	7,834 (61.0)
- proximal DVT	2,878 (22.4)
- isolated calf DVT	1,018 (7.9)
- other VTE sites	1,105 (8.6)
Risk factors of venous thrombosis	
- unprovoked	4,751 (37.0)
- minor persistent risk factors*	5,186 (40.4)
- minor transient risk factors**	2,898 (22.6)
Bleeding risk according to DOAC Score	
- very low (score 0-3)	7,697 (60.0)
- low (score 4-5)	2,088 (16.3)
- intermediate (score 6-7)	2,090 (16.3)
- high (score 8-9)	796 (6.2)
- very high (score ≥ 10)	164 (1.3)

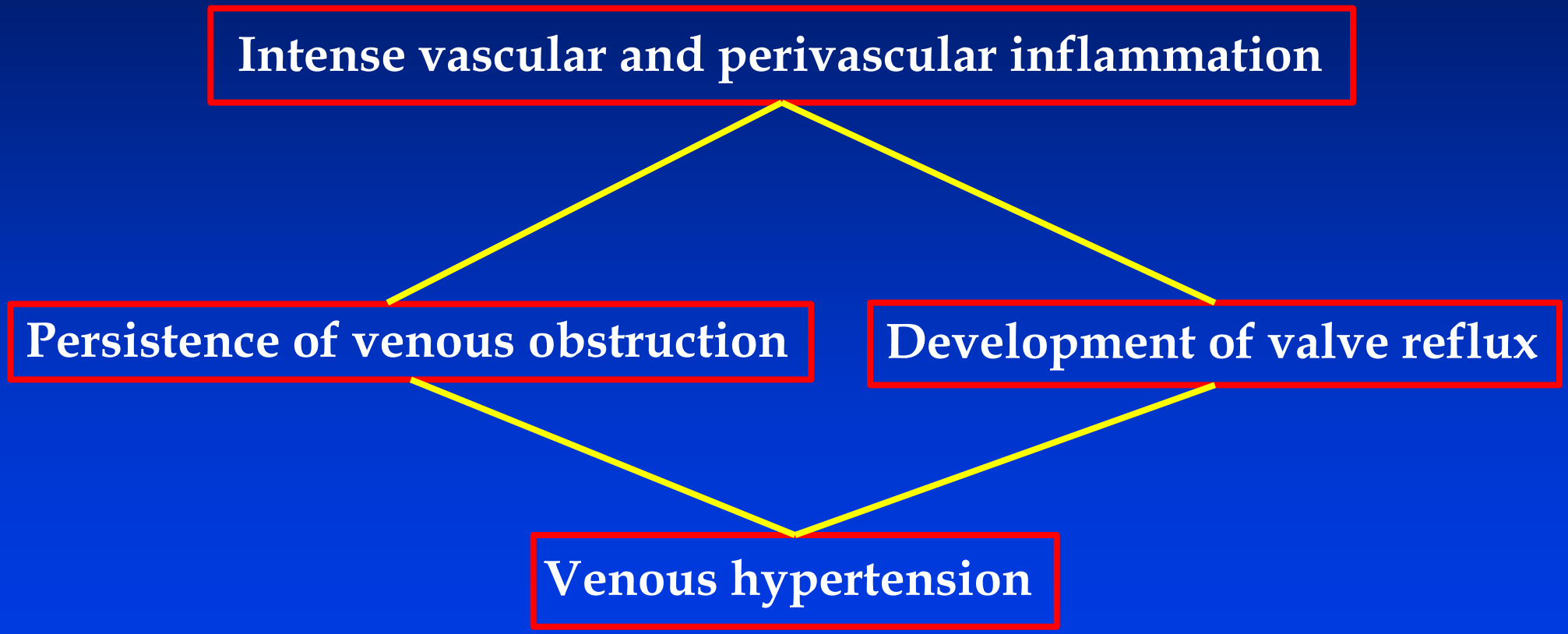
Cumulative incidence of major bleedings in each of the five subgroups of patients according to the DOAC score



C-index 0.72 (95% CI, 0.66 – 0.77)

