Προφυλακτική αγωγή υποτροπής στην πνευμονική εμβολή

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Disclosure

- ….. **no** conflict of interest

«τι έχει αλλάξει ?»

NOAC/DOAC

VTE

- proximal DVT + PE
- Χρόνια - υποτροπιάζουσα νόσο ?
- Χρόνια θεραπεία ?

8.4. Recommendations for the regimen and duration of anticoagulation after pulmonary embolism i[redacted]

Recommendations	Class[a]	Level[b]
Therapeutic anticoagulation for ⩾ 3 months is recommended for all patients with PE [347].	I	A
Patients in whom discontinuation of anticoagulation after 3 months is recommended		
For patients with first PE/VTE secondary to a major transient/reversible risk factor, discontinuation of therapeutic oral anticoagulation is recommended after 3 months [331, 340, 341].	I	B
Patients in whom extension of anticoagulation beyond 3 months is recommended		
Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor [358].	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with antiphospholipid antibody syndrome [359].	I	B

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παράταση αγωγής ?

- ↓ 80-90% μείζονα αιμορραγία

- Προγνωστικά σκορ κινδύνου υποτροπής
- Προγνωστικά μοντέλα εκτίμηση αιμορραγικού κινδύνου

upplementary Table 13 Validated prediction models for quantification of the risk of recurrent venous thromboembolism

Prediction model	Parameters	Points	Categories of recurrence risk	Risk group (for VTE recurrence) studied	Type of studies	Number of PE patients included	Remarks
Vienna prediction model[33–35]	• Male sex • Proximal DVT • Pulmonary embolism • D-dimer (continuous value)	n.a.	Continuous (nomogram)	Unprovoked VTE	Cohorts database (derivation, validation)	Derivation study: 438 (47% of cohort) Validation study: 291 (32%)	
HERDOO2[36,37]	• Hyperpigmentation, oedema or leg redness • D-dimer ≥250 mg/L (on VKAs) • Body mass index ≥30 kg/m^2 • Age ≥65 years	1 1 1 1	0—1 points: low risk; ≥2 points: high risk	Unprovoked VTE (derivation); unprovoked VTE, or with minor risk factors (validation)	Management study (derivation, internal validation)	Derivation study: 327 (49%) Management study: 1634 (59%)	Only applicable in women
DASH tool[38,39]	• D-dimer (post-VKA; normal or abnormal) • Age <50 years • Male sex • Hormonal therapy	2 1 1 —2	≤1 points: low risk; ≥2 points: high risk	Unprovoked VTE, or minor risk factors	Cohorts database (derivation, external validation)	Not reported	
DAMOVES[40,41]	• Age (continuous) • Sex • Obesity • Abnormal D-dimer • Factor VIII (continuous) • Genetic thrombophilia • Varicose veins	n.a.	Continuous (nomogram)	Unprovoked VTE	Prospective cohort (derivation) Retrospective cohort (external validation)	Derivation study: 270 (68%) Validation study: not reported	

Ottawa[a] [42,43]	• Female sex
	• Primary tumour site:
	  • lung
	  • breast
	• Tumour Node Metastasis stage I
	• History of VTE
		1
		1
		—1
		—2
		1
			≤0: low risk;
			≥1: high risk
				Patients with cancer	Retrospective cohort (derivation)
					Two RCTs (external validation)
						Not reported	Only applicable in patients with cancer

