Traitement curatif de la maladie thromboembolique veineuse

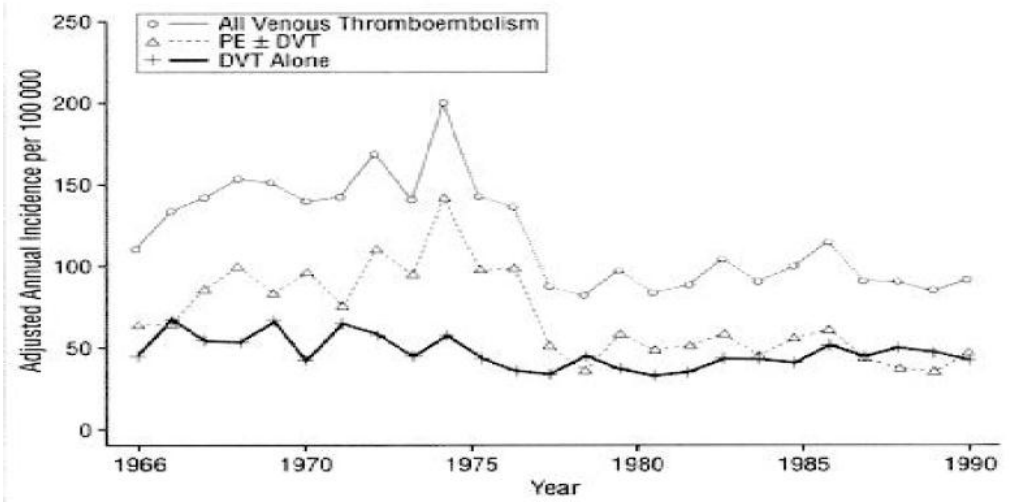
Jalila BEN KHELIL

Service de Réanimation Respiratoire

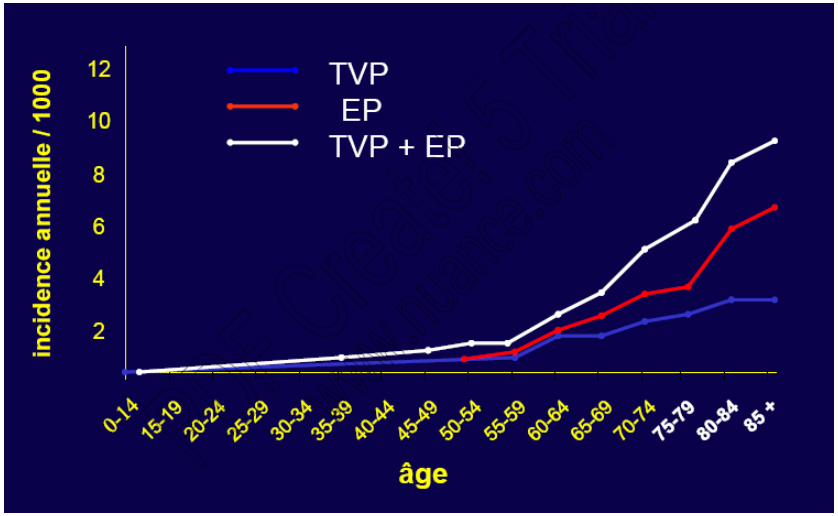
Hôpital A. Mami Ariana

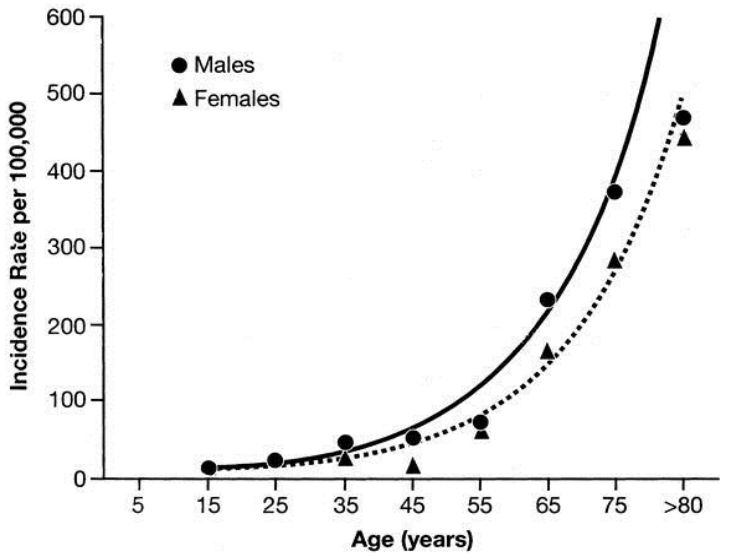
Introduction

Pathologie fréquente



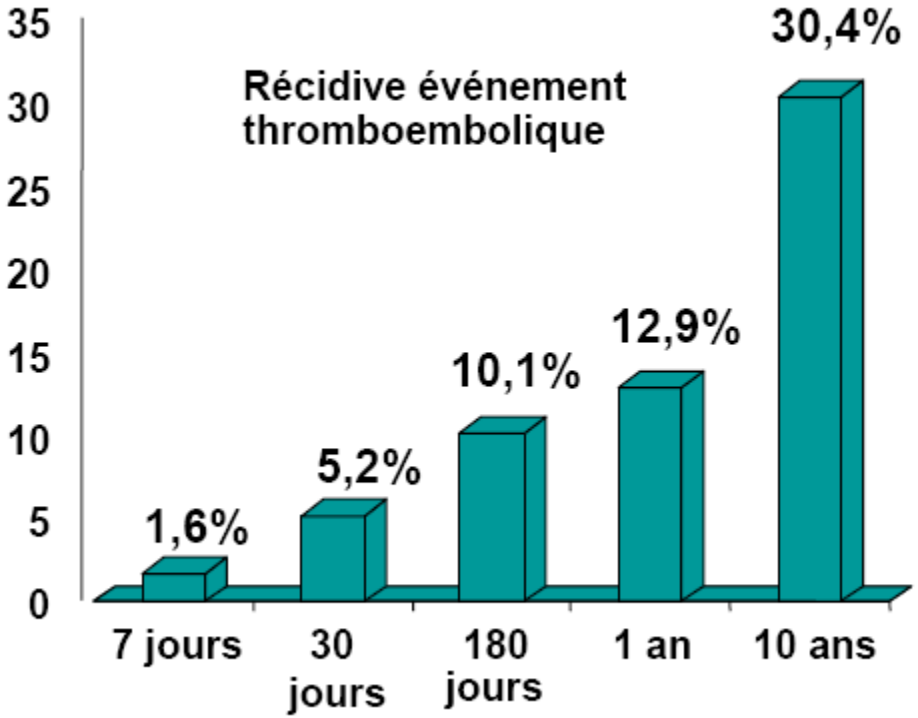
↑ Incidence avec l'âge : 0.28% entre 20 et 40 ans; 5% >75 ans





OgerE et al. ThromHaemost2000; SilversteinM, et al ArchInt Med 1998

Pathologie récidivante



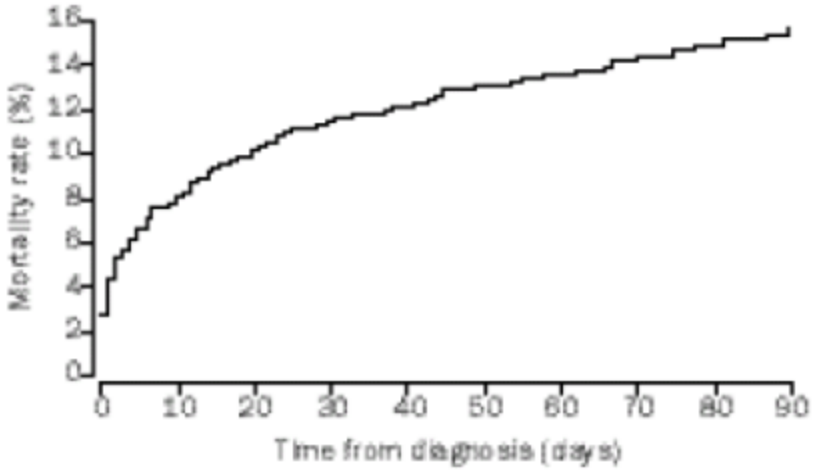
Mortalité à 3 mois en cas de récidive : 46,8%

Heit. ArchInternMed 2000;
Roy AnnInternMed 2006;
Goldhaber. Lancet1999; ICOPER

Pathologie mortelle

Une des premières causes de mortalité hospitalière

- 9 % des cas autopsiés (dg pré mortem fait dans 18 % des cas)
- Principale cause non carcinologique de mortalité des cancéreux.
- Première cause extra obstétricale de décès des parturientes



Mortalité> 15% à 3 mois

Facteurs de risque indépendants de mortalité à 3 mois

Variable	HR (IC 95%)
Âge > 70	1,6 (1,1-2,3)
Cancer	2,3 (1,5-3,5)
ICC	2,4 (1,5-3,7)
BPCO	1,8 (1,2-2,7)

GoldhaberSZ, et al. Lancet1999

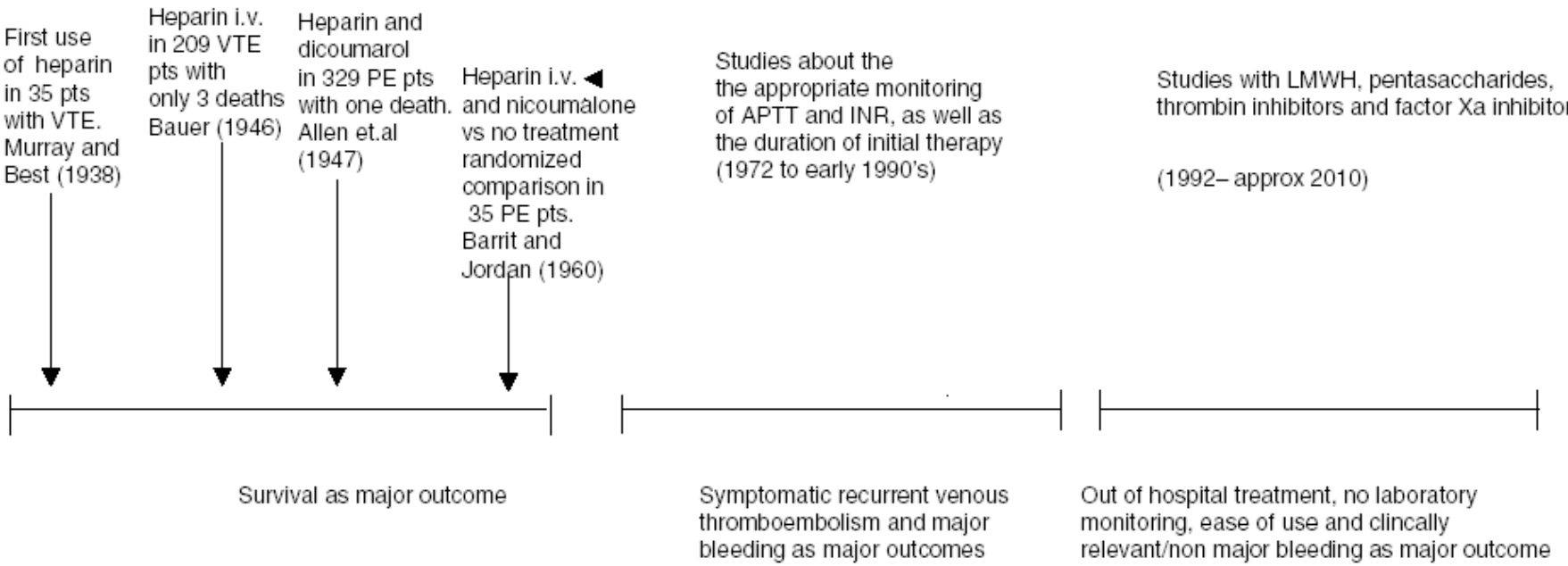


Fig. 1. The three phases in the evaluation of antithrombotic therapies in venous thromboembolism together with the three steps in the evolution of outcome assessments.

Büller & al, 2005

	BARRIT (1960)		BRANDJIS (1992)		p
	EP cliniquement suspectée		TVP proximale		
	HNF x 36 h + AVK x 2 semaines	Pas de traitement	HNF x 7j + AVK (n=60)	Placébo + AVK (n=60)	
Récidive (%)	-	-	7	20	0.058
Hémorragie (%)	-	-	3	5	NS
Décès (%)	0	26	-	-	-

	Hull (1986)	
	TVP proximale	
	HNF en IV continue dose thérapeutique	HNF en S/C Dose infra thérapeutique
Récidive (n,%)	1 (1.6)	13 (24.5)

Pas de traitement ou insuffisance de traitement :

Risque d'EP fatale

Risque de récidive

Questions

- Quelle prise en charge initiale d'une TVP proximale/ EP?
- Quel traitement au long cours (prévention de la récidive) ?
- Quel traitement des TV distales et des TV superficielles ?