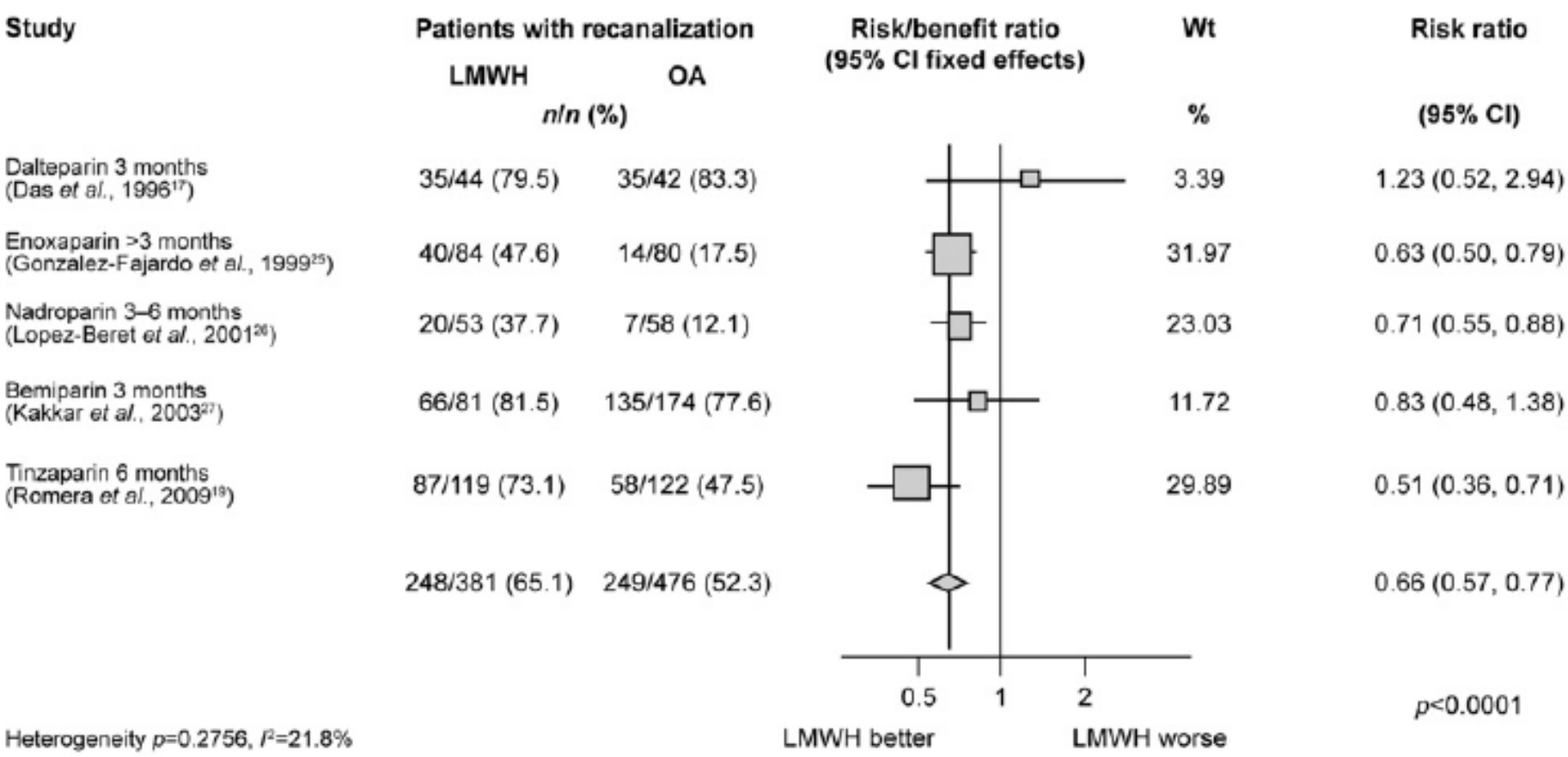
Nuove prospettive per la prevenzione della PTS

