Embolie Pulmonaire : thérapeutique et prise en charge en ambulatoire

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Plan

I. Anticoagulants oraux directs

II. Traitement ambulatoire de l'EP

III. Alternatives Thérapeutiques

IV. Conclusions.

Thérapeutique EP

Recommendations for acute phase treatment

Recommendations	Class[a]	Level[b]	Ref[c]
PE without shock or hypotension (intermediate-or low-risk)[d]			
Anticoagulation: combination of parenteral treatment with VKA			
Initiation of parenteral anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic work-up is in progress.	I	C	352

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Thérapeutique EP

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LMWH or fondaparinux is the recommended form of acute phase parenteral anticoagulation for most patients.	I	A	273, 274, 281, 353
In parallel to parenteral anticoagulation, treatment with a VKA is recommended, targeting an INR of 2.5 (range 2.0–3.0).	I	B	352, 354

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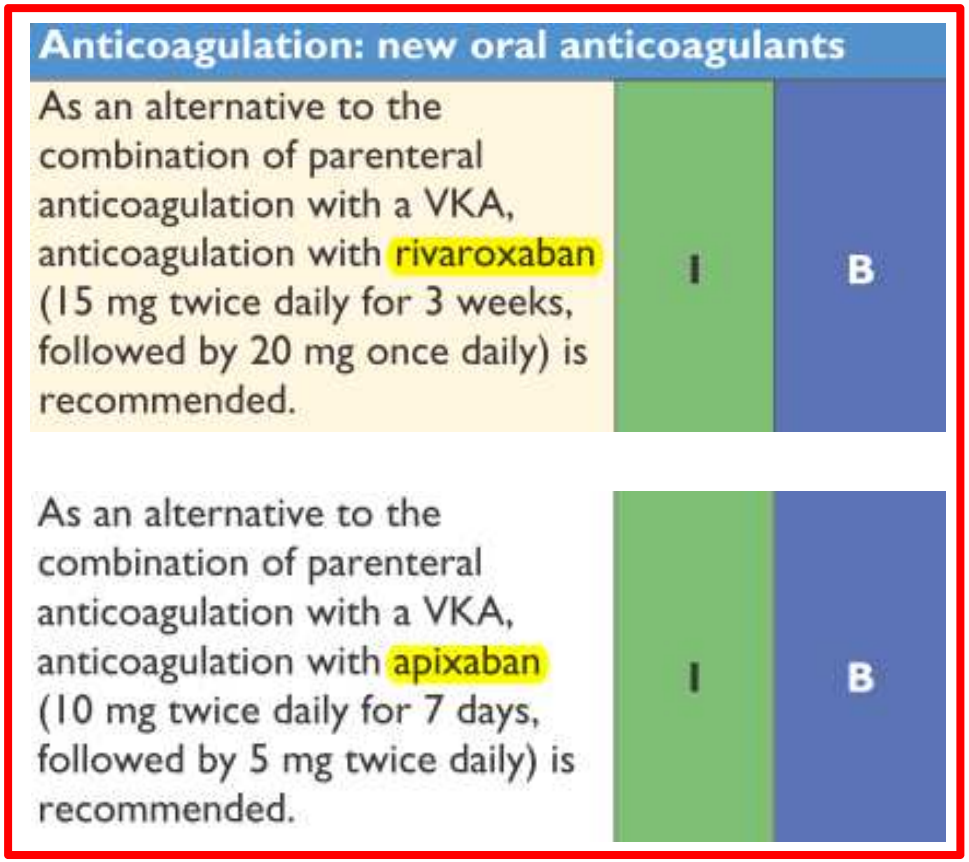
Thérapeutique EP

Anticoagulants oraux directs

France > 2500 patients inclus



Anticoagulation: new oral anticoagulants		
As an alternative to the combination of parenteral anticoagulation with a VKA, anticoagulation with rivaroxaban (15 mg twice daily for 3 weeks, followed by 20 mg once daily) is recommended.	I	B
As an alternative to the combination of parenteral anticoagulation with a VKA, anticoagulation with apixaban (10 mg twice daily for 7 days, followed by 5 mg twice daily) is recommended.	I	B

As an alternative to VKA treatment, administration of dabigatran (150 mg twice daily, or 110 mg twice daily for patients ≥80 years of age or those under concomitant verapamil treatment) is recommended following acute-phase parenteral anticoagulation.	I	B[e]
As an alternative to VKA treatment, administration of edoxaban* is recommended following acute-phase parenteral anticoagulation.	I	B