Supplementary Table 14 Prediction models for quantifying bleeding risk

Prediction model	Parameters	Points	Categories of bleeding risk	Validation status
OBRI[44]	Age ≥65 years History of stroke History of gastrointestinal bleeding Recent myocardial infarction, renal insufficiency, diabetes, or anaemia	1 1 1 1	0: low 1—2: intermediate 3—4: high	Validation showed modest accuracy in VKA cohorts (reviewed in Klok *et al.*[45]) No data in patients treated with NOACs
Kuijer *et al.*[46]	Age ≥60 years Female sex Malignancy	1.6 1.3 2.2	0: low 1—3: intermediate >3: high	
RIETE[47]	Age >75 years Recent bleeding Cancer Creatinine >1.2 mg/dL Anaemia PE (vs. DVT) index event	1 2 1 1.5 1.5 1	0: low 1—4: intermediate >4: high	
HAS-BLED[48,49]	Uncontrolled hypertension Abnormal liver/renal function Previous stroke Bleeding history or predisposition Labile INR (time in therapeutic range <60%) Age >65 years Concomitant drugs or alcohol	1 1 1 1 1 1 1	0—2: low ≥3: high	
VTE-BLEED[50]	Active cancer Male patient with uncontrolled hypertension Anaemia History of bleeding Age ≥60 years Renal dysfunction (CrCl 30—60 mL/min)	1.5 2 1 1.5 1.5 1.5	0—1: low ≥2: high	Validated in *post hoc* analysis of RCTs testing NOACs vs. VKAs after initial LMWH treatment[50,51]

πιθανότητα υποτροπής

TABLE 11 Categorization of risk factors for venous thromboembolism based on the risk of recurrence over the long-term

Estimated risk for long-term recurrence[a]	Risk factor category for index PE[b]	Examples[b]
Low (<3% per year)	Major transient or reversible factors associated with >10-fold increased risk for the index VTE event (compared to patients without the risk factor)	• Surgery with general anaesthesia for >30 min • Confined to bed in hospital (only "bathroom privileges") for ≥3 days due to an acute illness, or acute exacerbation of a chronic illness • Trauma with fractures
Intermediate (3-8% per year)	Transient or reversible factors associated with ≤10-fold increased risk for first (index) VTE	• Minor surgery (general anaesthesia for <30 min) • Admission to hospital for <3 days with an acute illness • Oestrogen therapy/contraception • Pregnancy or puerpium • Confined to bed out of hospital for ≥3 days with an acute illness • Leg injury (without fracture) associated with reduced mobility ≥3 days • Long-haul flight
	Non-malignant persistent risk factors	• Inflammatory bowel disease • Active autoimmune disease
	No identifiable risk factor	
High (>8% per year)		• Active cancer • One or more previous episodes of VTE in the absence of a major transient or reversible factor • Antiphospholipid antibody syndrome

PE: pulmonary embolism; VTE: venous thromboembolism. [a]If anticoagulation is discontinued after the first 3 months (based on data from Baglin *et al.* [340] and Iorio *et al.* [341]). [b]The categorization of risk factors for the index VTE event is in line with that proposed by the International Society on Thrombosis and Haemostasis [338]. The present Guidelines avoid terms such as "provoked", "unprovoked", or "idiopathic" VTE.

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CHEST

2021

Executive Summary

Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report

Scott M. Stevens, MD; Scott C. Woller, MD; Lisa Baumann Kreuziger, MD; Henri Bounameaux, MD; Kevin Doerschug, MD; Geert-Jan Geersing, MD, PhD; Menno V. Huisman, MD; Clive Kearon, MD, PhD; Christopher S. King, MD; Andrew J. Knighton, PhD; Erica Lake, MLS; Susan Murin, MD; Janine R. E. Vintch, MD; Philip S. Wells, MD; and Lisa K. Moores, MD

Guidance statements for antithrombotic therapy for VTE are arranged according to the descriptions of the phase of management:

- Initiation phase (~5-21 days): The initial provision of anticoagulants following VTE diagnosis
- Treatment phase (3 months): The period after initiation that completes treatment for the acute VTE event
- Extended phase (3 months-no planned stop date): The period of anticoagulant use at full or reduced dose for the goal of secondary prevention

Extended-Phase Therapy

22. In patients with VTE diagnosed in the setting of a major transient risk factor (see text), we recommend against offering extended-phase anticoagulation (strong recommendation, moderate-certainty evidence).

23. In patients with VTE diagnosed in the setting of a minor transient risk factor (see text), we suggest against offering extended-phase anticoagulation (weak recommendation, moderate-certainty evidence).