Mechanisms of PTS development



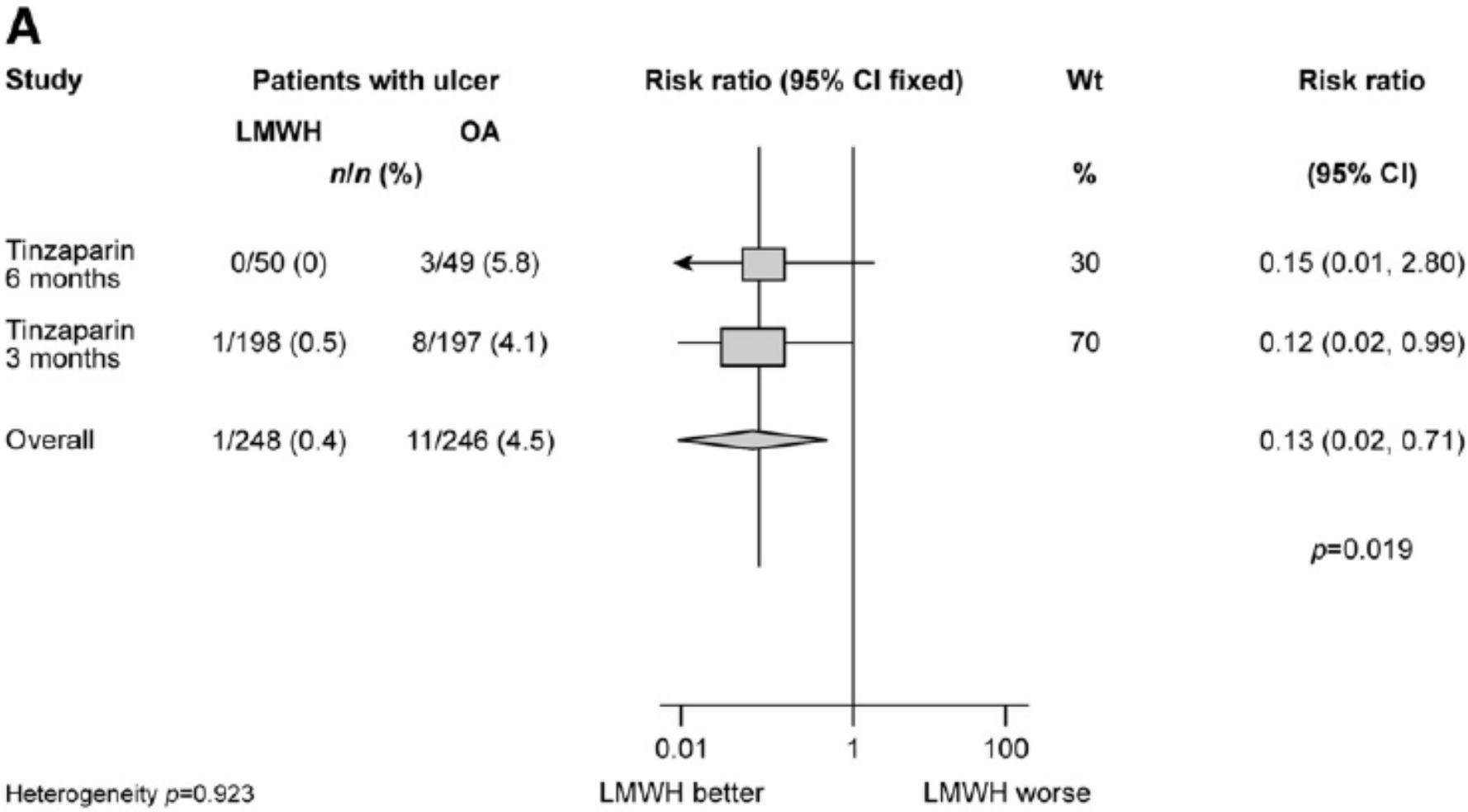
LMWH vs VKA for prevention of PTS: Veins recanalisation