💣Hors cancer, ins rénale/hépatique, interactions méd 💣

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Rappels AOD

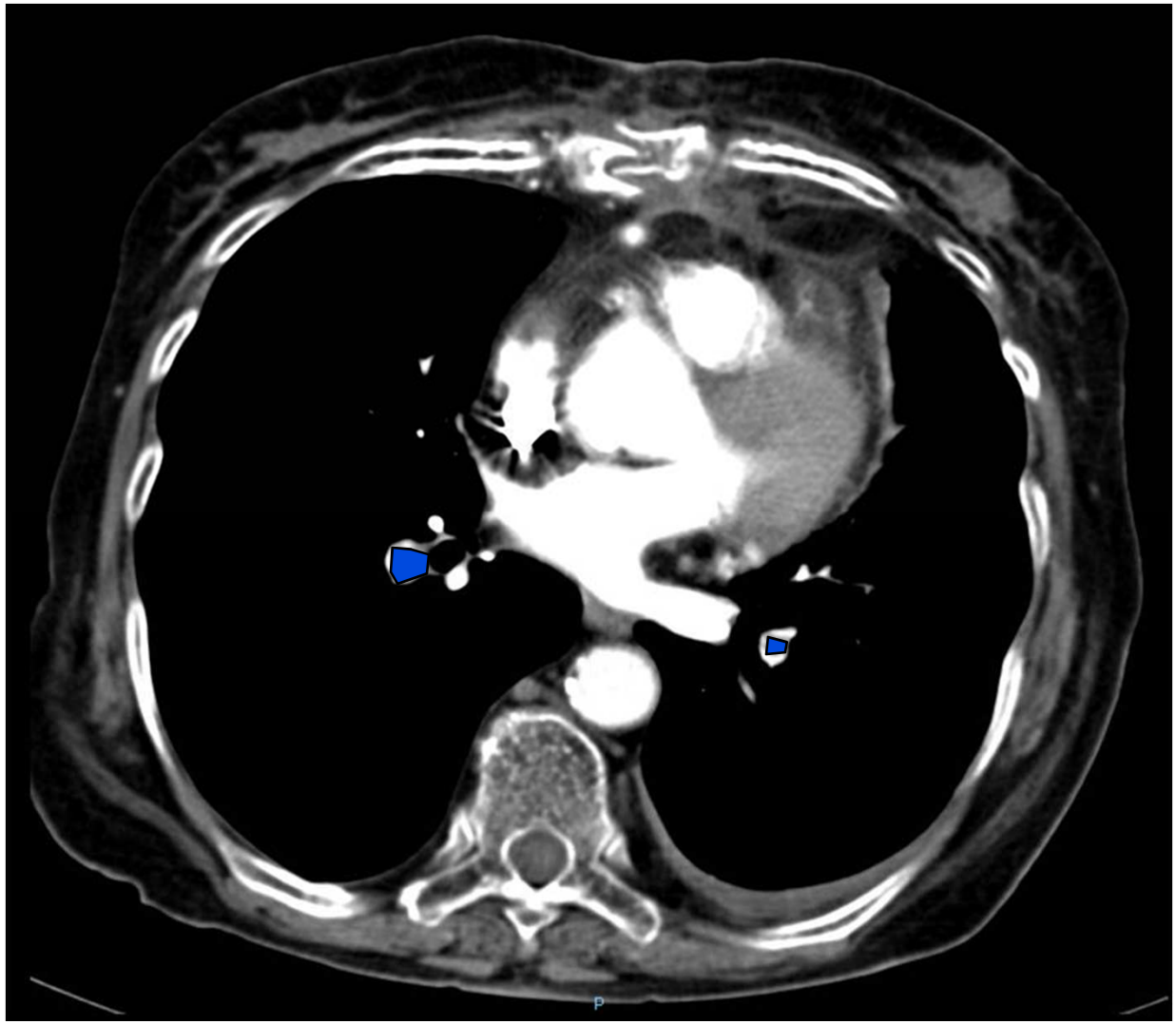
Indications validées
Indications en attente de prix

- Dabigatran (PRADAXA°):
  - Prévention post **PTH/PTG** : 110mg*2 (voire 75mg*2)
  - Prévention **AVC/FANR** : 150mg*2 (voire 110mg*2)
  - *Traitement **TVP/EP** : Hep puis 150mg*2 (voire 110mg*2)*

- Rivaroxaban (XARELTO°):
  - Prévention post **PTH/PTG** : 10mg
  - Prévention **AVC/FANR** : 20mg (voire 15mg)
  - ***Post-SCA** : 2,5mg*2, 6 mois*
  - Traitement **TVP/EP** : 15mg*2 - 21j, puis 20mg (voire 15mg)

- Apixaban (ELIQUIS°):
  - Prévention post **PTH/PTG** : 2.5mg*2
  - Prévention **AVC/FANR** : 5mg*2 (voire 2.5mg*2)
  - *Traitement **TVP/EP** : 10*2 pdt 7j puis 5mg*2*

EP sous dabigatran 110 * 2



Cancer

Recommendations	Class[a]	Level[b]
Incidental PE in patients with cancer should be managed in the same manner as symptomatic PE.	IIa	C
Negative D-dimer levels have the same negative diagnostic value as in non-cancer patients.	IIa	B
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 3–6 months.	IIa	B
For patients with PE and cancer, extended anticoagulation (beyond the first 3–6 months) should be considered for an indefinite period or until the cancer is cured.	IIa	C

HBPM = ↘ 30% ✞

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Cochrane. 2011

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EP « non à haut risque »

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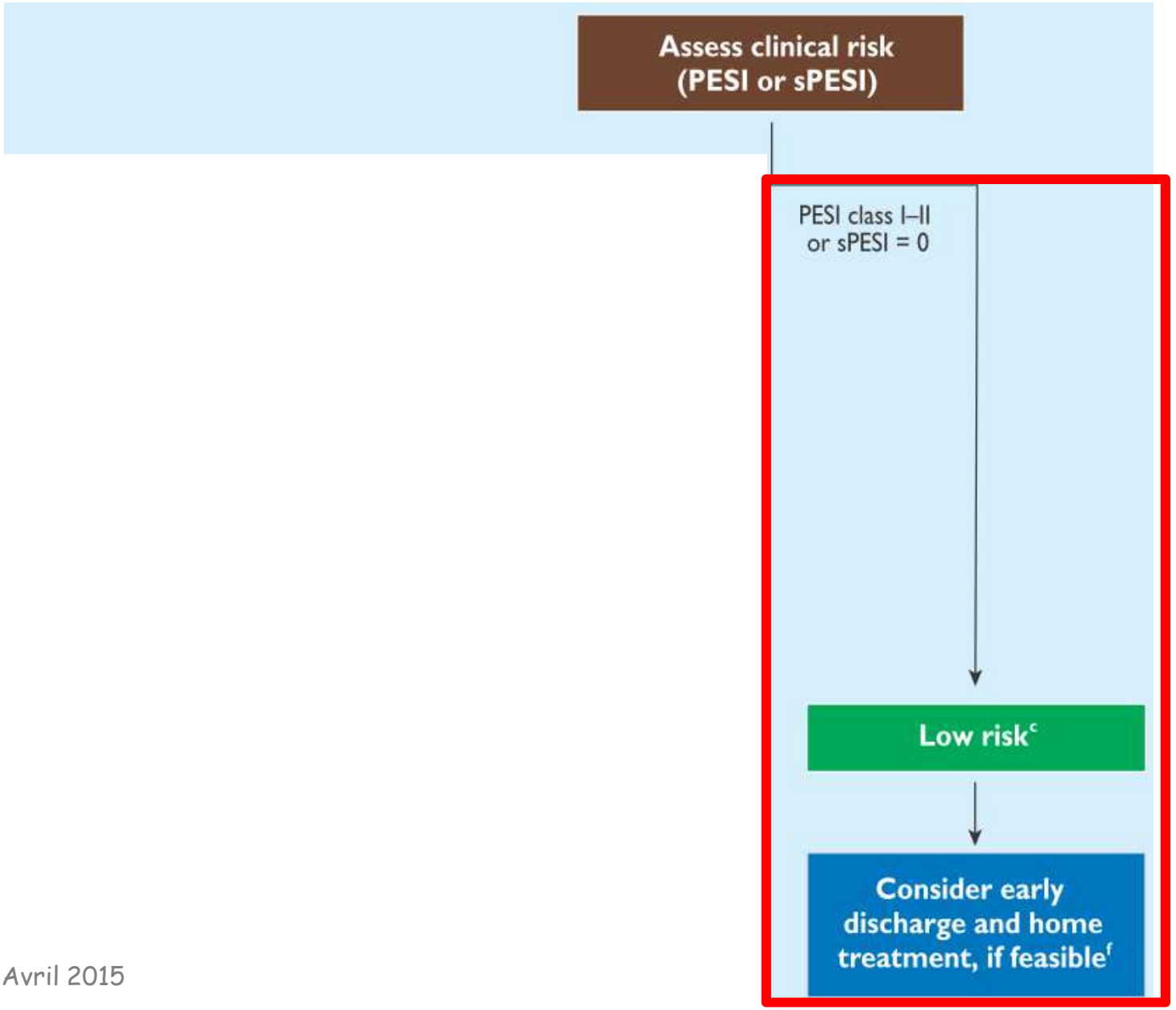
EP « non à haut risque »