24. In patients with VTE diagnosed in the absence of transient provocation (unprovoked VTE or provoked by persistent risk factor), we recommend offering extended-phase anticoagulation with a DOAC (strong recommendation, moderate-certainty evidence).

extended-phase therapy is defined as having no planned stop date,

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? Should extended-phase anticoagulant therapy vs no extended-phase anticoagulant therapy be provided to patients with venous thromboembolism who have completed the treatment phase of therapy?:

Duration of Treatment Phase of Anticoagulation

21. In patients with acute VTE who do not have a contraindication we recommend a 3-month treatment phase of anticoagulation (strong recommendation, moderate-certainty evidence).

Remark: On completion of the 3-month treatment phase of therapy, all patients should be assessed for extended-phase therapy.

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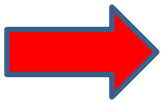
Patients in whom extension of anticoagulation beyond 3 months should be considered[c,d]

Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor [330, 331, 347, 351–353].	IIa	A
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a persistent risk factor other than antiphospholipid antibody syndrome [330, 352, 353].	IIa	C
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a minor transient or reversible risk factor [330, 331, 352].	IIa	C



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American Society of Hematology 2023 Guidelines for Management of Venous Thromboembolism: Thrombophilia Testing

Hereditary thrombophilia: heterozygous FVL mutation, heterozygous PGM, antithrombin deficiency, protein C deficiency, or protein S deficiency. For select questions, homozygous FVL and the combination of FVL mutation plus PGM were included as hereditary thrombophilia.

High-risk thrombophilia: antithrombin deficiency, protein C deficiency, or protein S deficiency. For select questions, homozygous FVL and the combination of FVL mutation plus PGM.

Low-risk thrombophilia: heterozygous FVL mutation or heterozygous PGM.

Panel testing for thrombophilia: testing for APLA and all hereditary thrombophilia types

Section 1: Thrombophilia testing in patients with symptomatic VTE

Question 1: *In patients with unprovoked VTE, should thrombophilia testing be performed to guide treatment duration?*

NO

Recommendation 1. In patients with unprovoked VTE who have completed primary short-term treatment, the ASH guideline panel suggests not to perform thrombophilia testing to guide the duration of anticoagulant treatment (conditional recommendation based on very low certainty of the evidence about effects ⨁◯◯◯).

Remarks:

- In the Treatment of VTE ASH guideline indefinite antithrombotic therapy is suggested in most patients with unprovoked VTE (recommendation 19).

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Question 2: In patients with VTE provoked by surgery, should thrombophilia testing be performed to guide treatment duration? NO

Recommendation 2. In patients with VTE provoked by surgery who have completed primary short-term treatment, the ASH guideline panel suggests not to perform thrombophilia testing to determine the duration of anticoagulant treatment (conditional recommendation based on very low certainty of the evidence about effects ⨁◯◯◯).

Remarks:

- According to the Treatment of VTE ASH guideline most patients with VTE provoked by temporary risk factors will discontinue anticoagulant therapy after completion of the primary treatment.

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Question 3: In patients with VTE provoked by a non-surgical major transient risk factor, should thrombophilia testing be performed to guide treatment duration? YES

Recommendation 3. In patients with VTE provoked by a non-surgical major transient risk factor who have completed primary short-term treatment, the ASH guideline panel suggests testing for thrombophilia to guide anticoagulant treatment duration. The panel suggests indefinite anticoagulant treatment in patients with thrombophilia and stopping anticoagulant treatment in patients without thrombophilia (conditional recommendation based on very low certainty of the evidence about effects ⨁◯◯◯).

- Non-surgical major transient risk factors: e.g. confinement to bed in hospital for at least 3 days with an acute illness ("bathroom privileges only"), or a combination of minor transient risk factors such as admission to hospital for less than 3 days with an acute illness, confinement to bed out of hospital for at least 3 days with an acute illness, or leg injury associated with decreased mobility for at least 3 days. (

- This recommendation refers to testing for hereditary and acquired types of thrombophilia.