B

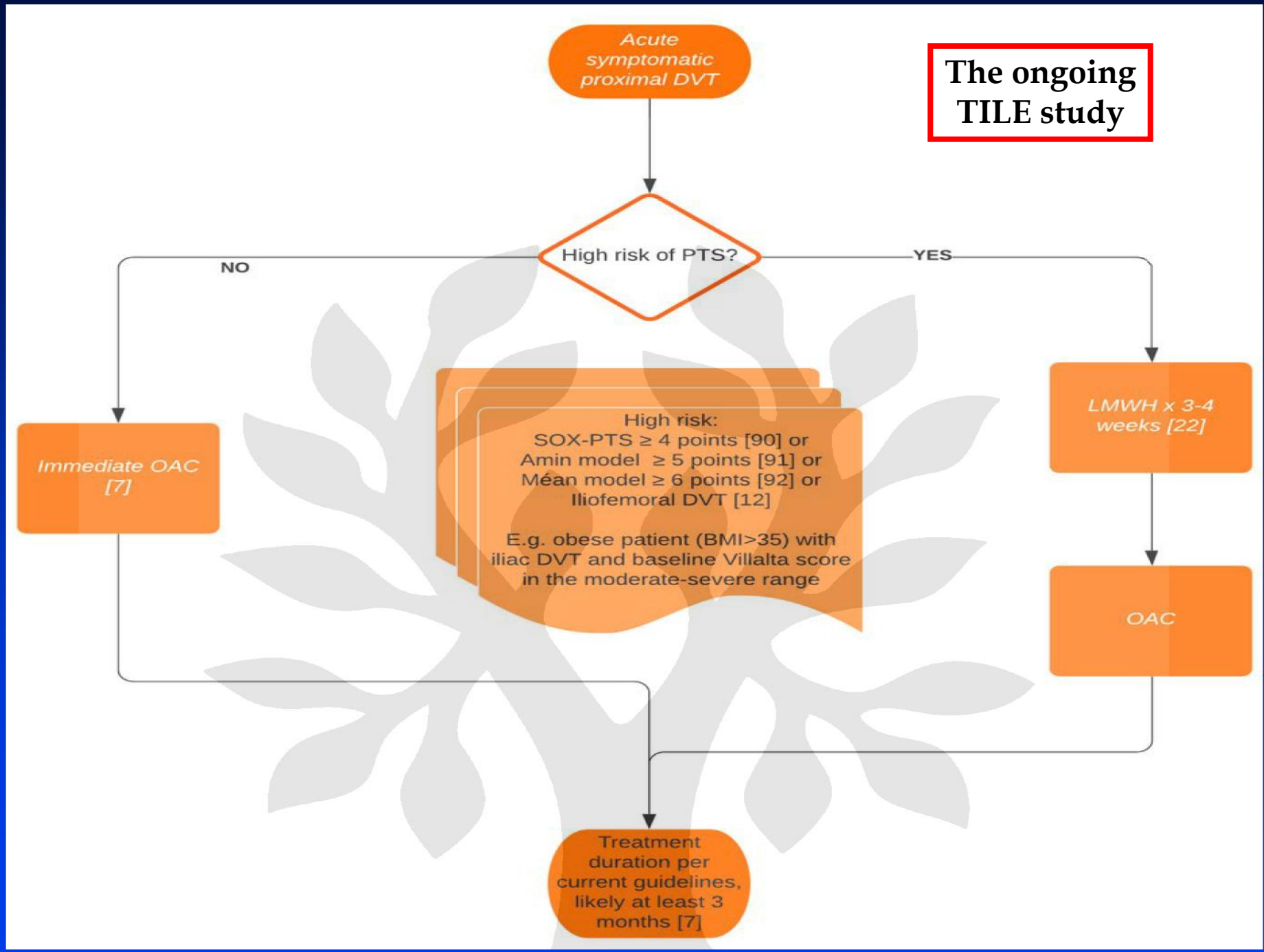


R Hull, Am J Med 2011

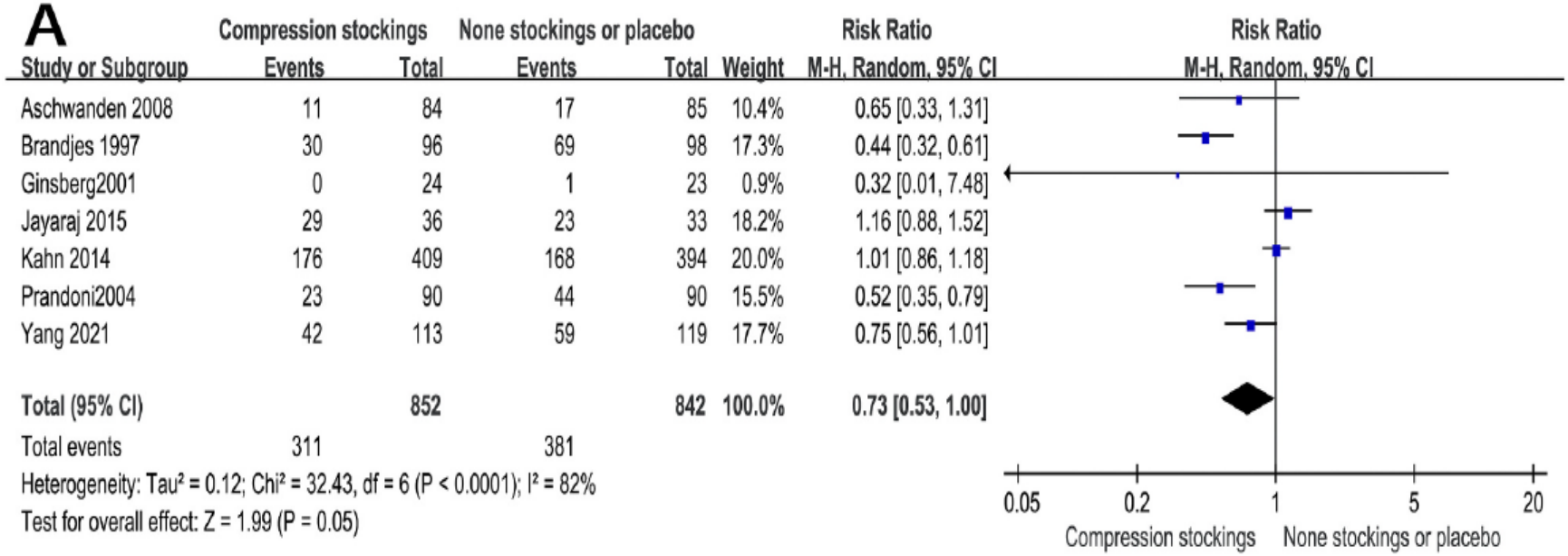
LMWH vs VKA for prevention in PTS: Skin ulcer



R Hull, Am J Med 2011


Acute symptomatic proximal DVT
The ongoing TILE study
High risk of PTS?
NO
YES
Immediate OAC [7]
High risk:
SOX-PTS ≥ 4 points [90] or
Amin model ≥ 5 points [91] or
Méan model ≥ 6 points [92] or
Iliofemoral DVT [12]
E.g. obese patient (BMI>35) with iliac DVT and baseline Villalta score in the moderate-severe range
LMWH x 3-4 weeks [22]
OAC
Treatment duration per current guidelines, likely at least 3 months [7]

Compression Stockings to Prevent PTS
Metanalysis of RCTs



A

Study or Subgroup	Compression stockings Events	Total	None stockings or placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Aschwanden 2008	11	84	17	85	10.4%	0.65 [0.33, 1.31]
Brandjes 1997	30	96	69	98	17.3%	0.44 [0.32, 0.61]
Ginsberg2001	0	24	1	23	0.9%	0.32 [0.01, 7.48]
Jayaraj 2015	29	36	23	33	18.2%	1.16 [0.88, 1.52]
Kahn 2014	176	409	168	394	20.0%	1.01 [0.86, 1.18]
Prandoni2004	23	90	44	90	15.5%	0.52 [0.35, 0.79]
Yang 2021	42	113	59	119	17.7%	0.75 [0.56, 1.01]
Total (95% CI)		**852**		**842**	**100.0%**	**0.73 [0.53, 1.00]**
Total events	311		381			