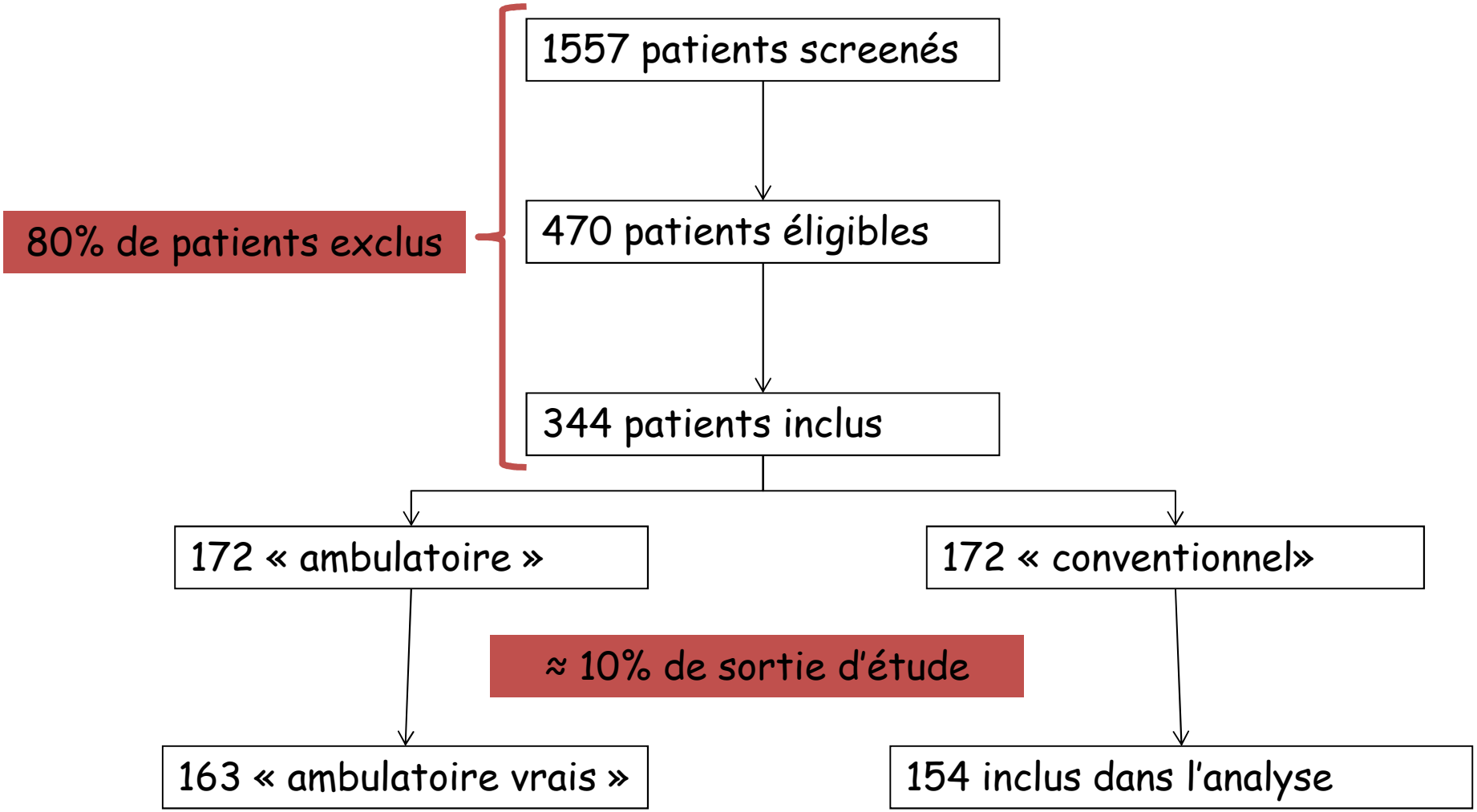
Mortalité J30 : 1%

EP « non à haut risque »



Thérapeutique EP

- Etude OTPE : EP confirmée, faible risque (PESI I ou II)



Aujesky D et al. Lancet 2011

Thérapeutique EP

Traitement ambulatoire

- Etude OTPE : EP confirmée, faible risque (PESI I ou II)