Objectifs du traitement

- Prévenir l’extension du thrombus
- Prévenir l’embolisation si TBPH
- Prévenir les complications locales et générales
- Prévenir les récidives

En urgence : quelle stratégie thérapeutique devant une MTEV?

- Nombreuses publications
- Nombreuses recommandations
  - ACCP 2004, 2008, 02/2012
  - ESC 2008
  - Recommandations Afssaps 2009

Guidelines on the diagnosis and management of acute pulmonary embolism

The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC)

Severity of pulmonary embolism

The severity of PE should be understood as an individual estimate of PE-related early mortality risk rather than the anatomical burden and the shape and distribution of intrapulmonary emboli. Therefore, current guidelines suggest replacing potentially misleading terms such as 'massive', 'submassive' and 'non-massive' with the estimated level of the risk of PE-related early death.

European Heart Journal (2008) **29**, 2276–2315
doi:10.1093/eurheartj/ehn310

Guidelines on the diagnosis and management of acute pulmonary embolism

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Severity of pulmonary embolism

➢La gravité de l'EP doit aujourd'hui être interprétée en fonction du *risque de décès* lié au phénomène thromboembolique, et non plus en fonction de la sévérité de l'amputation vasculaire pulmonaire.

European Heart Journal (2008) **29**, 2276–2315
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Severity of pulmonary embolism

➢Nouvelles recommandations (SEC) : remplacer la terminologie des EP massives, sub-massives, ou non massives, par une terminologie basée sur le risque de décès précoce intra hospitalier ou à 30 jours.

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Severity of pulmonary embolism

PE can be stratified into several levels of risk of early death (understood as in-hospital or 30-day mortality) based on the presence of risk markers. For practical purposes, risk markers useful for risk stratification in PE can be classified into three groups (*Table 4*).

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The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC)

Severity of pulmonary embolism

- L'EP peut être stratifiée en plusieurs niveau de risque de mortalité à l'hôpital et à 30 jours basée sur la présence de marqueurs évaluant l'existence :
  - ✓D'une instabilité hémodynamique
  - ✓D'une dysfonction ventriculaire droite
  - ✓D'une ischémie myocardique

European Heart Journal (2008) **29**, 2276–2315
doi:10.1093/eurheartj/ehn310

Table 4 Principal markers useful for risk stratification in acute pulmonary embolism

Clinical markers	Shock
	Hypotension[a]
Markers of RV dysfunction	RV dilatation, hypokinesis or pressure overload on echocardiography
	RV dilatation on spiral computed tomography
	BNP or NT-proBNP elevation
	Elevated right heart pressure at RHC
Markers of myocardial injury	Cardiac troponin T or I positive[b]

BNP = brain natriuretic peptide; NT-proBNP = N-terminal proBNP; RHC = right heart catheterization; RV = right ventricle.

[a]Defined as a systolic blood pressure <90 mmHg or a pressure drop of ≥40 mmHg for >15 min if not caused by new-onset arrhythmia, hypovolaemia or sepsis.

[b]Heart-type fatty acid binding protein (H-FABP) is an emerging marker in this category, but still requires confirmation.

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doi:10.1093/eurheartj/ehn310

Table 5 Risk stratification according to expected pulmonary embolism-related early mortality rate

PE-related early MORTALITY RISK	RISK MARKERS		
	CLINICAL (shock or hypotension)	RV dysfunction	Myocardial injury
HIGH >15%	+	(+)[a]	(+)[a]

[a]In the presence of shock or hypotension it is not necessary to confirm RV dysfunction/injury to classify as high risk of PE-related early mortality.

PE = pulmonary embolism; RV = right ventricle.

Table 5 Risk stratification according to expected pulmonary embolism-related early mortality rate

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HIGH >15%	+	(+)[a]	(+)[a]
NON HIGH			

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NON HIGH	Intermediate 3–15%	–	+	+
			+	–
			–	+

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HIGH >15%		+	(+)[a]	(+)[a]
NON HIGH	Inter mediate 3–15%	–	+	+
			+	–
			–	+
	Low <1%	–	–	–

[a]In the presence of shock or hypotension it is not necessary to confirm RV dysfunction/injury to classify as high risk of PE-related early mortality.

PE = pulmonary embolism; RV = right ventricle.

Immediate bedside clinical assessment for the presence or absence of clinical markers allows stratification into high-risk and non-high-risk PE (*Table 5*). This classification should also be applied to patients with suspected PE, as it helps in the choice of the optimal diagnostic strategy and initial management.

European Heart Journal (2008) **29**, 2276–2315
doi:10.1093/eurheartj/ehn310

Quel traitement initial d'une TVP proximale/EP?

- Thrombolyse/HNF/HBPM/Fondaparinux/ chirurgie/interruption cave/?
- Hospitalier/ambulatoire

Table 5 Risk stratification according to expected pulmonary embolism-related early mortality rate

PE-related early MORTALITY RISK		RISK MARKERS			Potential treatment implications
		CLINICAL (shock or hypotension)	RV dysfunction	Myocardial injury	
HIGH >15%		+	(+)[a]	(+)[a]	Thrombolysis or embolectomy
NON HIGH	Intermediate 3–15%	–	+	+	
			+	–	
			–	+	
	Low <1%	–	–	–	

[a]In the presence of shock or hypotension it is not necessary to confirm RV dysfunction/injury to classify as high risk of PE-related early mortality.

PE = pulmonary embolism; RV = right ventricle.

2012

Antithrombotic Therapy for VTE Disease : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Clive Kearon, Elie A. Akl, Anthony J. Comerota, Paolo Prandoni, Henri Bounameaux, Samuel Z. Goldhaber, Michael E. Nelson, Philip S. Wells, Michael K. Gould, Francesco Dentali, Mark Crowther and Susan R. Kahn

5.6 Systemic Thrombolytic Therapy for Patients With PE

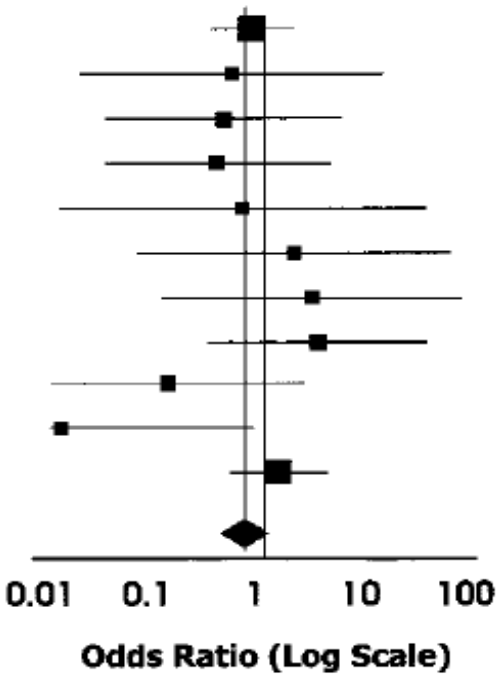
5.6.1.1. In patients with acute PE associated with hypotension (eg, systolic BP < 90 mm Hg) who do not have a high bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy (Grade 2C).

5.6.1.2. In most patients with acute PE not associated with hypotension, we recommend against systemically administered thrombolytic therapy (Grade 1C).

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

11 RCT (**5 incluant EPM**) : 748 patients

Study	Thrombolysis	Heparin	OR	95% CI
UPET, 1973	10/82	14/78	0.63	0.26 - 1.53
Tibbutt et al, 1974	0/13	1/17	0.41	0.02 - 10.83
Ly et al, 1978	1/14	2/11	0.35	0.03 - 4.42
Dotter et al, 1979	1/15	3/16	0.31	0.03 - 3.36
Marini et al, 1988	0/20	0/10	0.51	0.01 - 27.68
PIOPED, 1990	1/9	0/4	1.59	0.05 - 47.52
Levine et al, 1990	1/33	0/25	2.35	0.09 - 60.24
Dalla-Volta et al, 1992	3/20	1/16	2.65	0.25 - 28.24
Goldhaber et al, 1993	0/46	4/55	0.12	0.01 - 2.35
Jerjes-Sanchez et al, 1995	0/4	4/4	0.01	0.00 - 0.77
Konstantinides et al, 2002	8/118	7/138	1.36	0.48 - 3.87
Total	**25/374**	**36/374**	**0.67**	**0.40 - 1.12**



Métanalyse : Thrombolyse vs heparin Wan et al, 2004

Outcome	Thrombolysis, n/N (%)	Heparin, n/N (%)	OR (95% CI)
Major bleeding	34/374 (9.1)	23/374 (6.1)	1.42 (0.81–2.46)*
Nonmajor bleeding	53/233 (22.7)	22/221 (10.0)	2.63 (1.53–4.54)†
Intracranial hemorrhage	2/374 (0.5)	1/374 (0.3)	1.04 (0.36–3.04)‡

bénéfice sur **taux de décès ou récidive d'EP**

	Thrombolyse	Héparine	OR [IC 95%]
RCT incluant EPM	9%	19%	0.45 [0.22-0.92]
RCT excluant EPM	5.3%	4.8%	1.07 [0.5-2.3]

Table 13 Approved thrombolytic regimens for pulmonary embolism

Streptokinase	250 000 IU as a loading dose over 30 min, followed by 100 000 IU/h over 12–24 h
	Accelerated regimen: 1.5 million IU over 2 h
Urokinase	4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg/h over 12–24 h
	Accelerated regimen: 3 million IU over 2 h
rtPA	100 mg over 2 h
	or 0.6 mg/kg over 15 min (maximum dose 50 mg)

rtPA = recombinant tissue plasminogen activator.

2012

Antithrombotic Therapy for VTE Disease : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Clive Kearon, Elie A. Akl, Anthony J. Comerota, Paolo Prandoni, Henri Bounameaux, Samuel Z. Goldhaber, Michael E. Nelson, Philip S. Wells, Michael K. Gould, Francesco Dentali, Mark Crowther and Susan R. Kahn

5.6.2.1. In patients with acute PE, when a thrombolytic agent is used, we suggest short infusion times (eg, a 2-h infusion) over prolonged infusion times (eg, a 24-h infusion) (Grade 2C).

5.6.2.2. In patients with acute PE when a thrombolytic agent is used, we suggest administration through a peripheral vein over a pulmonary artery catheter (Grade 2C).

Table 14 Contraindications to fibrinolytic therapy

Absolute contraindications[a]

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in preceding 6 months
- Central nervous system damage or neoplasms
- Recent major trauma/surgery/head injury (within preceding 3 weeks)
- Gastrointestinal bleeding within the last month
- Known bleeding

Relative contraindications

- Transient ischaemic attack in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week post partum
- Non-compressible punctures
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure >180 mmHg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

From reference 263.

[a]Contraindications to thrombolysis that are considered absolute, e.g. in acute myocardial infarction, might become relative in a patient with immediately life-threatening high-risk PE.

Stabilisation hémodynamique :
Remplissage vasculaire

13 patients EP avec IC<2.5 l/mn/m² sans hypoTA, 500 cc colloïdes :

↑Diamètre TDVD et l'IC p<0.05

sans ↑RAP.

Corrélation inverse entre↑IC et le ratio VD/VG initial p<0.05

- Optimisation du remplissage sous contrôle ETT avec une limite de ratio VD/VG à 1
- Prudence si hypotension : risque d'aggravation de l'ischémie VD → plutôt vasopresseurs

Mercat et al, Crit Care Med 1999

Catécholamines

- Noradrénaline
  - études animales (1971-1991):
  - amélioration de l'IC et du pronostic
  - veinoconstriction : Maintien précharge VD
  - vasoconstriction systémique : réduit l'ischémie du VD
  - effet inotrope β1
  - peu d'effet péjoratif sur les RVP
- Dobutamine :
  - 2 études non comparatives : efficacité sur l'IC et le TO2
  - Parfois effet hypoxémiant par altération des V/Q
  - Action vasodilatatrice β2
  - Utile à un degré moindre de défaillance (TA conservée) : Gare à l'aggravation de l'ischémie VD

Ventilation mécanique

- Traitement de l'hypoxie et de la défaillance circulatoire
- Effets délétères de la VM en Ppositive
  - Diminution du retour veineux
  - Augmentation des RVP.
  - Baisse du DC peut être majeure dans ce contexte
- tonus sympathique entravé par la sédation

- Pas de controverse sur le traitement de l'EP avec instabilité hémodynamique
- Qu'en est-il de l'EP sans instabilité hémodynamique mais avec dysfonction VD?