Heterogeneity: Tau² = 0.12; Chi² = 32.43, df = 6 (P < 0.0001); I² = 82%

Test for overall effect: Z = 1.99 (P = 0.05)

Meng J et al, Thromb Res 2023

The value of compression elastic stockings for prevention of PTS in patients with and without RVT and/or PVR: sub-analysis of a prospective cohort study

Paolo Prandoni, Anthonie WA Lensing, Martin H Prins, Sabina Villalta, Raffaele Pesavento, Daniela Tormene, Franco Noventa, Gualtiero Palareti

Haematologica 2022

PTS development in patients with and without CES, according to the presence of vein abnormalities

PTS	No RVT and/or PVI		RVT and/or PVI	
	NO ES (N=139)	ES (N=183)	NO ES (N=211)	ES (N=328)
Overall	42 (30.2)	48 (26.2)	135 (64.0)	114 (34.8)
p	0.430		0.001	
Mild	36 (25.9)	43 (23.5)	116 (55.0)	100 (30.5)
Severe	6 (4.3)	5 (2.7)	19 (9.0)	14 (4.3)
p	0.625		0.001	

Implicazioni per la pratica clinica

- Prolungamento della terapia eparinica iniziale nei soggetti a più alto rischio di PTS?

- Impiego delle calze elastiche in tutti i pazienti con TVP prossimale e loro prolungamento in quelli con residuo trombotico venoso a distanza di 3 mesi dalla TVP (da indagare!)

25 mm Hg versus 35 mm Hg elastic compression stockings to prevent post-thrombotic syndrome after deep vein thrombosis (CELEST): a randomised, double-blind, non-inferiority trial

*Jean-Philippe Galanaud, Céline Genty-Vermorel, Marie-Thérèse Barrellier, François Becker, Violaine Jabbour, Sophie Blaise, Alessandra Bura-Rivière, Alexa Comte, Claire Grange, Herve Guenneguez, Mario Maufus, Pierre Ouvry, Cécile Richaud, Carole Rolland, Jeannot Schmidt, Marie-Antoinette Sevestre, François Verrière, Jean-Luc Bosson for the CELEST trial investigators**

Lancet Haematol 2022; 9: e886-96

	25 mm Hg ECS group (n=171*)	35 mm Hg ECS group (n=170*)
Patients' characteristics†		
Median age, years	59 (47–69)	59 (44–71)
Sex		
Female	54 (32%)	54 (32%)
Male	117 (68%)	116 (68%)
Initial in-hospital management‡	129 (75%)	128 (75%)
BMI		
<25 kg/m²	66 (39%)	58/169 (34%)
25–30 kg/m²	69 (40%)	77/169 (46%)
≥30 kg/m²	36 (21%)	34/169 (20%)
Previous venous thromboembolism	40 (23%)	30/166 (18%)
Cancer	20 (12%)	19/169 (11%)
Baseline contralateral Villalta score ≥5	14 (8%)	14/166 (8%)
DVT characteristics		
Unprovoked DVT	101/160 (63%)	92/152 (61%)
Time from DVT diagnosis to randomisation <3 days	124 (73%)	134 (79%)
Right leg DVT	70 (41%)	71 (42%)
Most proximal DVT extent		
Iliac	27/170 (16%)	27/158 (17%)
Femoral	82/170 (48%)	70/158 (44%)
Popliteal	61/170 (36%)	61/158 (39%)
Anticoagulant treatment		
Duration of treatment		
≤90 days	9/131 (7%)	9/126 (7%)
91–180 days	18/131 (14%)	19/126 (15%)
>180 days	104/131 (79%)	98/126 (78%)
Initial anticoagulant treatment low-molecular-weight heparin	119 (70%)	105/168 (63%)
Median duration of low-molecular-weight heparin, days	4 (2–19; n=103)	4 (2–8; n=88)
Long-term anticoagulant treatment		
Vitamin K antagonist	49/153 (32%)	45/152 (30%)
Direct oral anticoagulant	104/153 (68%)	107/152 (70%)