	Outpatient group (n=171)	Inpatient group (n=168)
Age (years)	47 (16)	49 (15)
Male sex	84 (49%)	85 (51%)
Body-mass index (kg/m²)	26·1 (5·0)	26·8 (4·9)
Localisation of PE‡		
Central	24 (14%)	16 (10%)
Lobar	60 (35%)	66 (39%)
Segmental	110 (64%)	100 (60%)
Subsegmental	52 (30%)	44 (26%)
History of venous thromboembolism	31 (18%)	40 (24%)
Cancer§	1 (1%)	3 (2%)
Oestrogen therapy	39 (23%)	34 (20%)
History of thrombophilic condition¶	7 (4%)	6 (4%)
History of heart failure‖	2 (1%)	2 (1%)
History of lung disease**	7 (4%)	6 (4%)

Aujesky D et al. Lancet 2011

Thérapeutique EP

Traitement ambulatoire

- Etude OTPE : EP confirmée, faible risque (PESI I ou II)

	Outpatient group	Inpatient group	Difference in percentages ($\%_{outpatient}-\%_{inpatient}$)	Upper 95% CL for difference	p value*
Primary analysis outcomes within 90 days†					
Recurrent VTE	1 (0·6%)‡	0	0·6%	2·7%	0·011
Major bleeding	3 (1·8%)	0	1·8%	4·5%	0·086
Intramuscular	2 (1·2%)	0	1·2%	3·6%	0·031
Menometrorrhagia	1 (0·6%)	0	0·6%	2·7%	0·011
Overall mortality	1 (0·6%)§	1 (0·6%)¶	0%	2·1%	0·005

« Parcours de soins EP »

Early discharge and home treatment		
Patients with acute low-risk PE should be considered for early discharge and continuation of treatment at home if proper outpatient care and anticoagulant treatment can be provided.	IIa	B

Aujesky D et al. Lancet 2011

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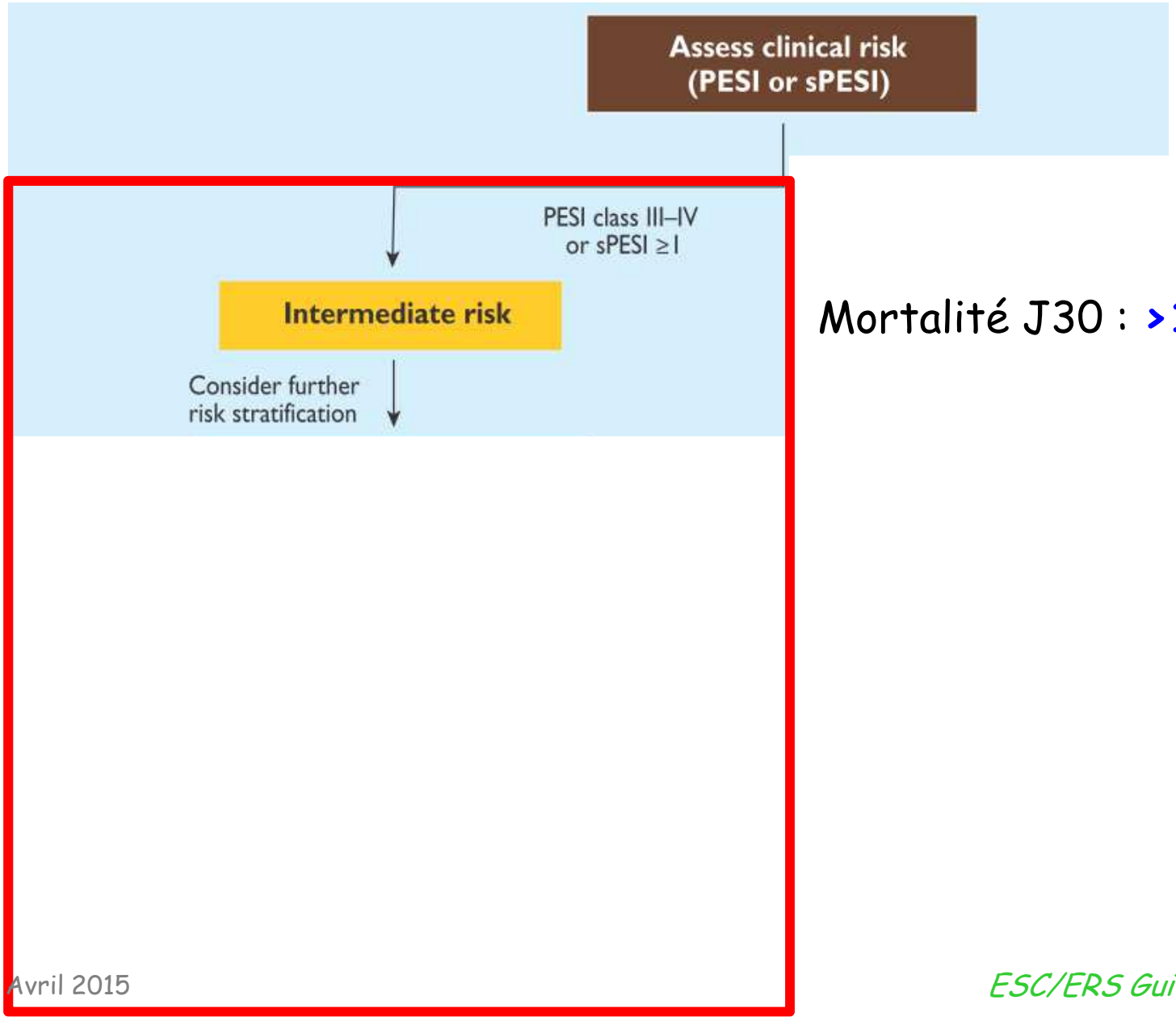
EP « non à haut risque »