Table 5 Risk stratification according to expected pulmonary embolism-related early mortality rate

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		CLINICAL (shock or hypotension)	RV dysfunction	Myocardial injury	
HIGH >15%		+	(+)[a]	(+)[a]	Thrombolysis or embolectomy
NON HIGH	Intermediate 3–15%	–	+	+	Hospital admission
			+	–	
			–	+	
	Low <1%	–	–	–	

[a]In the presence of shock or hypotension it is not necessary to confirm RV dysfunction/injury to classify as high risk of PE-related early mortality.

PE = pulmonary embolism; RV = right ventricle.

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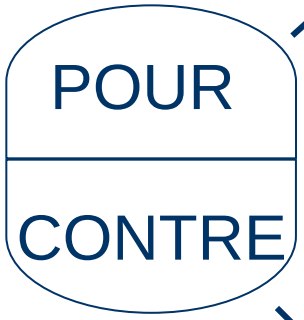
In summary, thrombolytic therapy is the first-line treatment in patients with high-risk PE presenting with cardiogenic shock and/or persistent arterial hypotension, with very few absolute contraindications. Routine use of thrombolysis in non-high-risk patients is not recommended, but may be considered in selected patients with intermediate-risk PE and after thorough consideration of conditions increasing the risk of bleeding. Thrombolytic therapy should be not used in patients with low-risk PE.



- Cause de décès par EP = IVDroite
- Signes de dysfonction VD = marqueurs pronostiques
- RCT : amélioration de certains de ces marqueurs après TL
- Traitement étiologique rapide en situation encore compensée
- Diminution des récidives
- Diminution du risque d'HTAP II

-Circulation bronchique collatérale de recours
-Risque hémorragique notamment encéphalique
-Coût supérieur
-RCT : pas de diminution de mortalité

HEPARIN PLUS ALTEPLASE COMPARED WITH HEPARIN ALONE IN PATIENTS WITH SUBMASSIVE PULMONARY EMBOLISM

STAVROS KONSTANTINIDES, M.D., ANNETTE GEIBEL, M.D., GERHARD HEUSEL, PH.D., FRITZ HEINRICH, M.D., AND WOLFGANG KASPER, M.D., FOR THE MANAGEMENT STRATEGIES AND PROGNOSIS OF PULMONARY EMBOLISM-3 TRIAL INVESTIGATORS*

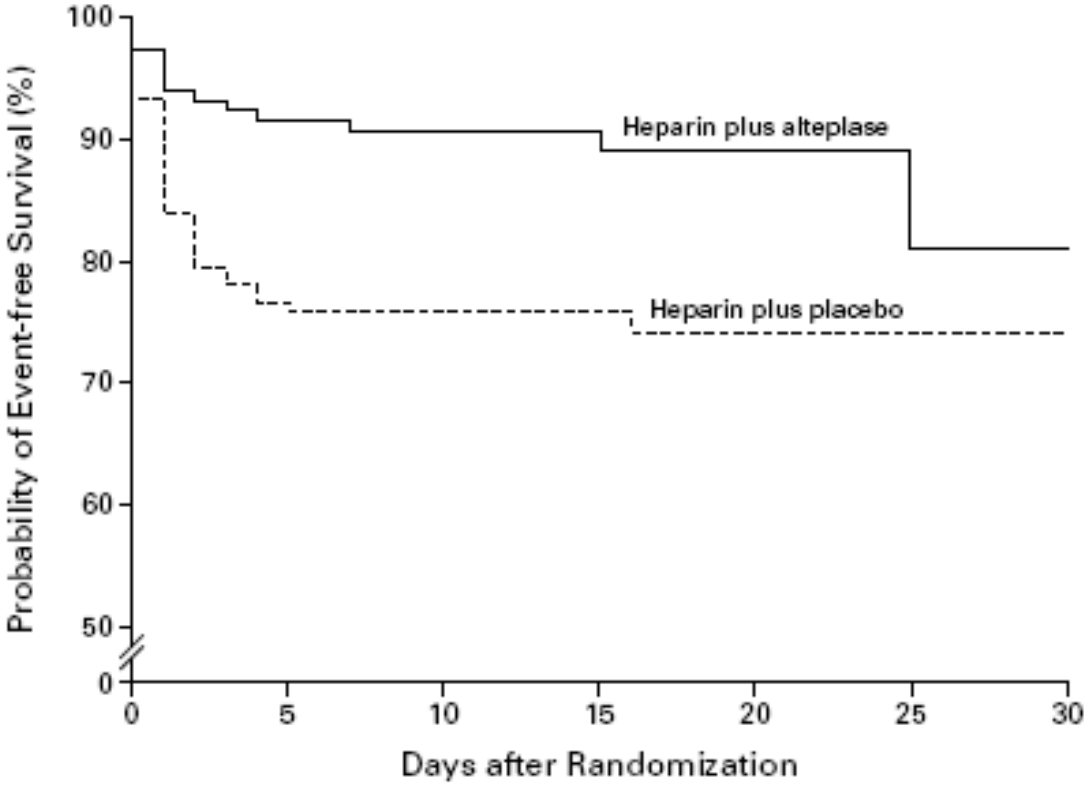
N Engl J Med, Vol. 347, No. 15 · October 10, 2002

TABLE 1. BASE-LINE CHARACTERISTICS OF THE STUDY PATIENTS.*

CHARACTERISTIC	HEPARIN PLUS ALTEPLASE (N=118)	HEPARIN PLUS PLACEBO (N=138)	P VALUE
Clinical			
Sex — no. (%)			0.66
Male	54 (45.8)	68 (49.3)	
Female	64 (54.2)	70 (50.7)	
Age — yr			
Men	61.2±10.1	60.5±9.7	0.70
Women	64.4±9.5	62.2±12.4	0.25
Weight — kg			
Men	86.5±16.2	86.7±16.0	0.70
Women	75.2±15.3	75.6±13.6	0.25
Previous or concomitant disease — no. (%)			
Cardiovascular	84 (71.2)	92 (66.7)	0.52
Pulmonary	40 (33.9)	51 (37.0)	0.71
Gastrointestinal or hepatobiliary	38 (32.2)	56 (40.6)	0.21
Diabetes mellitus	46 (39.0)	57 (41.3)	0.80
Renal	28 (23.7)	25 (18.1)	0.34
Musculoskeletal or dermatologic	45 (38.1)	55 (39.9)	0.88
Neurologic	9 (7.6)	12 (8.7)	0.94
Blood pressure — mm Hg			
Systolic	133±19	133±20	1.00
Diastolic	79.7±12.0	80.8±13.0	0.49
Heart rate — beats/min	103±18.9	100±17	0.18
Respiratory rate — breaths/min	23.0±6.3	22.5±6.1	0.52
Partial pressure of arterial oxygen — mm Hg	63.9±28.7	59.6±24.6	0.20
Partial pressure of arterial carbon dioxide — mm Hg	29.4±8.7	28.7±9.9	0.55
Electrocardiographic			
S waves in lead I plus Q waves in lead III — no. (%)	41 (34.7)	76 (55.1)	0.002
Complete right bundle-branch block — no. (%)	12 (10.2)	13 (9.4)	0.99
Incomplete right bundle-branch block — no. (%)	34 (28.8)	50 (36.2)	0.26
Inverted T waves in leads V_1, V_2, and V_3 — no. (%)	53 (44.9)	67 (48.6)	0.65
Echocardiographic†			
Right ventricular dysfunction — no. (%)	37 (31.4)	43 (31.2)	0.92
Laboratory			
Hematocrit — %	40.9±5.0	41.3±4.7	0.51
Platelet count — per mm³	221,000±73,600	223,000±95,900	0.87

TABLE 2. IN-HOSPITAL CLINICAL EVENTS.*

EVENT	HEPARIN PLUS ALTEPLASE (N=118)	HEPARIN PLUS PLACEBO (N=138)	P VALUE†
	no. (%)		
Primary end point	13 (11.0)	34 (24.6)	0.006
Death from all causes	4 (3.4)	3 (2.2)	0.71
Escalation of treatment	12 (10.2)	34 (24.6)	0.004
Catecholamine infusion (for persistent hypotension or shock)	3 (2.5)	8 (5.8)	0.33
Secondary thrombolysis	9 (7.6)	32 (23.2)	0.001
Endotracheal intubation	3 (2.5)	3 (2.2)	0.85
Cardiopulmonary resuscitation	0	1 (0.7)	1.0
Embolectomy or thrombus fragmentation	0	1 (0.7)	1.0
Secondary end points			
Recurrent pulmonary embolism‡	4 (3.4)	4 (2.9)	0.89
Major bleeding§	1 (0.8)	5 (3.6)	0.29
Fatal bleeding	0	1 (0.7)	1.0
Hemorrhagic stroke¶	0	0	—
Ischemic stroke¶	0	1 (0.7)	1.0



No. at Risk							
Heparin plus alteplase	118	107	96	57	26	11	6
Heparin plus placebo	137	105	87	53	24	3	2

Figure 1. Kaplan–Meier Estimates of the Probability of Event-free Survival among Patients with Acute Submassive Pulmonary Embolism, According to Treatment with Heparin plus Alteplase or Heparin plus Placebo.

- Plusieurs articles récents démontrent que la dysfonction droite est associée avec une moins bonne évolution

European Heart Journal (2003) 24, 1447–1454

ELSEVIER

EUROPEAN SOCIETY OF CARDIOLOGY

In-hospital and long-term outcome after sub-massive and massive pulmonary embolism submitted to thrombolytic therapy

Nicolas Meneveau[a*], Liu Pin Ming[b], Marie France Séronde[a], Nursen Mersin[a], François Schiele[a], Fiona Caulfield[a], Yvette Bernard[a], Jean-Pierre Bassand[a]

Table 3 In-hospital clinical course

	n=249
In-hospital uneventful clinical course	165 (66%)
Death	22 (8.8%)
Refractory shock	4
Recurrent PE	11
Major bleeding	6
Cancer	1
Recurrent PE (fatal and non fatal)	19 (7.6%)
Repeat thrombolysis	20 (8%)
Surgical embolectomy	13 (5%)
Cava filter insertion	51 (20%)
Bleeding complications (total)	43 (17.3%)
Major bleedings	24 (9.6%)
Cerebral	3
Gastrointestinal	3
Hematoma (vascular access)	16
Other	2

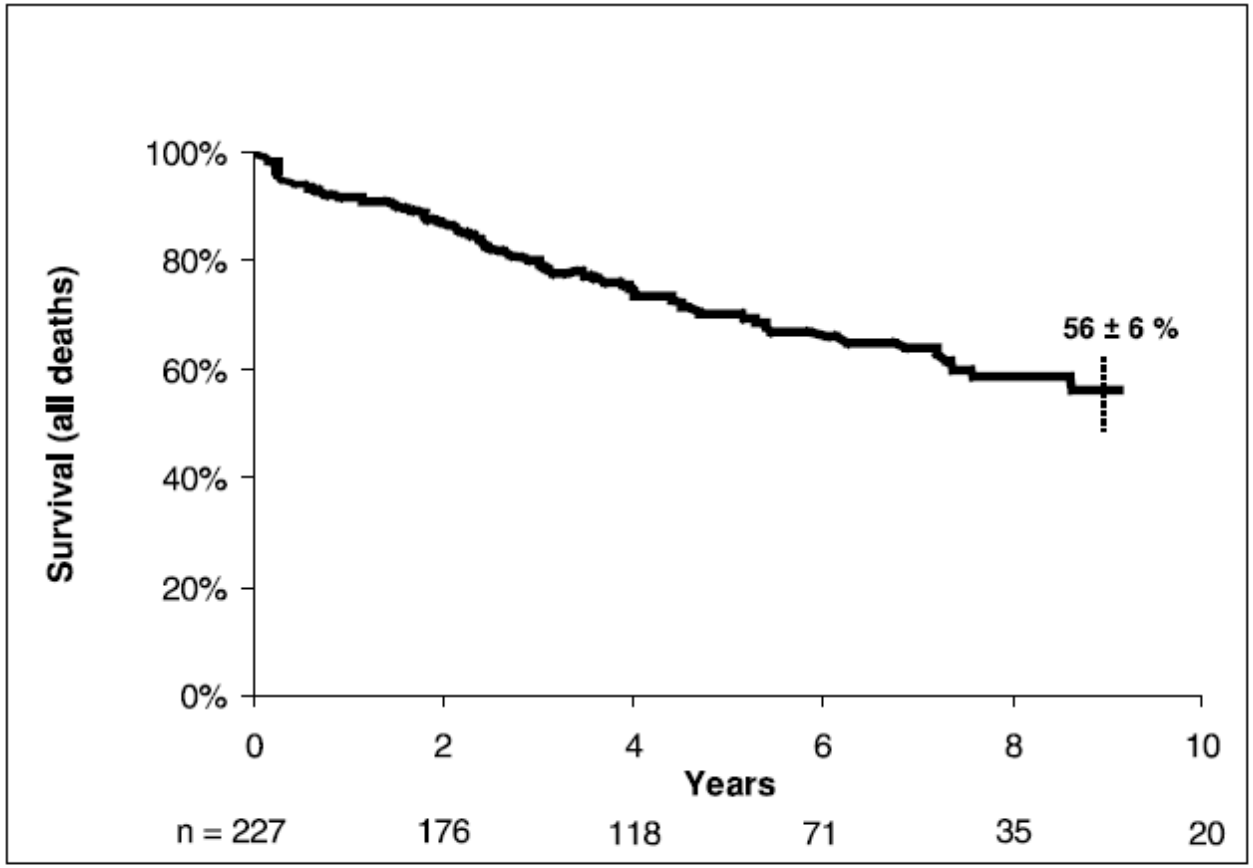


Fig. 1 Global survival after thrombolysis in patients who survived the acute phase