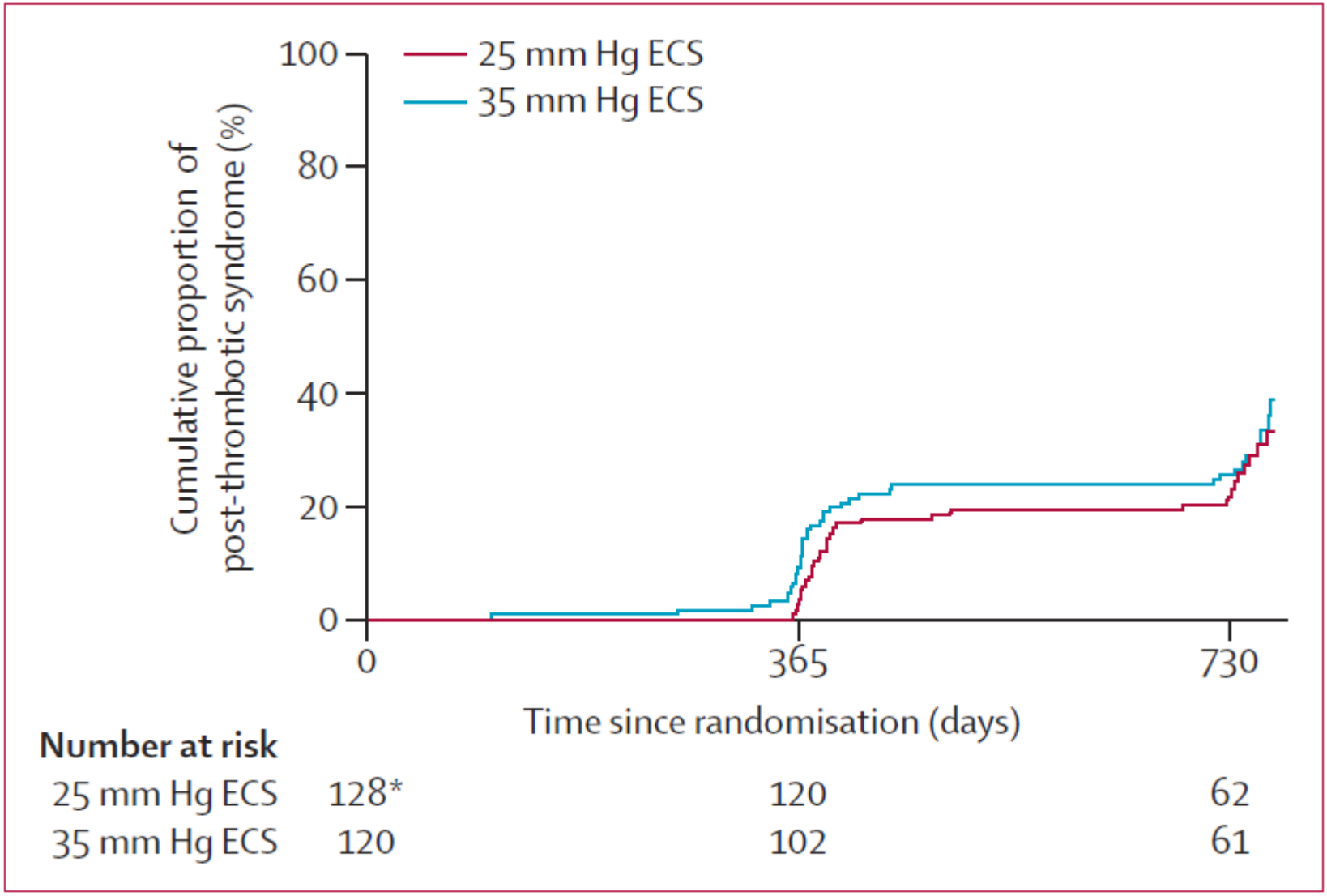
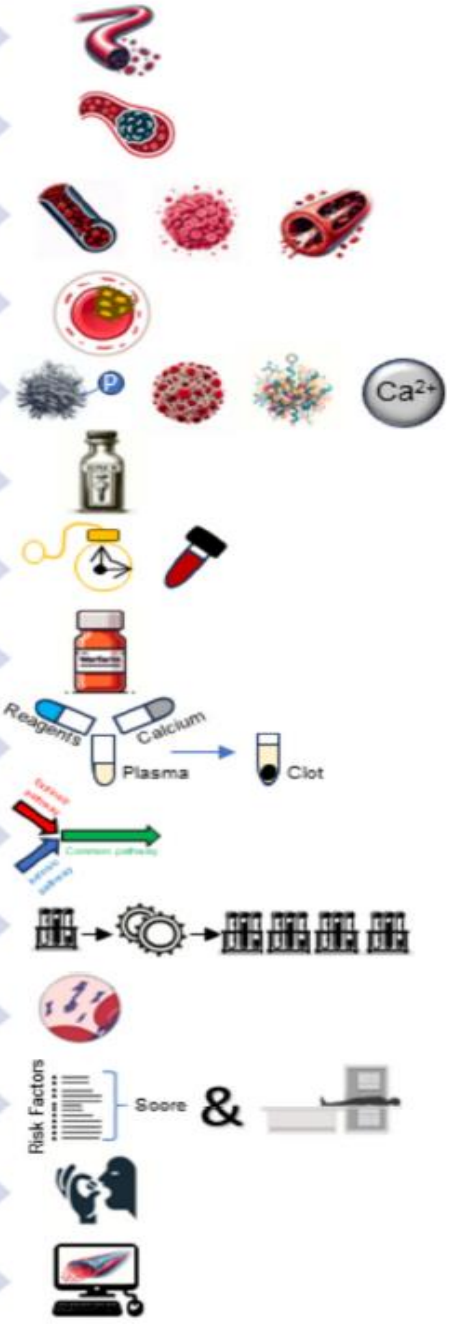