Mortalité J30 : **>10%**

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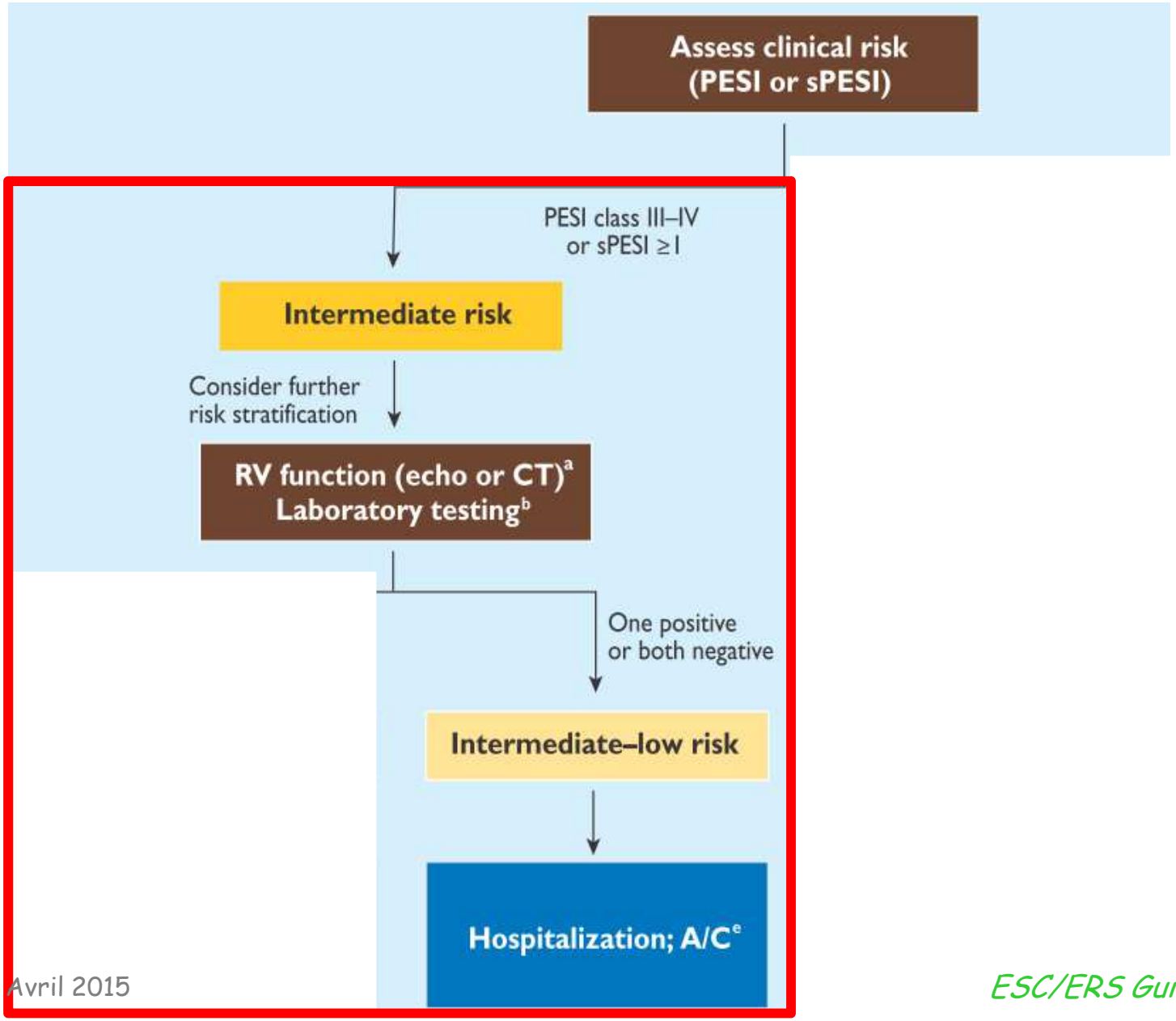
EP « non à haut risque »



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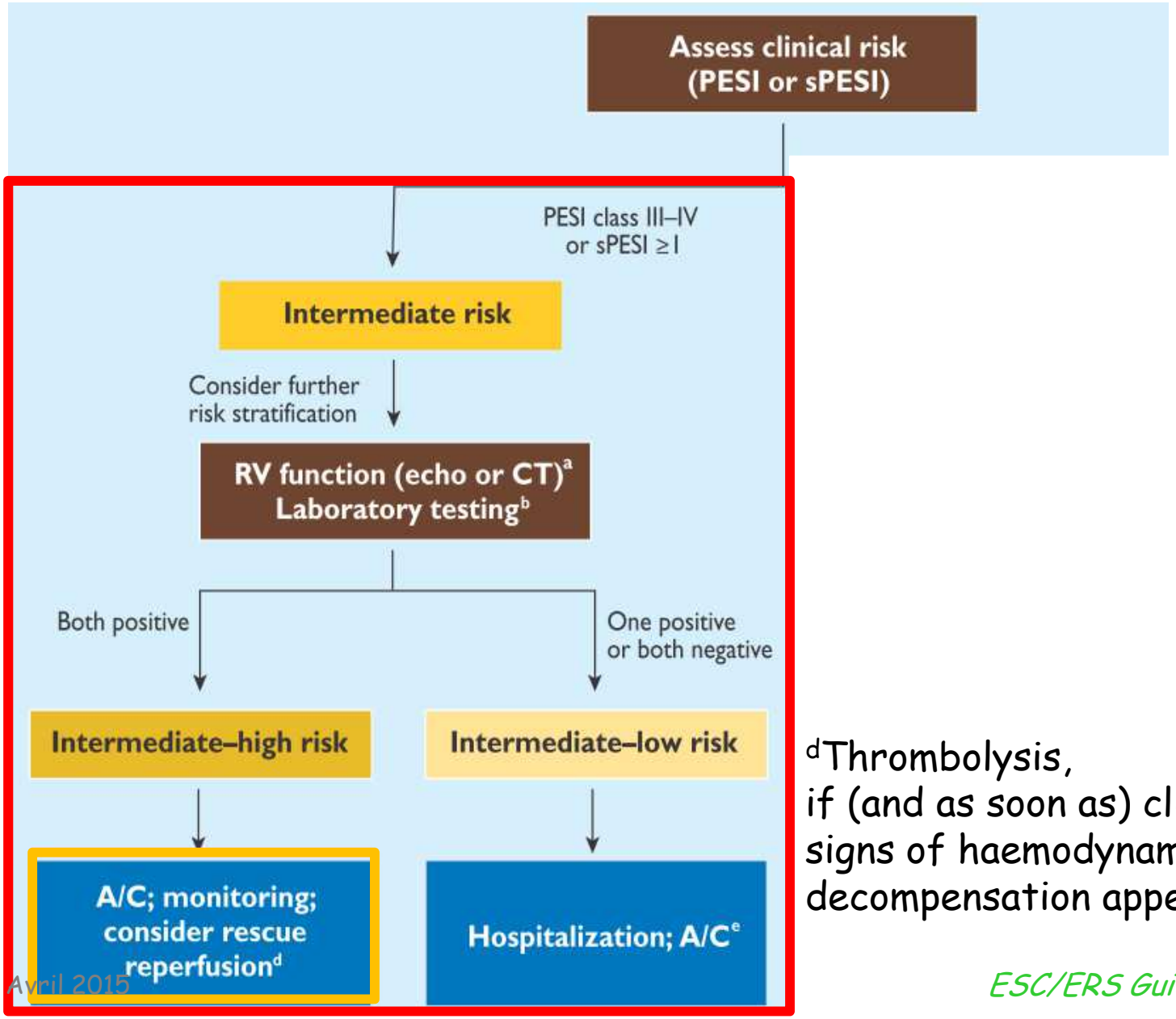
EP « non à haut risque »