Question 4: In women with VTE provoked by pregnancy or postpartum, should thrombophilia testing be performed to guide treatment duration?

YES

Recommendation 4. In women with VTE provoked by pregnancy or postpartum who have completed primary treatment, the ASH guideline panel suggests thrombophilia testing to guide anticoagulant treatment duration. The panel suggests indefinite anticoagulant treatment in women with thrombophilia and stopping anticoagulant treatment in women without thrombophilia (conditional recommendation based on very low certainty of the evidence about effects ⨁◯◯◯).

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Question 5: In women with VTE associated with combined oral contraceptives, should thrombophilia testing be performed to guide treatment duration? YES

Recommendation 5. In women with VTE associated with combined oral contraceptives who have completed primary short-term treatment, the ASH guideline panel suggests testing for thrombophilia to guide anticoagulant treatment duration. The panel suggests indefinite anticoagulant treatment in women with thrombophilia and stopping anticoagulant treatment in women without thrombophilia (conditional recommendation based on very low certainty of the evidence about effects ⨁◯◯◯).

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επιλογή αγωγής

NOAC dose in extended anticoagulation[e]

If extended oral anticoagulation is decided after PE in a patient without cancer, a reduced dose of the NOACs apixaban (2.5 mg b.i.d.) or rivaroxaban (10 mg o.d.) should be considered after 6 months of therapeutic anticoagulation [352, 353].

IIa | A

Extended treatment with alternative antithrombotic agents

In patients who refuse to take or are unable to tolerate any form of oral anticoagulants, aspirin or sulodexide may be considered for extended VTE prophylaxis [355–357].

IIb | B

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επιλογή αγωγής

Reduced-Dose vs Full-Dose Anticoagulation for Extended Treatment of VTE

Guidance statement:

26. In patients offered extended-phase anticoagulation, we suggest the use of reduced-dose apixaban or rivaroxaban over full-dose apixaban or rivaroxaban (weak recommendation, very low-certainty evidence).

Remark: Reduced dose refers to apixaban 2.5 mg twice daily and rivaroxaban 10 mg once daily.

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επιλογή αγωγής

Aspirin for Extended Treatment of VTE

27. In patients offered extended-phase anticoagulation, we recommend reduced-dose DOAC over aspirin or no therapy (strong recommendation, low-certainty evidence) and suggest rivaroxaban over aspirin (weak recommendation, moderate-certainty evidence).

28. In patients with an unprovoked proximal DVT or PE who are stopping anticoagulant therapy and do not have a contraindication to aspirin, we suggest aspirin over no aspirin to prevent recurrent VTE (weak recommendation, low-certainty evidence).

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επιλογή αγωγής, Cancer

8.6. Recommendations for the regimen and the duration of anticoagulation after pulmonary embolism in patients with active cancer

Recommendations	Class[a]	Level[b]
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs [360–363].	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer [366].	IIa	B
Rivaroxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer [367].	IIa	C
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months)[c] should be considered for an indefinite period or until the cancer is cured [378].	IIa	B
In patients with cancer, management of incidental PE in the same manner as symptomatic PE should be considered, if it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with proven DVT [376, 377].	IIa	B

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επιλογή αγωγής, Cancer

16. In patients with acute VTE in the setting of cancer (cancer-associated thrombosis) we recommend an oral Xa inhibitor (apixaban, edoxaban, rivaroxaban) over LMWH for the initiation and treatment phases of therapy (strong recommendation, moderate-certainty evidence).

Remark: Edoxaban and rivaroxaban appear to be associated with a higher risk of GI major bleeding than LMWH in patients with cancer-associated thrombosis (CAT) and a luminal gastrointestinal malignancy, while apixaban does not. Apixaban or LMWH may be the preferred option in patients with luminal GI malignancies.

Follow-up

Follow-up of the patient under anticoagulation

In patients who receive extended anticoagulation, it is recommended that their drug tolerance and adherence, hepatic and renal[f] function, and bleeding risk be reassessed at regular intervals [259].

ευχαριστώ πολύ για την πρόσκληση και την προσοχή σας