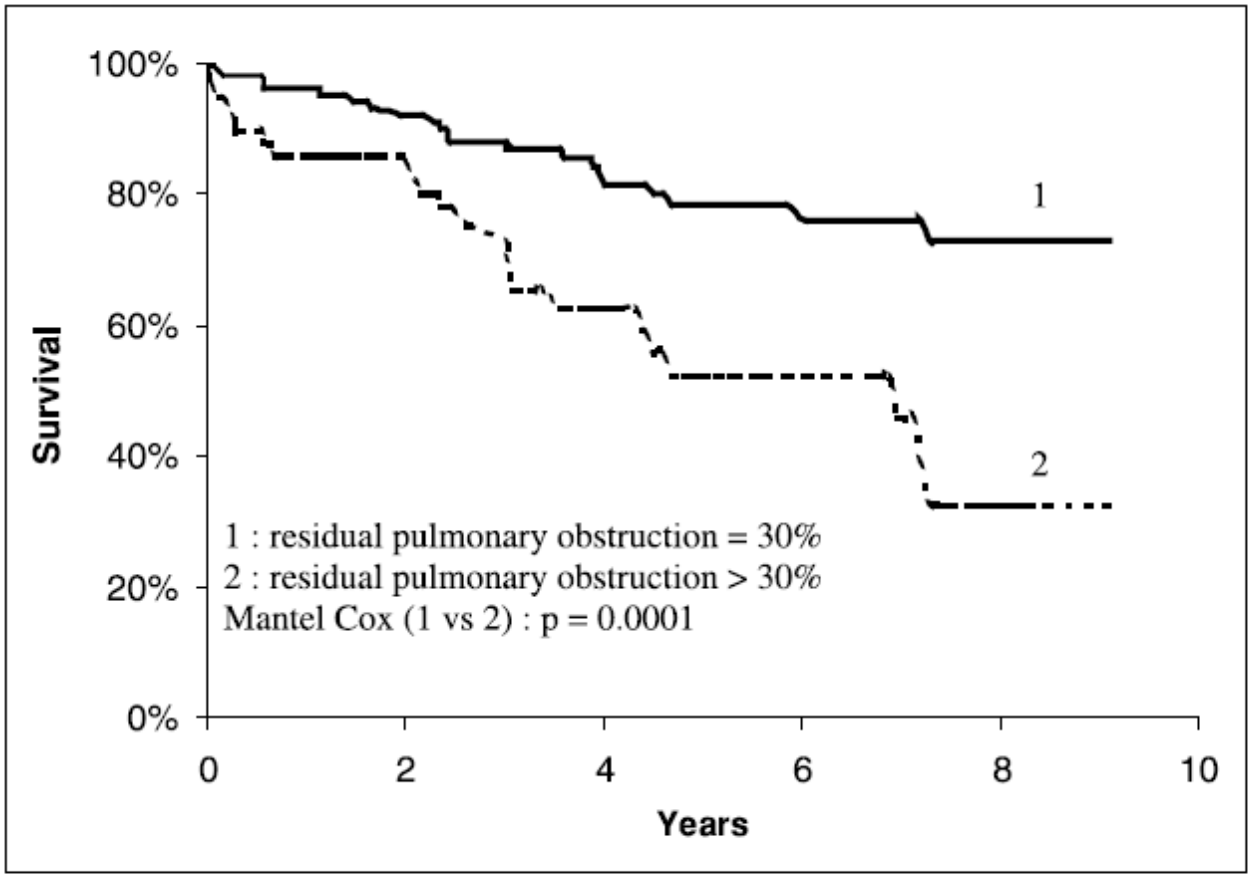


Fig. 2 Survival according to residual pulmonary vascular obstruction after thrombolysis

Table 5 Predictors of long-term mortality by univariate and cox proportional hazards multivariate analysis

Variables	Predictors of Long-term Mortality		
	Univariate	Multivariate	
	P	RR [95% CI]	*P*
Age >75 years	0.0003	2.73 [2.18;3.21]	0.0002
Residual pulmonary vascular obstruction >30%	0.004	2.22 [1.69;2.74]	0.003
Cancer	0.08	2.03 [1.40;2.65]	0.04
Cava filter insertion	0.02	–	ns
Systolic blood pressure=90 mmHg	0.08	–	ns
PaO2 <55 mmHg	0.04	–	ns

Étude personnelle

61 patients thrombolysés

- 43 pour CPA échographique (5 décès)
- 18 pour état de choc (18 décès)

Facteurs prédictifs d'échec de la thrombolyse chez les patients en CPA (analyse multivariée)

Variables	OR	IC 95%	P
IGS (≥28)	11,945	1,79-79,72	0,01
Fg (≤ 3,3)	18,248	1,427-233,356	0,026
PAPs (>68)	9,456	1,138-78,558	0,038

Ce travail suggère qu'une THL précoce chez les patients à risque intermédiaire de mortalité pourrait être bénéfique

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5.6.1.3. In selected patients with acute PE not associated with hypotension and with a low bleeding risk whose initial clinical presentation, or clinical course after starting anticoagulant therapy, suggests a high risk of developing hypotension, we suggest administration of thrombolytic therapy (Grade 2C).

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Thrombolyse et thrombophlébite

2.10 Systemic Thrombolytic Therapy for Patients With Acute DVT

2.10. In patients with acute proximal DVT of the leg, we suggest anticoagulant therapy alone over systemic thrombolysis (Grade 2C).

- TVP extensive iliofémorale
  - Avec des symptômes < 7 js,
  - Risque hémorragique faible et
  - Âge < 60 ans
- Phlegmacia caeruléa dolens ou phlébite bleue en l'absence de contre indications
- Accord du malade

Traitement anticoagulant

Molécule	Site d'action	Surveillance biologique
Héparine non fractionnée, pentasaccharide	Facteur IIa et Facteur Xa	Héparinémie TCA
HBPM,	Facteur Xa	Facteur anti Xa
Antivitamine K	II, VII, IX et X	INR
Hirudine Hirulog Lepirudine	antithrombine	
Fondaparinux (Arixtra*)		non

Molécule	Dose	Dosage	Surveillance
HNF	500UI/kg/j IVSE 1mg = 100UI	4 h début et 4h après chaque modif dose	TCA (2-3 x témoin), héparinémie (0.3-0.6) Plaquettes 2X/sem
HBPM	100UI anti Xa/kg 2 fois/j à 12 d'intervalle en SC	4h après la deuxieme injection	Anti Xa pas nécessaire sauf cas particuliers Plaquettes 2X/sem
Fondaparinux (Arixtra*)	1 injection SC/j de 2.5mg à la même heure	non	Adaptation à la clairance créatinine et respect strict horaires

Héparine : HBPM

- 2 injections / jour :
  - Énoxaparine (Lovenox) 100 UI/kg/12h
  - Nadroparine (Fraxiparine) 0.1 ml/kg/12h
  - Daltéparine (Fragmine) 100 UI/Kg/12h
- 1 injection /jour :
  - Tinzaparine (Inohep) 175 UI/Kg
  - Nadroparine (Fraxodi) 0.1 ml/10kg

	Dose	Interval
Enoxaparin	1.0 mg/kg	Every 12 h
Tinzaparin	175 U/kg	Once daily
Fondaparinux	5 mg (body weight <50 kg) 7.5 mg (body weight 50–100 kg) 10 mg (body weight >100 kg)	Once daily

Les études comparant HBPM et HNF sont :

- Nombreuses
- S'accordent pour dire que HBPM :
  - Aussi efficaces que HNF
  - Équivalentes pour les récidives TE
  - Et des complications hémorragiques
  - Moins de complications hématologiques
  - Pharmacocinétique plus stable
  - ½ vie prolongée
  - Ne nécessitent pas de surveillance biologique

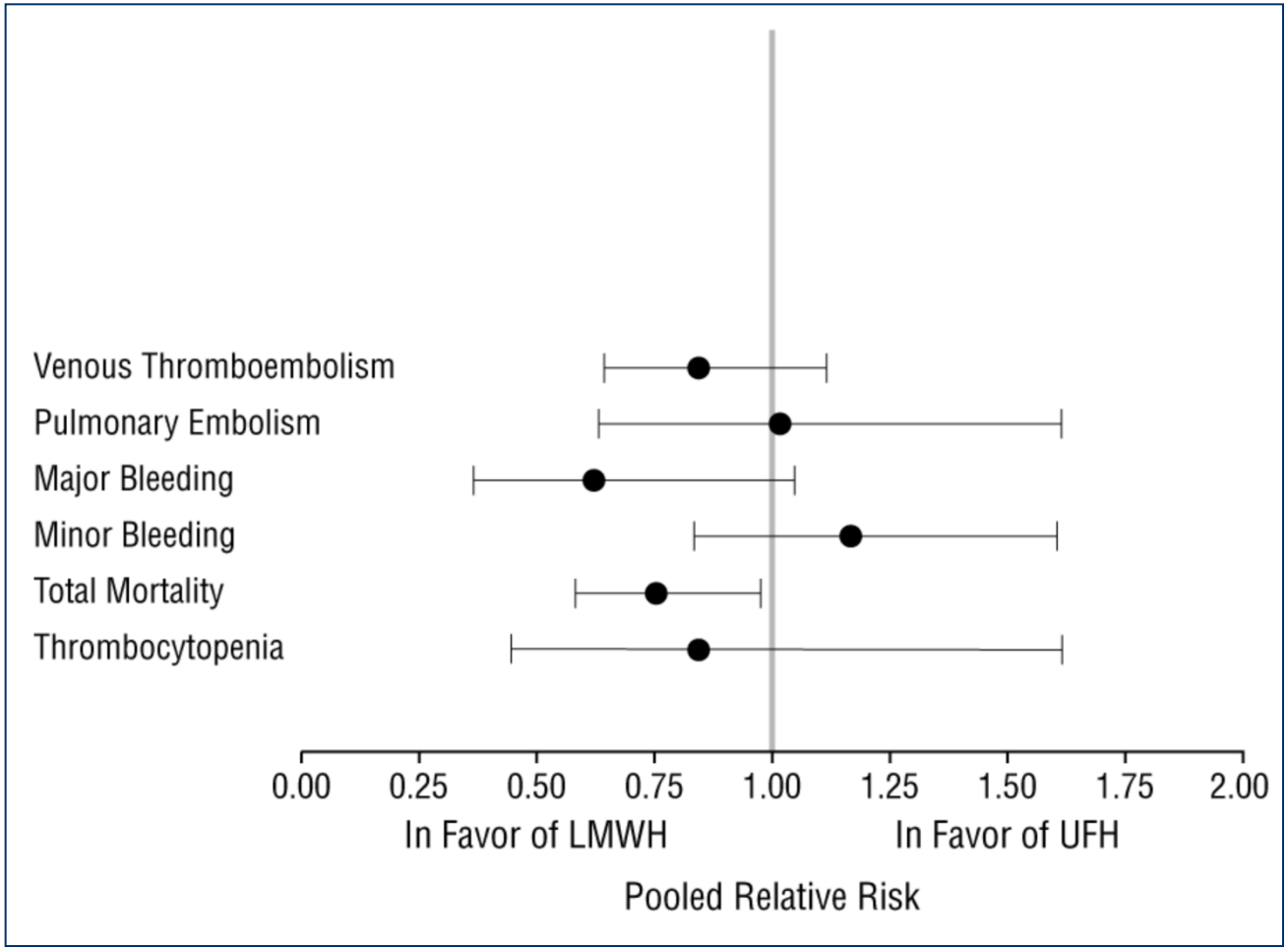
A Meta-analysis Comparing Low-Molecular-Weight Heparins With Unfractionated Heparin in the Treatment of Venous Thromboembolism