[d]Thrombolysis,
if (and as soon as) clinical signs of haemodynamic decompensation appear

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Thérapeutique EP

Reperfusion treatment		
Routine use of primary systemic thrombolysis is not recommended in patients not suffering from shock or hypotension.	III	B
Close monitoring is recommended in patients with intermediate-high risk PE to permit early detection of haemodynamic decompensation and timely initiation of 'rescue' reperfusion therapy.	I	B
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation.	IIa	B
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high.[g]	IIb	C
Percutaneous catheter-directed treatment may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high.[g]	IIb	B

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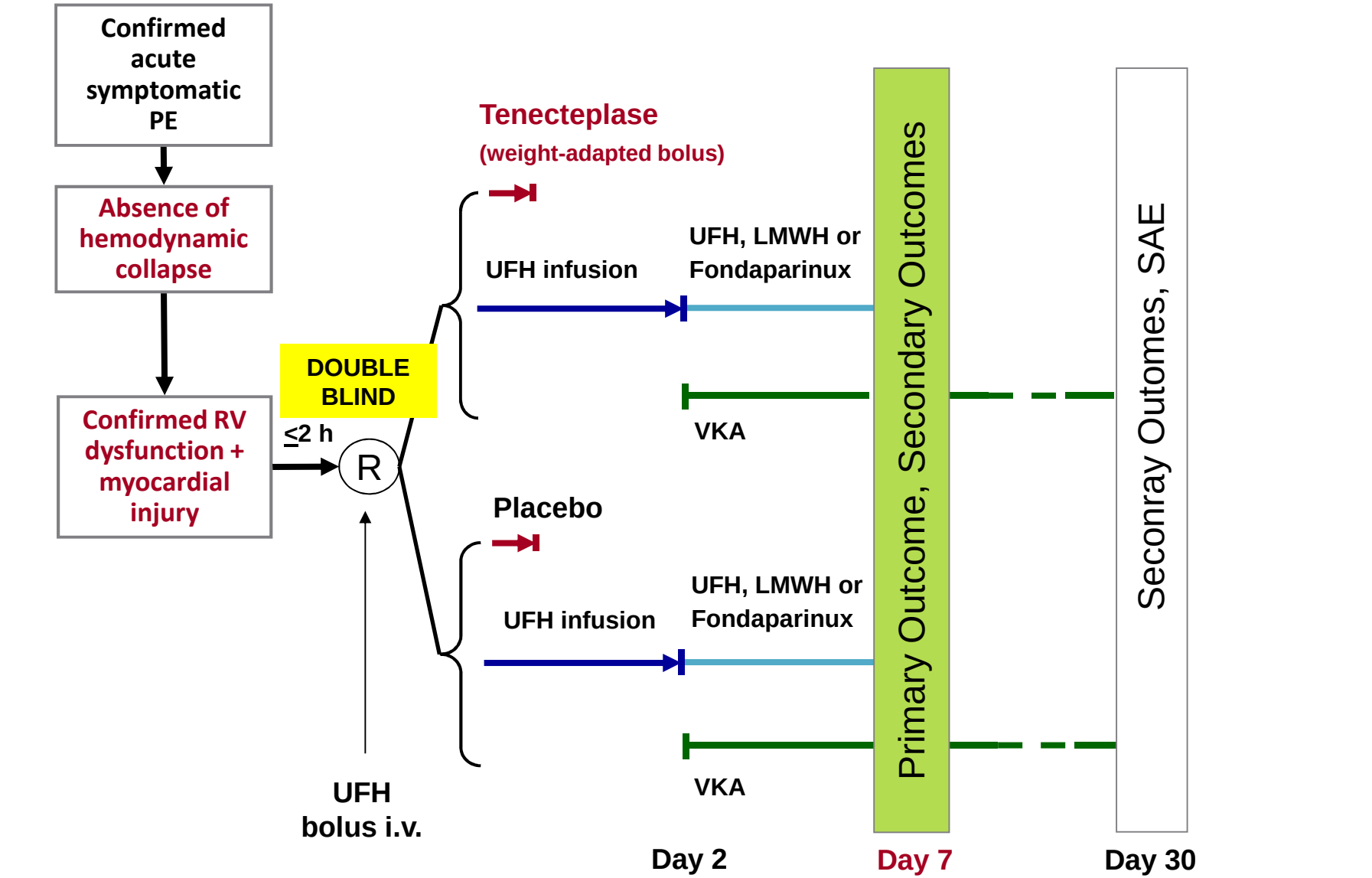
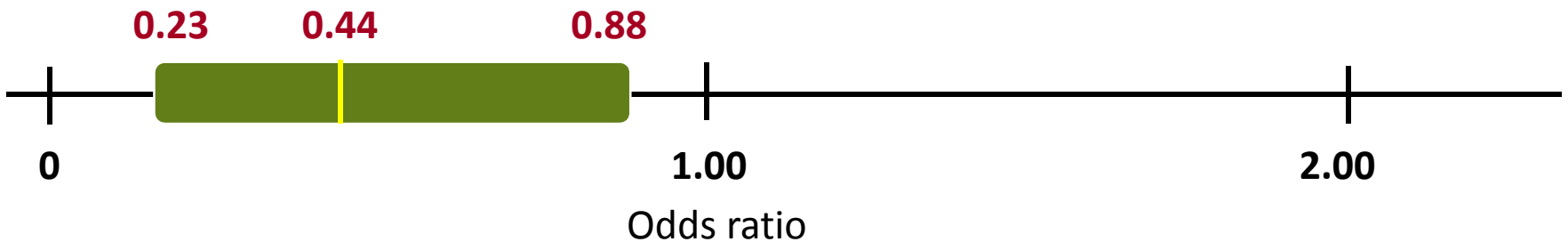
Fibrinolyse