Figure 2: Cumulative proportions of post-thrombotic syndrome, in the 249 patients with complete datasets for the primary outcome

L’arrivo dell’Intelligenza Artificiale: un terremoto di portata epocale

1628	*Blood circulation*	William Harvey describes the importance of blood circulation
1835	*Tissue factor*	Andrew Buchanan discovers blood clots
1856	*Virchow's triad*	Stasis, Hypercoagulability, Endothelial injury
1882	*Platelets*	Giulio Bizzozero discovers platelets adhering to damaged vessels under the microscope
1905	*Coagulation*	Paul Morawitz coins the term coagulation, citing 4 factors: thrombokinase, fibrinogen, prothrombin and calcium
1916	*Heparin*	Jay McLean discovers Heparin. Since 1935, thrombosis associated mortality has decreased from 18% to 0.4% thanks to Heparin
1935	*Prothrombin Time Test*	Armand Quick invents the first prothrombin time test
1939	*Anticoagulants*	Warfarin is discovered
1953	*Activated Partial Thromboplastin Time Test (aPTT)*	R.D. Langdell, R.H. Wagner, and K.M. Brinkhoua develop the aPTT
1964	*Coagulation Cascade*	Two independent teams, separately led by Macfarlane and Ratnoff, describe the waterfall coagulation cascade
1980s	*Automation*	Automation of coagulation instruments occurs
1993	*D-Dimer Test*	The D-Dimer Test is developed for ruling out pulmonary embolism
1998	*Pulmonary Embolism Diagnosis*	The Wells Score is developed for prediction of pulmonary embolism, and Computed Tomography Pulmonary Angiography (CTPA) is introduced for diagnosing PE
2010s	*Oral Treatment*	Direct oral anticoagulants (DOACs) are developed
2020s-Future	*Artificial Intelligence???*	Studies of Machine Learning in VTE medicine Can AI be utilized in the practice of VTE prevention/ diagnosis/ management?



Vi aspetto sulla mia pagina di aggiornamento bibliografico e culturale sulle malattie trombotiche:

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