Arch Intern Med. 2000;160(2):181-188. doi:10.1001/archinte.160.2.181

- 775 articles
  - 33 études randomisées
    - 20 études éliminées (méthodologie…..)
      - 13 études retenues
        - 4657 patients

A Meta-analysis Comparing Low-Molecular-Weight Heparins With Unfractionated Heparin in the Treatment of Venous Thromboembolism

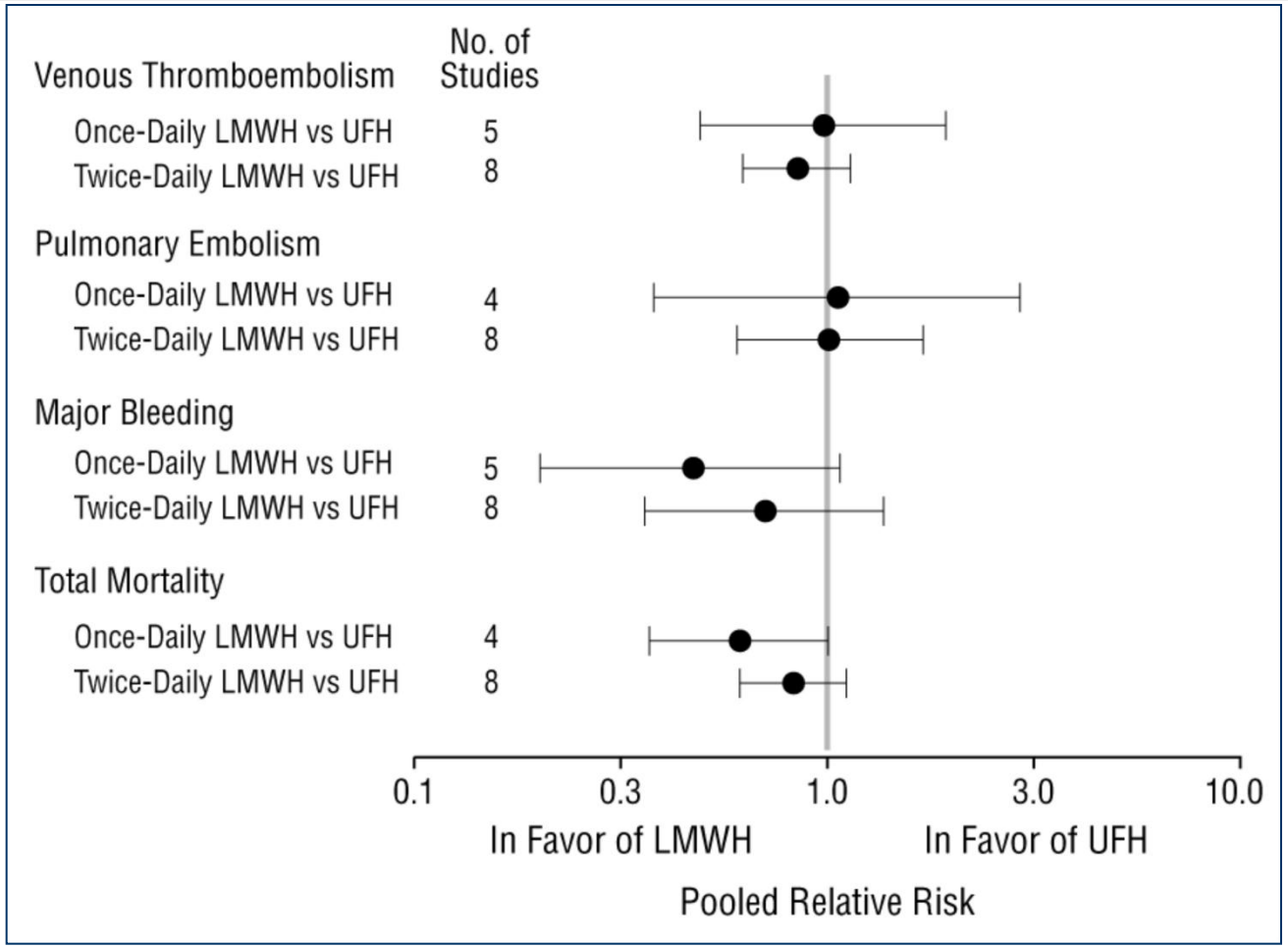
Arch Intern Med. 2000;160(2):181-188. doi:10.1001/archinte.160.2.181



The effects of low-molecular-weight heparin (LMWH) vs unfractionated heparin (UFH) in the acute treatment of venous thromboembolism.

A Meta-analysis Comparing Low-Molecular-Weight Heparins With Unfractionated Heparin in the Treatment of Venous Thromboembolism

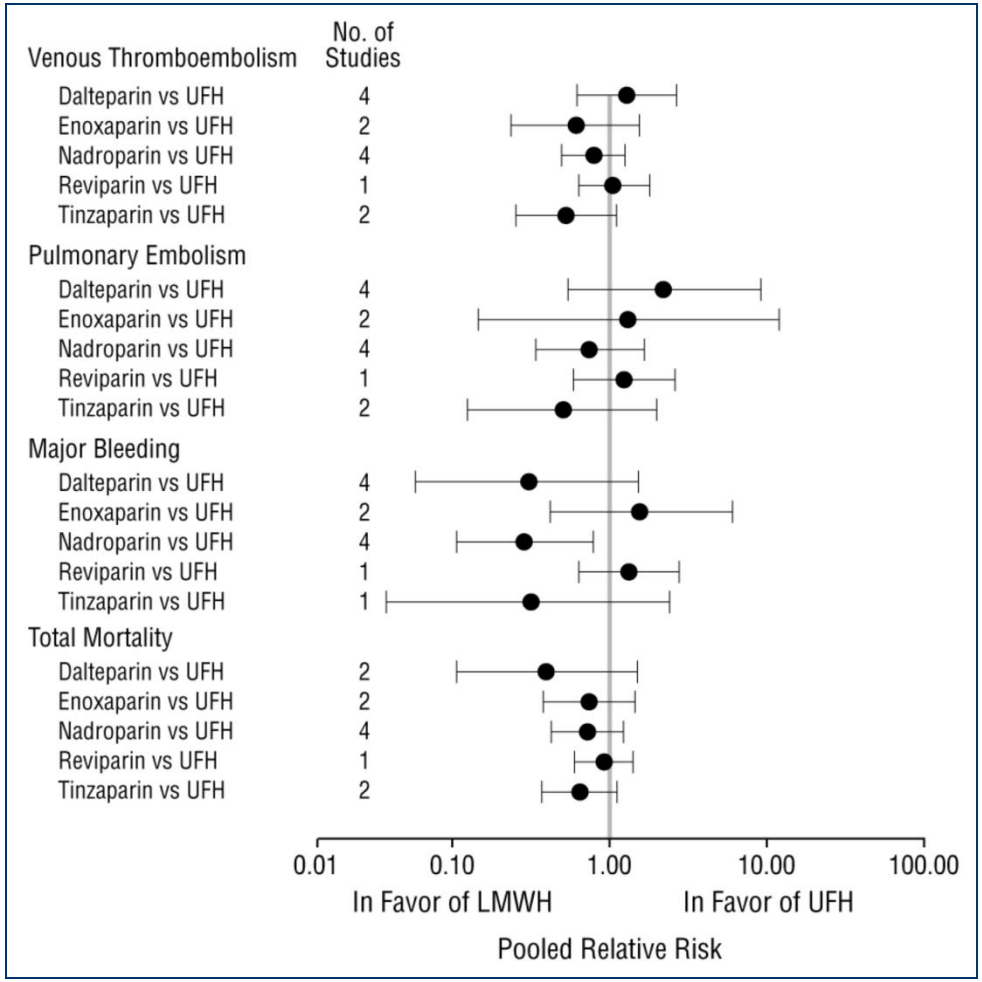
Arch Intern Med. 2000;160(2):181-188. doi:10.1001/archinte.160.2.181



A comparison of once-daily or twice-daily low-molecular-weight heparin (LMWH) vs unfractionated heparin (UFH).

A Meta-analysis Comparing Low-Molecular-Weight Heparins With Unfractionated Heparin in the Treatment of Venous Thromboembolism

Arch Intern Med. 2000;160(2):181-188. doi:10.1001/archinte.160.2.181



A comparison of different low-molecular-weight heparin (LMWH) products vs unfractionated heparin (UFH).

Surveillance de la réponse anticoagulante

- HNF :
  - TCA 2 – 3 fois le témoin
  - Anti Xa : 0.3 – 0.6 u/ml
- HBPM :
  - La réponse anticoagulante est prévisible
  - Elle est dose dépendante
  - Dose est ajustée au poids
  - Pas de surveillance biologique
    - sauf si obésité > 120kg
    - ou insuffisance rénale
    - Activité anti Xa : 0.6 – 1 U/ml si 2 injections et 1 – 2 UI/ml si 1 injection (4h après l'injection)

Complications

- Les complications hémorragiques
- Allergie
- TIH : type 1 et 2
- Alopécie
- Ostéoporose
- Nécroses cutanées
- Augmentation des transaminases

Contre indications aux HBPM

- Absolues :
  - Sensibilité (TIH2, allergie)
  - Enfant < 3 ans
  - AVCH récent
  - Insuffisance rénale (clairance < 30 ml)
  - Anesthésie péridurale
- Relatives
  - AVCI
  - Clairance créatinine < 30 ml/min en préventif

Problème de résistance à l'héparine

- Doses d'héparine > 35000 U I/ 24 h avec TCA normal
- Dosage de l'activité anti Xa
- Causes de résistance:
  - Déficit du facteur antithrombine
  - Augmentation de la clairance de l'héparine
  - Augmentation du facteur VIII
  - Augmentation heparine binding protein
  - Augmentation fibrinogène
  - Augmentation platelet factor 4

Fondaparinux (Arixtra)

- Produit synthétique, inhibiteur spécifique du facteur Xa
- Anticoagulant injectable puissant
- ½ vie longue (17h) 1 seule prise /jour
- Élimination rénale
- Efficacité démontrée pour le traitement de la TVP et de l'EP
- TIH peu probable mais numération plaquettes souhaitée
- Pas d'antidote
- Attention aux sujets fragiles : Ice rénale ,age> 75 ans, poids < 50 kg

Fondaparinux or Enoxaparin for the Initial Treatment of Symptomatic Deep Venous Thrombosis

A Randomized Trial

Ann Intern Med. 2004;140:867-873.

Harry R. Büller, MD; Bruce L. Davidson, MD; Hervé Decousus, MD; Alexander Gallus, MD; Michael Gent, DSc; Franco Piovella, MD; Martin H. Prins, MD; Gary Raskob, PhD; Annelise E.M. Segers, MD; Roger Cariou, MD; Oscar Leeuwenkamp, PhD; and Anthonie W.A. Lensing, MD; for The Matisse Investigators*

Table 1. Demographic and Baseline Characteristics of Randomly Assigned Patients*

Characteristic	Fondaparinux Group (n = 1098)	Enoxaparin Group (n = 1107)
Age, *y*	61.1 ± 16.7	61.5 ± 16.5
Men/women, *n/n*	581/517	578/529
Body weight, *kg*	79.4 ± 17.4	80.1 ± 17.2
<50 kg, *n (%)*	31 (2.8)	24 (2.2)
50–100 kg, *n (%)*	948 (86.3)	974 (88.0)
>100 kg, *n (%)*	119 (10.8)	109 (9.8)
Creatinine clearance, *n (%)*†		
<0.5 mL/s	25 (2.3)	19 (1.7)
0.5–0.84 mL/s	471 (43.6)	513 (46.8)
>0.84 mL/s	584 (54.1)	563 (51.4)
Time between first symptoms and first active study drug, *d*	6.9 ± 8.7	7.4 ± 9.7
Diagnostic method, *n (%)*‡		
Ultrasonography	1045 (95.2)	1042 (94.1)
Venography	39 (3.6)	48 (4.3)
Location of deep venous thrombosis, *n (%)*		
Femoral or Iliac	601 (54.7)	595 (53.7)
Popliteal or trifucation	493 (44.9)	505 (45.6)
Bilateral	5 (0.5)	12 (1.1)
Risk factors, *n (%)*		
Previous venous thromboembolism	273 (24.9)	280 (25.3)
Active cancer§	126 (11.5)	111 (10.0)
Active cancer or history of cancer	202 (18.4)	186 (16.8)
Surgery or trauma (<3 mo)	251 (22.9)	251 (22.7)
Estrogen use	126 (11.5)	140 (12.6)
Known prothrombotic state	58 (5.3)	63 (5.7)
≥2 of the above	293 (26.7)	283 (25.6)

Table 4. Incidence of Recurrent Venous Thromboembolism (during the 3-Month Study Period) and Major Bleeding (during the Initial Treatment Period) for the Various Body Weight Categories*

Treatment	Recurrent Venous Thromboembolism			Major Bleeding		
	Body Weight < 50 kg	Body Weight, 50–100 kg	Body Weight > 100 kg	Body Weight < 50 kg	Body Weight, 50–100 kg	Body Weight > 100 kg
	← *n/n (%)* →					
Fondaparinux	1/31 (3.2)	37/948 (3.9)	5/119 (4.2)	1/31 (3.2)	11/942 (1.2)	0/118
Enoxaparin	3/24 (12.5)	39/974 (4.0)	3/109 (2.8)	0/24	12/967 (1.2)	1/110 (0.9)

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2.5 Choice of Initial Anticoagulant Regimen in Patients With Proximal DVT

2.5.1. In patients with acute DVT of the leg, we suggest LMWH or fondaparinux over IV UFH (Grade 2C) **and over SC UFH** (Grade 2B for LMWH; Grade 2C for fondaparinux).