Konstantinides for the PEITHO Steering Committee. Am Heart J 2012

PEITHO: Primary efficacy outcome

	Tenecteplase (n=506)		Placebo (n=499)		*P* value
	n	(%)	n	(%)	
All-cause mortality or hemodynamic collapse within 7 days of randomization	13	(2.6)	28	(5.6)	0.015



Thrombolysis superior

ITT population

Dia : Guy MEYER
The PEITHO Investigators

PEITHO: Safety outcomes (within 7 days of randomization)

	Tenecteplase (n=506)		Placebo (n=499)		*P* value
	n	(%)	n	(%)	
Non-intracranial bleeding					
Major	32	(6.3)	6	(1.5)	<0.001
Minor	165	(32.6)	43	(8.6)	<0.001
Strokes by day 7	**12**	**(2.4)**	**1**	**(0.2)**	**0.003**
Hemorrhagic	10		1		
Ischemic	2		0		

- Sous groupe > 75 ans : excès de risque hémorragique → bénéfice si < 75 ans ?

ITT population

Dia : Guy MEYER
The PEITHO Investigators

Filtres caves

Recommendations for venous filters

Recommendations	Class[a]	Level[b]	Ref[c]
IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation.	IIa	C	
IVC filters should be considered in case of recurrence of PE, despite therapeutic levels of anticoagulation.	IIa	C	
Routine use of IVC filters in patients with PE is not recommended.	III	A	341, 355

IVC = inferior *vena cava*; PE = pulmonary embolism.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.

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Filtres Caves temporaires

- Filtre Cave en cas de TVP : ↘ risque d'EP, ↗ celui de TVP

Décousus et al. New Eng J Med 1998
Laporte et al. Circulation 2005

- Filtre Cave temporaire : retirable en pratique courante

Mismetti et al. Chest 2008

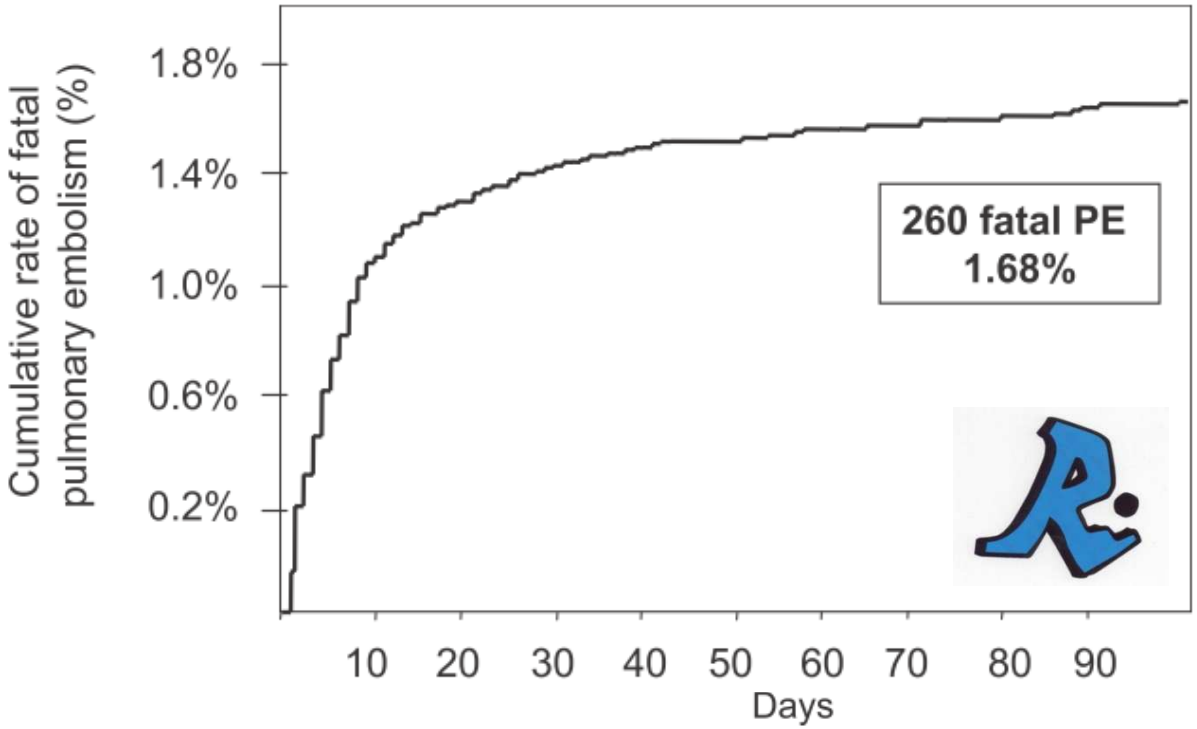


Figure. Cumulative rate of fatal PE.