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

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5.1 Initial Anticoagulation for Patients With Acute Pulmonary Embolism (PE)

5.1. In patients with acute PE, we recommend initial treatment with parenteral anticoagulation (LMWH, fondaparinux, IV UFH, or SC UFH) over no such initial treatment (Grade 1B).

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5.4 Choice of Initial Parenteral Anticoagulant Regimen in Patients With PE

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

5.4.2. In patients with acute PE treated with LMWH, we suggest once- over twice-daily administration (Grade 2C).

AVK

- Traitement au long cours de la MTEV
- Action retardée : démarré même jour que l'héparine
- Efficacité testée par dosage de l'INR : 2 – 3 fois (2 prélèvements consécutifs à 24 h d'intervalle)

Médicament	Demi-vie (h)	Durée d'action (h)	Posologie (mg/j)	Dose par cp (mg)
Sintrom® (acénocoumarol)	8-9	48-96	2-10	1 ou 4
Pindione® (phénindione)	5-10	24-48	50-100	50
Tioclomarol® (Apegmone)	24	48-72	4-8	4
Préviscan® (fluindione)	30	48	5-40	20
Coumadine® (warfarine)	35-45	96-120	2-15	2 ou 10

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2.4 Timing of Initiation of VKA and Associated Duration of Parenteral Anticoagulant Therapy

2.4. In patients with acute DVT of the leg, we recommend early initiation of VKA (eg, same day as parenteral therapy is started) over delayed initiation, and continuation of parenteral anticoagulation for a minimum of 5 days and until the international normalized ratio (INR) is 2.0 or above for at least 24 h (Grade 1B).

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3.2 Intensity of Anticoagulant Effect

3.2. In patients with DVT of the leg who are treated with VKA, we recommend a therapeutic INR range of 2.0 to 3.0 (target INR of 2.5) over a lower (INR < 2) or higher (INR 3.0-5.0) range for all treatment durations (Grade 1B).

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 14, 2003 VOL. 349 NO. 7

Comparison of Low-Intensity Warfarin Therapy with Conventional-Intensity Warfarin Therapy for Long-Term Prevention of Recurrent Venous Thromboembolism

Clive Kearon, M.B., Ph.D., Jeffrey S. Ginsberg, M.D., Michael J. Kovacs, M.D., David R. Anderson, M.D., Philip Wells, M.D., Jim A. Julian, M.Math., Betsy MacKinnon, M.Sc., Jeffrey I. Weitz, M.D., Mark A. Crowther, M.D., Sean Dolan, M.D., Alexander G. Turpie, M.B., William Geerts, M.D., Susan Solymoss, M.D., Paul van Nguyen, M.D., Christine Demers, M.D., Susan R. Kahn, M.D., Jeannine Kassis, M.D., Marc Rodger, M.D., Julie Hambleton, M.D., and Michael Gent, D.Sc., for the Extended Low-Intensity Anticoagulation for Thrombo-Embolism Investigators*

- Prospective, randomisée
- 738 patients traités par Warfarin
- 2 groupes comparables :
  - Low intensity group : INR = 1;5 – 1.9 (369 malades)
  - Conventionnal intensity group : INR = 2 – 3 (369 malades)

Table 2. Main Outcomes According to Treatment Group.*

Outcome	Low-Intensity–Therapy Group (N=369)		Conventional-Intensity–Therapy Group (N=369)		Hazard Ratio (95% CI)	Difference between Rates (95% CI)	P Value
	No. of Events	No./100 Person-Yr	No. of Events	No./100 Person-Yr			
						no./100 person-yr	
Major bleeding episode	9	1.1	8	0.9	1.2 (0.4 to 3.0)	0.1 (–0.8 to 1.1)	0.76
Any bleeding episode	39	4.9	31	3.7	1.3 (0.8 to 2.1)	1.2 (–0.8 to 3.2)	0.26
Recurrent venous thromboembolism	16	1.9	6	0.7	2.8 (1.1 to 7.0)	1.2 (0.2 to 2.7)	0.03
Death	16	1.9	8	0.9	2.1 (0.9 to 4.8)	1.0 (–0.2 to 2.1)	0.09

* Because of rounding, the figures given for the differences between rates may not match the differences calculated from the rates given for each group. CI denotes confidence interval.

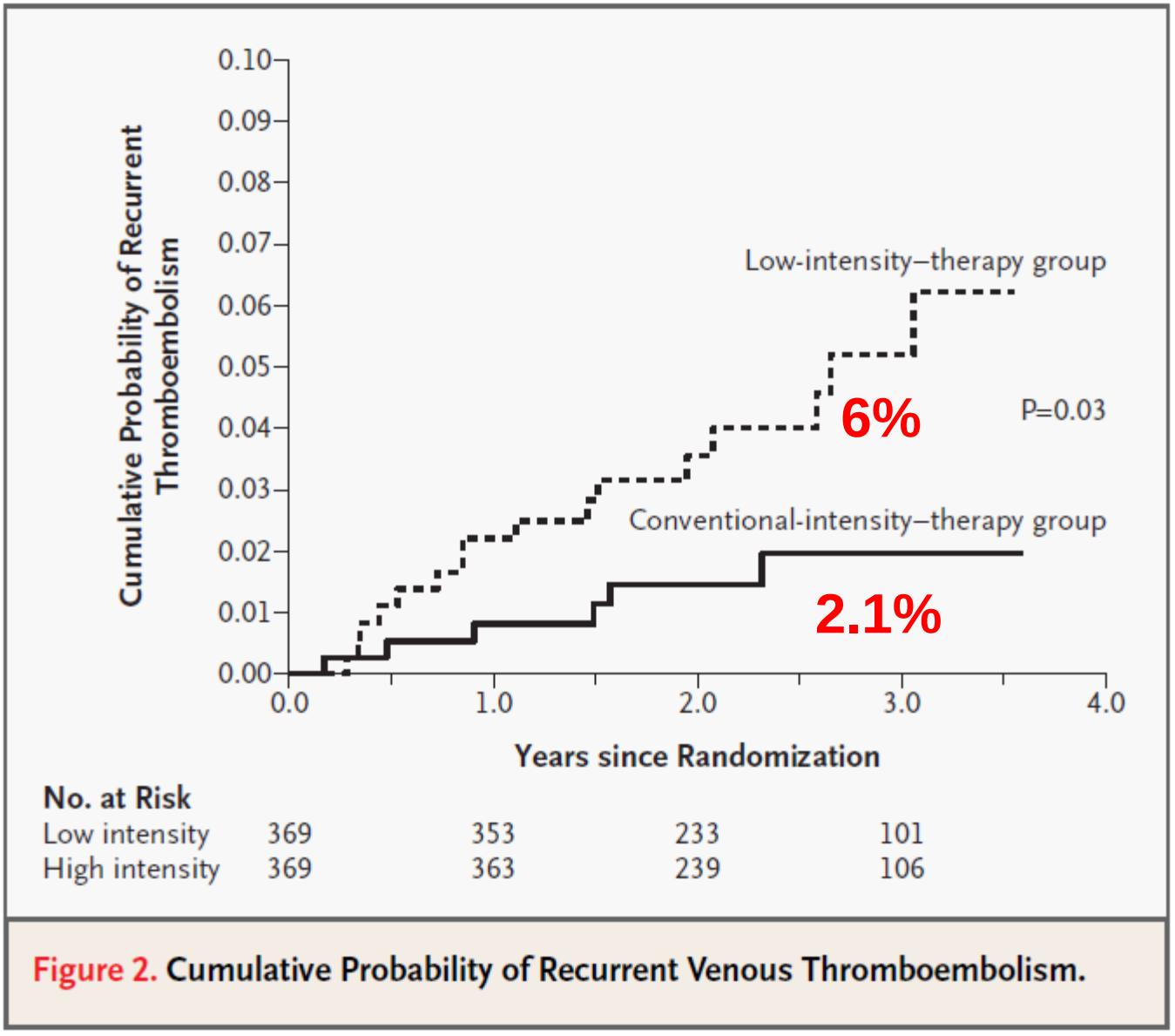

Figure 2. Cumulative Probability of Recurrent Venous Thromboembolism.

Durée du traitement

The New England
Journal of Medicine

Volume 332 JUNE 22, 1995 Number 25

A COMPARISON OF SIX WEEKS WITH SIX MONTHS OF ORAL ANTICOAGULANT THERAPY AFTER A FIRST EPISODE OF VENOUS THROMBOEMBOLISM

SAM SCHULMAN, M.D., ANN-SOFIE RHEDIN, M.D., PER LINDMARKER, M.D., ANDERS CARLSSON, M.D., GERD LÄRFARS, M.D., PETER NICOL, M.D., ENNO LOOGNA, M.D., ELSE SVENSSON, M.D., BENGT LJUNGBERG, M.D., HANS WALTER, M.D., STANKA VIERING, M.D., SUNE NORDLANDER, M.D., BARBRO LEIJD, M.D., KJELL-ÅKE JÖNSSON, M.D., MARTIN HJORTH, M.D., OLLE LINDER, M.D., JONAS BOBERG, M.D., AND THE DURATION OF ANTICOAGULATION TRIAL STUDY GROUP*

- Multicentrique, randomisée
- Anticoagulants 6 semaines : n = 443
- Anticoagulants 6 mois : n = 454

Récidive à 6 mois : 12.1 vs 24.1
Récidive à 24 mois : 9.5 vs 18.1
Pas de différence pour
la mortalité et
les événements hémorragiques

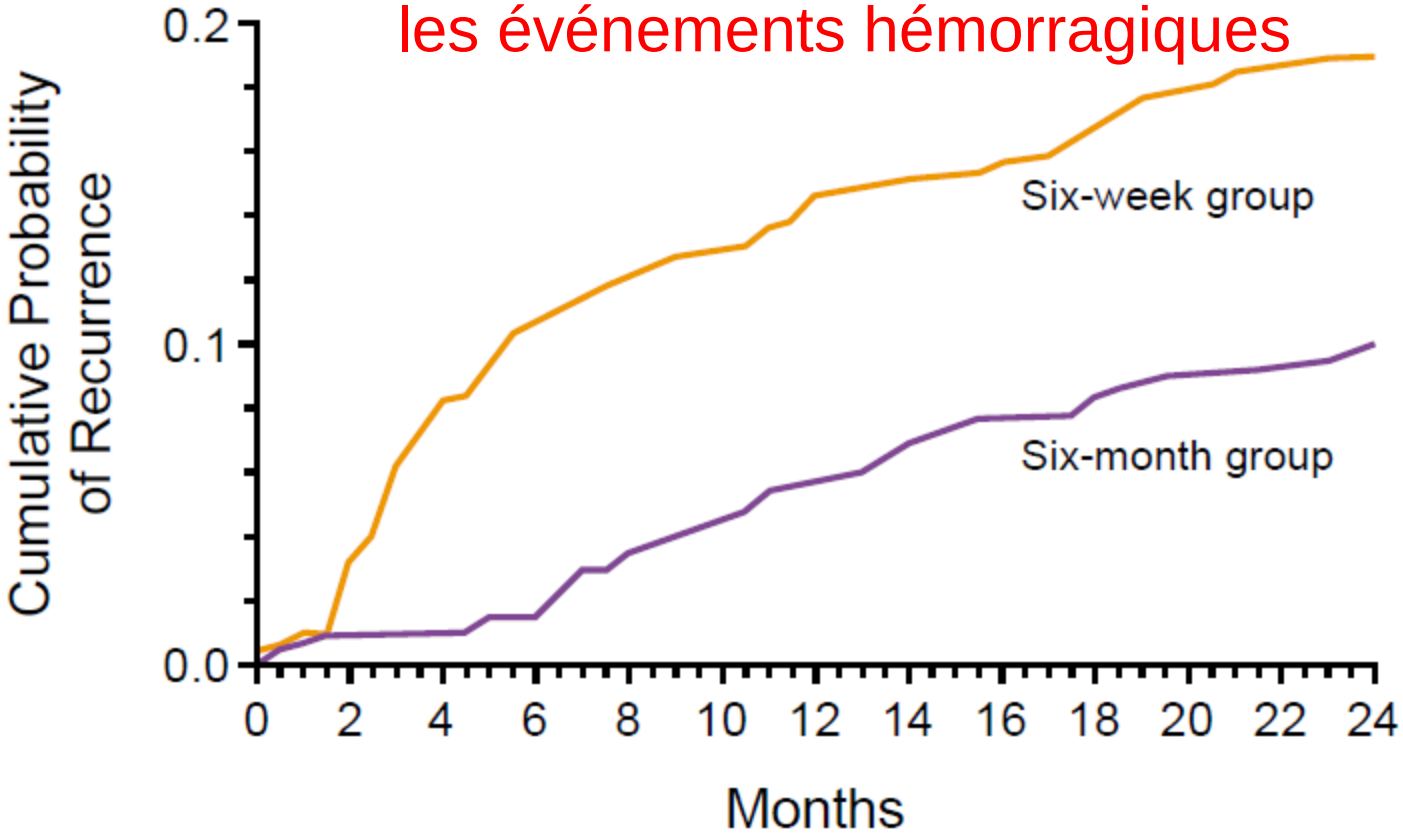

Figure 1. Cumulative Probability of Recurrent Venous Thromboembolism after a First Episode, According to the Duration of Anticoagulation.