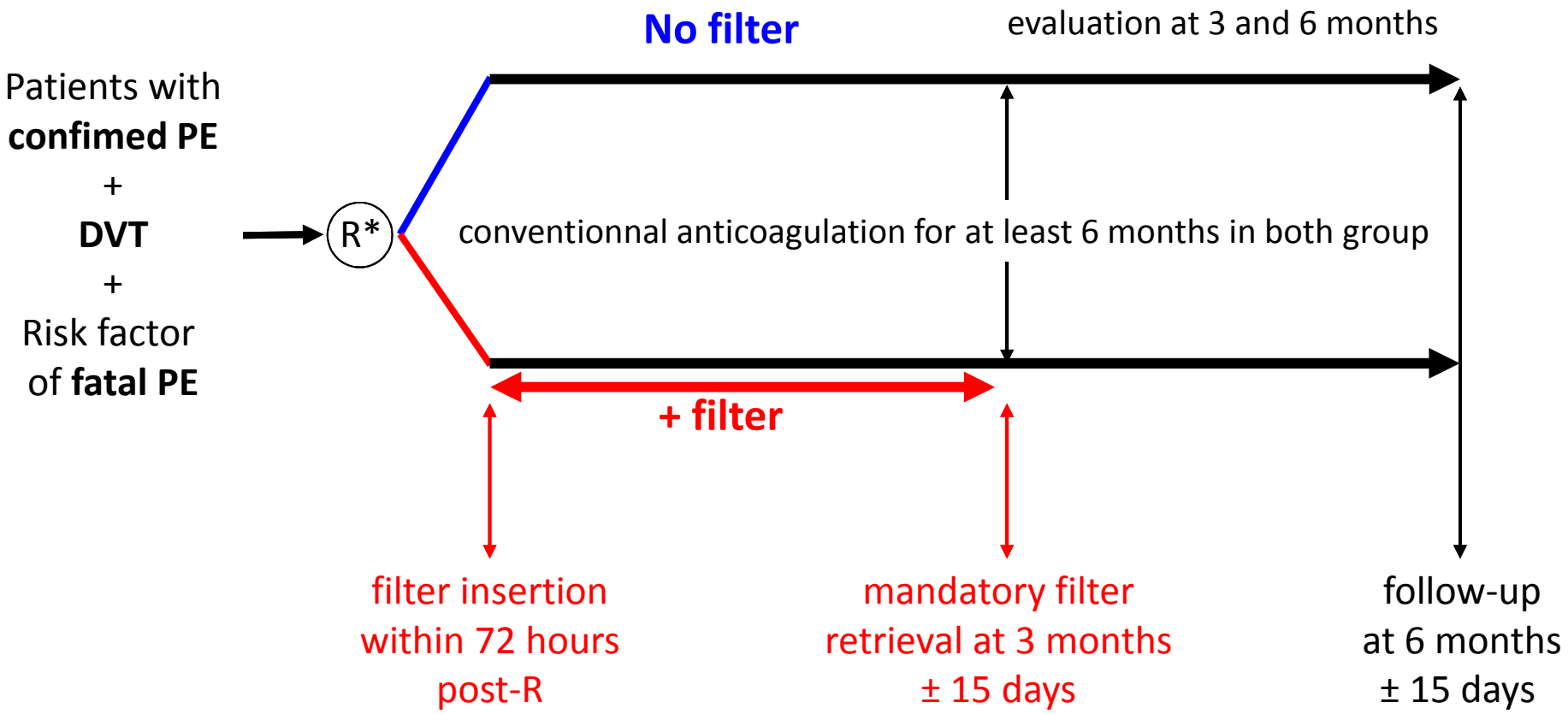
Laporte et al, for the RIETE registry, Circulation 2008

- 15 500 TVP et/ou EP
- Evolution ss ttt AVK

=> **FDR d'EP Fatale**

Filtres Caves temporaires

PREPIC-2
Plan expérimental



** centrally randomized, stratified by center and severe renal insufficiency (CrCl < 30 mL/mn)*

Mismetti for the PREPIC-2 study group, JAMA e-pub 28 Avril 2015

PREPIC-2
Population étudiée

- **399 patients** entre Août 2006 et Juillet 2012 (17 **centres Français**)

	Filter, n = 200	**No Filter,** n = 199
age (yrs)	74.2 ± 10.8	72.7 ± 12.4
Female (%)	51.0%	52.8%
BMI > 30 kg/m^2	27.7%	25.0%
CrCl < 50 ml/min	21.0%	19.6%
History of VTE	35.0%	35.7%
Active cancer	24.1%	26.1%
Chronic heart/resp insufficiency	24.0%	17.6%

Mismetti for the PREPIC-2 study group, JAMA e-pub 28 Avril 2015

Filtres Caves temporaires

PREPIC-2
Récidive d'EP

	Filter n = 193	No Filter n = 199	
PE: modified ITT*	4 (**2.1%**)	3 (**1.5%**)	**1.37** [0.31 ; 6.06] p=0.72
• Fatal PE	2.1%	1.0%	
• Non fatal PE	0.0%	0.5%	

- ITT modifiée: n=**193** pour le bras filtre :
  - 2 décès avant pose,
  - 3 sans EP,
  - 2 échecs de pose (compression extrinsèque, allergie à l'iode).

Mismetti for the PREPIC-2 study group, JAMA e-pub 28 Avril 2015

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Thérapeutique de l'EP

Take Home Message

1. **Modification de la thérapeutique = AOD**
   - Simplification de la prise en charge (sous réserve de bon usage)
   - Difficulté de savoir « ***quel médicament pour quel patient*** ? »
   - non utilisables si cancer (HBPM), insuffisance rénale, …
2. **Traitement ambulatoire de l'EP :**
   - **Avenir** possible pour une population sélectionnée (sPESI=0)
   - sous réserve d'un **parcours de soins** efficient
3. **Prise en charge EP intermédiaires reste à préciser : fibrinolyse ?**