THREE MONTHS VERSUS ONE YEAR OF ORAL ANTICOAGULANT THERAPY FOR IDIOPATHIC DEEP VENOUS THROMBOSIS

GIANCARLO AGNELLI, M.D., PAOLO PRANDONI, M.D., PH.D., MARIA GABRIELLA SANTAMARIA, M.D., PAOLA BAGATELLA, M.D., ALFONSO IORIO, M.D., MARIO BAZZAN, M.D., MARCO MOIA, M.D., GIULIANA GUAZZALOCA, M.D., ADRIANO BERTOLDI, M.D., CRISTINA TOMASI, M.D., GIANLUIGI SCANNAPIECO, M.D., WALTER AGENO, M.D., AND THE WARFARIN OPTIMAL DURATION ITALIAN TRIAL INVESTIGATORS*

N Engl J Med, Vol. 345, No. 3 · July 19, 2001

- Étude randomisée
- Anticoagulants
  - 3 mois (n = 134) vs
  - 1 an (n = 133)

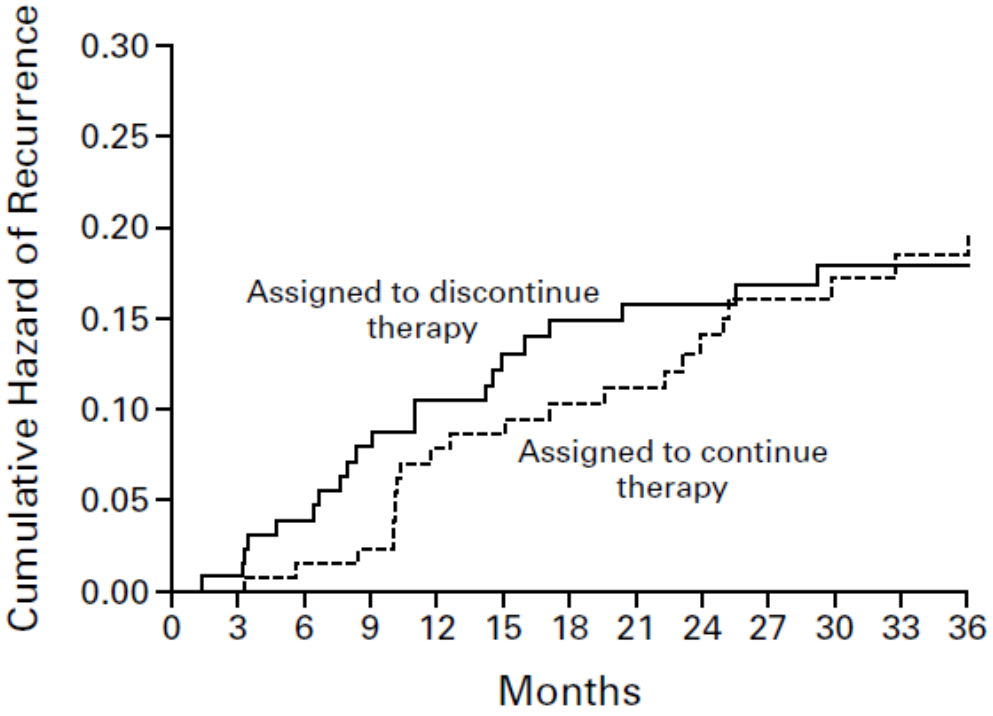

Figure 1. Cumulative Hazard of Recurrent Venous Thromboembolism in Patients Assigned to Discontinue Oral Anticoagulant Therapy and Those Assigned to Continue Oral Anticoagulant Therapy (Intention-to-Treat Population).

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6.0 Long-term Treatment of Patients With PE

6.1. In patients with PE provoked by surgery, we recommend treatment with anticoagulation for 3 months over (i) treatment of a shorter period (Grade 1B), **(ii) treatment of a longer time-limited period (eg, 6 or 12 months)** (Grade 1B), **or (iii) extended therapy** (Grade 1B regardless of bleeding risk).

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6.2. In patients with PE provoked by a non-surgical transient risk factor, we recommend treatment with anticoagulation for 3 months over (i) treatment of a shorter period (Grade 1B), **(ii) treatment of a longer time-limited period (eg, 6 or 12 months)** (Grade 1B), **and (iii) extended therapy if there is a high bleeding risk** (Grade 1B). **We suggest treatment with anticoagulation for 3 months over extended therapy if there is a low or moderate bleeding risk** (Grade 2B).

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6.3. In patients with an unprovoked PE, we recommend treatment with anticoagulation for at least 3 months over treatment of a shorter duration (Grade 1B). **After 3 months of treatment, patients with unprovoked PE should be evaluated for the risk-benefit ratio of extended therapy.**

6.5. In patients with PE who are treated with VKA, we recommend a therapeutic INR range of 2.0 to 3.0 (target INR of 2.5) over a lower (INR < 2) or higher (INR 3.0-5.0) range for all treatment durations (Grade 1B).

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3.1 Duration of Long-term Anticoagulant Therapy

3.1.1. In patients with a proximal DVT of the leg provoked by surgery, we recommend treatment with anticoagulation for 3 months over (i) treatment of a shorter period (Grade 1B), **(ii) treatment of a longer time-limited period (eg, 6 or 12 months)** (Grade 1B), **or (iii) extended therapy** (Grade 1B regardless of bleeding risk).

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3.1.2. In patients with a proximal DVT of the leg provoked by a nonsurgical transient risk factor, we recommend treatment with anticoagulation for 3 months over (i) treatment of a shorter period (Grade 1B), **(ii) treatment of a longer time-limited period (eg, 6 or 12 months)** (Grade 1B), **and (iii) extended therapy if there is a high bleeding risk** (Grade 1B). **We suggest treatment with anticoagulation for 3 months over extended therapy if there is a low or moderate bleeding risk** (Grade 2B).

Embolectomie

Embolectomie percutanée

- Techniques : aspiration, fragmentation, pulvérisation
- Indications : Contre Indications à la thrombolyse
  Echec de thrombolyse
- Gare à l'impact hémodynamique des produits de contraste
- Séries rétrospectives :
  80% d'efficacité immédiate sur l'hémodynamique
  Mortalité variable de 0 à 25%
  succédant ou couplé à la thrombolyse le plus souvent

Modern surgical treatment of massive pulmonary embolism: Results in 47 consecutive patients after rapid diagnosis and aggressive surgical approach

Marzia Leacche, MD,[a] Daniel Unic, MD,[a] Samuel Z. Goldhaber, MD,[b] James D. Rawn, MD,[a] Sary F. Aranki, MD,[a] Gregory S. Couper, MD,[a] Tomislav Mihaljevic, MD,[a] Robert J. Rizzo, MD,[a] Lawrence H. Cohn, MD,[a] Lishan Aklog, MD,[c] and John G. Byrne, MD[a]

The Journal of Thoracic and Cardiovascular Surgery • May 2005

TABLE 2. Indications for surgical embolectomy (n = 47)

Indication	N (%)
Contraindications to thrombolysis	21 (45%)
Recent surgical intervention	10 (21%)
Active bleeding	3 (6%)
Stroke	4 (9%)
Other	4 (9%)
Failed medical treatment	5 (10%)
Failure of thrombolytics	4 (9%)
Failure of catheter embolectomy	1 (2%)
Large RA-RV thrombus	5 (10%)
RV hemodynamic dysfunction	15 (32%)
Large PFO	1 (2%)

RA-RV, Right atrium–right ventricle; *PFO*, patent foramen ovale.

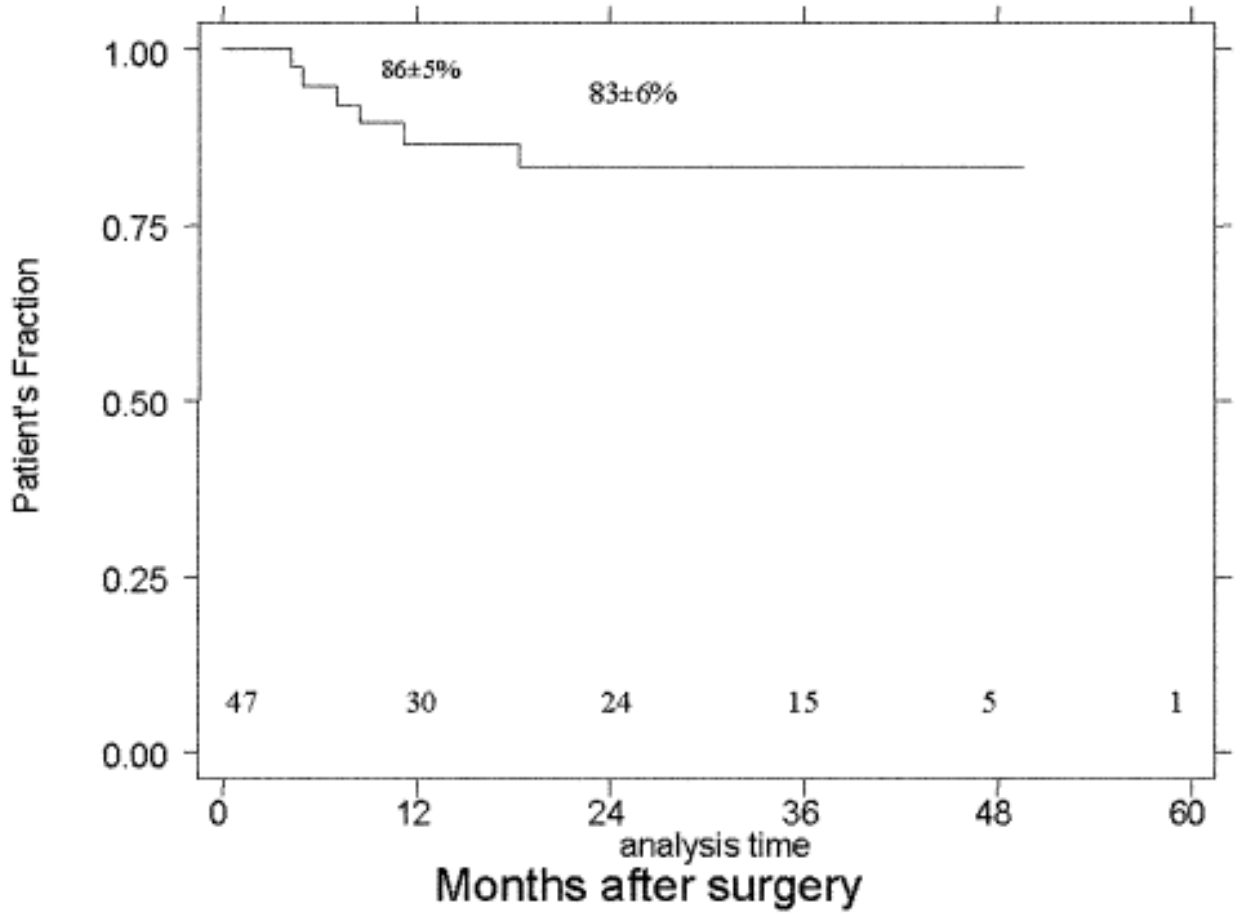

Figure 3. Kaplan-Meier survival curve after surgical pulmonary embolectomy (n = 47 patients, including the 3 operative deaths).

A retenir

- Nette diminution du taux de mortalité chirurgicale au cours des années (57% à 6%)
- Approche diagnostique agressive (ct/écho)
- Besoin d'un embole central pour faire embolectomie
- Mauvais pronostic demeure pour ceux avec arrêt cardio-respiratoire préalable

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2.11 Operative Venous Thrombectomy for Acute DVT

2.11. In patients with acute proximal DVT of the leg, we suggest anticoagulant therapy alone over operative venous thrombectomy (Grade 2C).

5.7 Catheter-Based Thrombus Removal for the Initial Treatment of Patients With PE

5.7. In patients with acute PE associated with hypotension and who have (i) contraindications to thrombolysis, (ii) failed thrombolysis, or (iii) shock that is likely to cause death before systemic thrombolysis can take effect (eg, within hours), if appropriate expertise and resources are available, we suggest catheter-assisted thrombus removal over no such intervention (Grade 2C).

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5.8 Surgical Embolectomy for the Initial Treatment of Patients With PE

5.8. In patients with acute PE associated with hypotension, we suggest surgical pulmonary embolectomy over no such intervention if they have (i) contraindications to thrombolysis, (ii) failed thrombolysis or catheter-assisted embolectomy, or (iii) shock that is likely to cause death before thrombolysis can take effect (eg, within hours), provided surgical expertise and resources are available (Grade 2C).

Filtres Caves

- Filtre définitif ou temporaire (jusqu'à 1 an)

- Indications :
  - Contre indication absolue d'emblée aux ATC
  - Obligation d'interrompre les ATC
  - Décès probable si récurrence d'EP
  - échec traitement médical et avant embolectomie

  (*Aklog et al, Circulation 2002)*

- Incidence de TVP > avec FC vs sans FC.

  (*PREPIC study group, Circulation 2005)*

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5.9. Vena Cava Filters for the Initial Treatment of Patients With PE

5.9.1. In patients with acute PE who are treated with anticoagulants, we recommend against the use of an IVC filter (Grade 1B).

5.9.2. In patients with acute PE and contraindication to anticoagulation, we recommend the use of an IVC filter (Grade 1B).

5.9.3. In patients with acute PE and an IVC filter inserted as an alternative to anticoagulation, we suggest a conventional course of anticoagulant therapy if their risk of bleeding resolves (Grade 2B).

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2.13 Vena Cava Filters for the Initial Treatment of Patients With DVT

2.13.1. In patients with acute DVT of the leg, we recommend against the use of an IVC filter in addition to anticoagulants (Grade 1B).

2.13.2. In patients with acute proximal DVT of the leg and contraindication to anticoagulation, we recommend the use of an IVC filter (Grade 1B).

2.13.3. In patients with acute proximal DVT of the leg and an IVC filter inserted as an alternative to anticoagulation, we suggest a conventional course of anticoagulant therapy if their risk of bleeding resolves (Grade 2B).

Table 5 Risk stratification according to expected pulmonary embolism-related early mortality rate

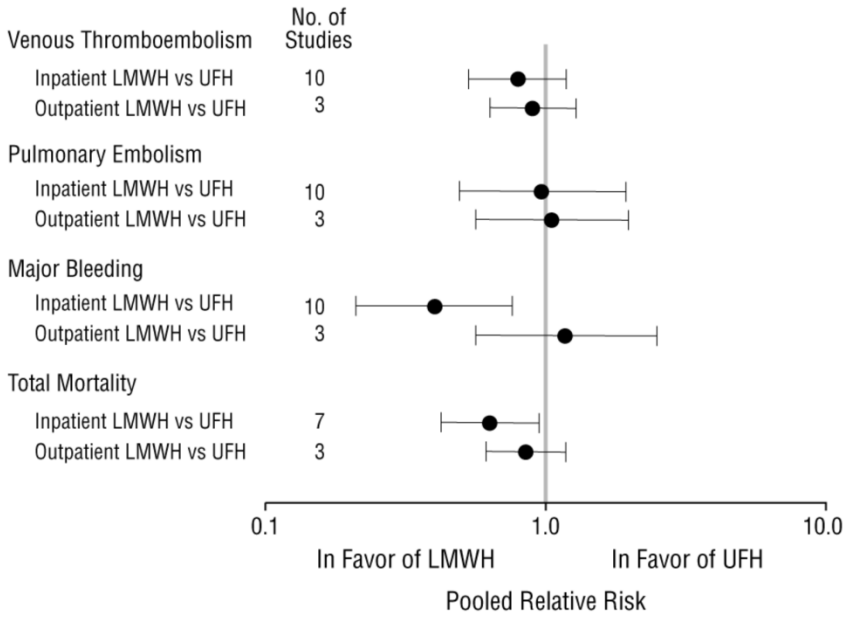
PE-related early MORTALITY RISK		RISK MARKERS: CLINICAL (shock or hypotension)	RISK MARKERS: RV dysfunction	RISK MARKERS: Myocardial injury	Potential treatment implications
HIGH >15%		+	(+)[a]	(+)[a]	Thrombolysis or embolectomy
NON HIGH	Intermediate 3–15%	–	+	+	Hospital admission
			+	–	
			–	+	
	Low <1%	–	–	–	Early discharge or home treatment

[a]In the presence of shock or hypotension it is not necessary to confirm RV dysfunction/injury to classify as high risk of PE-related early mortality.

PE = pulmonary embolism; RV = right ventricle.

A Meta-analysis Comparing Low-Molecular-Weight Heparins With Unfractionated Heparin in the Treatment of Venous Thromboembolism
Location of Treatment, Product Type, and Dosing Frequency

Arch Intern Med. 2000;160(2):181-188. doi:10.1001/archinte.160.2.181



A comparison of inpatient vs outpatient treatment with low-molecular-weight heparin (LMWH) vs unfractionated heparin (UFH).

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8.1 Treatment of Patients With Superficial Vein Thrombosis

8.1.1. In patients with superficial vein thrombosis of the lower limb of at least 5 cm in length, we suggest the use of a prophylactic dose of fondaparinux or LMWH for 45 days over no anticoagulation (Grade 2B).

8.1.2. In patients with superficial vein thrombosis who are treated with anticoagulation, we suggest fondaparinux 2.5 mg daily over a prophylactic dose of LMWH (Grade 2C).

Hospitalier/ambulatoire

2012

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2.7 At-Home vs In-Hospital Initial Treatment of Patients With DVT

2.7. In patients with acute DVT of the leg and whose home circumstances are adequate, we recommend initial treatment at home over treatment in hospital (Grade 1B).

Uptake of new treatment strategies for deep vein thrombosis: an international audit

DRAHOMIR A. AUJESKY[1], JACQUES CORNUZ[1], JEAN-LUC BOSSON[2], HENRI BOUNAMEAUX[3], JOSEPH EMMERICH[4], RUSSELL D. HULL[5], ELIZABETH MACKAY[5], ARNAUD PERRIER[3], HUDE QUAN[6], ROSS T. TSUYUKI[7] AND WILLIAM A. GHALI[5]

International Journal for Quality in Health Care 2004; **Volume 16, Number 3**: pp. 193–200

Objective. Study of the uptake of new medical technologies provides useful information on the transfer of published evidence into usual practice. We conducted an audit of selected hospitals in three countries (Canada, France, and Switzerland) to identify clinical predictors of low-molecular-weight (LMW) heparin use and outpatient treatment, and to compare the pace of uptake of these new therapeutic approaches across hospitals.

Setting and participants. We reviewed the medical records of 3043 patients diagnosed with deep vein thrombosis (DVT) in five Canadian, two French, and two Swiss teaching hospitals from 1994 to 1998.

Measures. We explored independent clinical variables associated with LMW heparin use and outpatient treatment, and determined crude and adjusted rates of LMW heparin use and outpatient treatment across hospitals.

Results. For the years studied, the overall rates of LMW heparin use and outpatient treatment in the study sample were 34.1 and 15.8%, respectively, with higher rates of use in later years. Many comorbidities were negatively associated with outpatient treatment, and risk-adjusted rates of use of these new approaches varied significantly across hospitals.

9

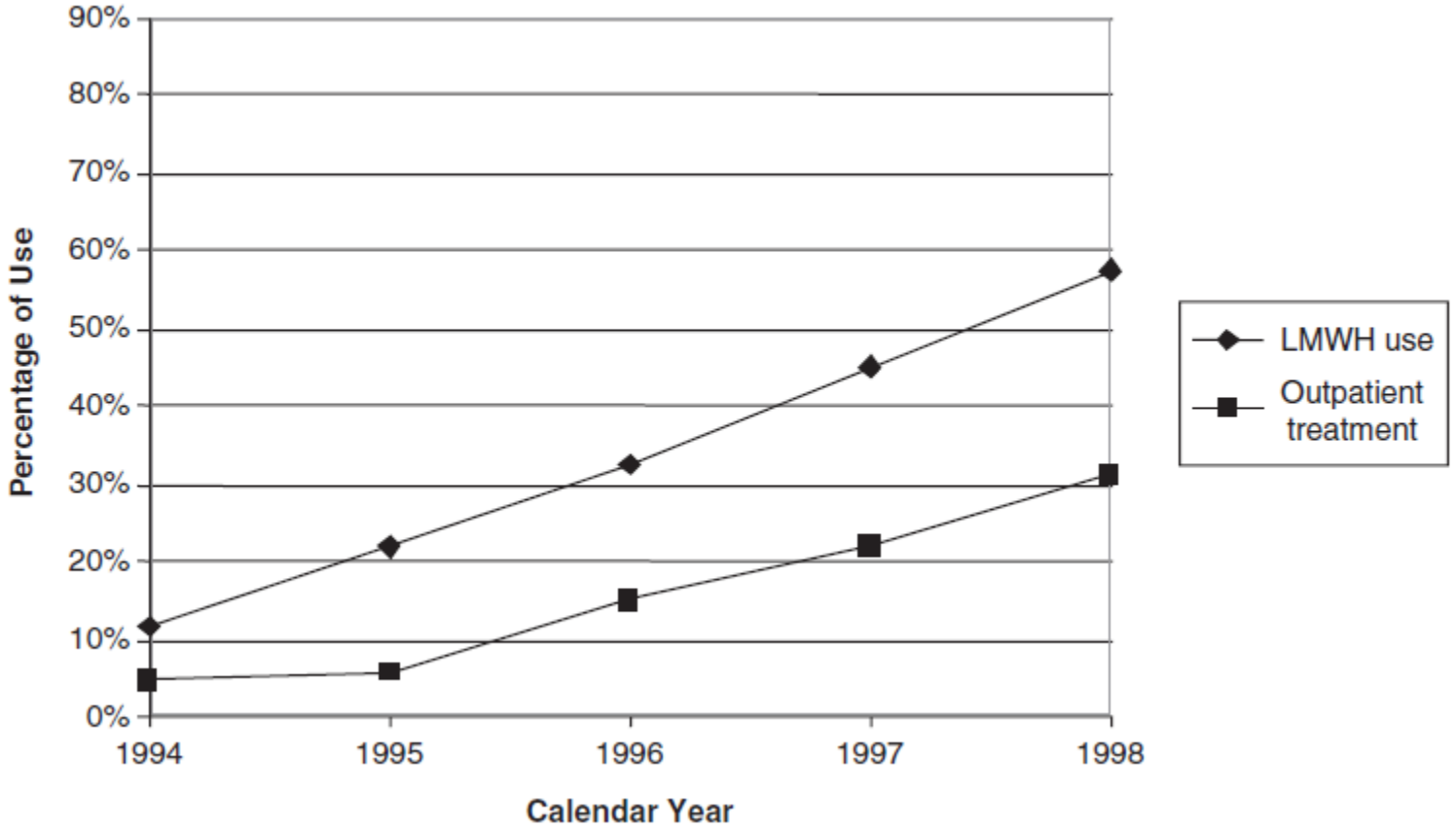

Figure 1 Overall low-molecular-weight heparin use and outpatient treatment for all nine hospitals. LMWH, low-molecular-weight heparin.

Conclusion. There has been a relatively rapid uptake of LMW heparins and outpatient treatment for DVT in their early years of availability, but the pace of uptake has varied considerably across hospitals and countries.


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C'EST QU'IL N'Y A PAS DE PROBLÈME.


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