Optimisation du Traitement de l'Embolie Pulmonaire

Journée d'Actualités Thérapeutiques ACCA Nice
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Liens d’intérêt

Research Support

- Bayer HealthCare, Bristol-Myers Squibb, Pfizer, Daiichi-Sankyo, Boerhinger

Consultant

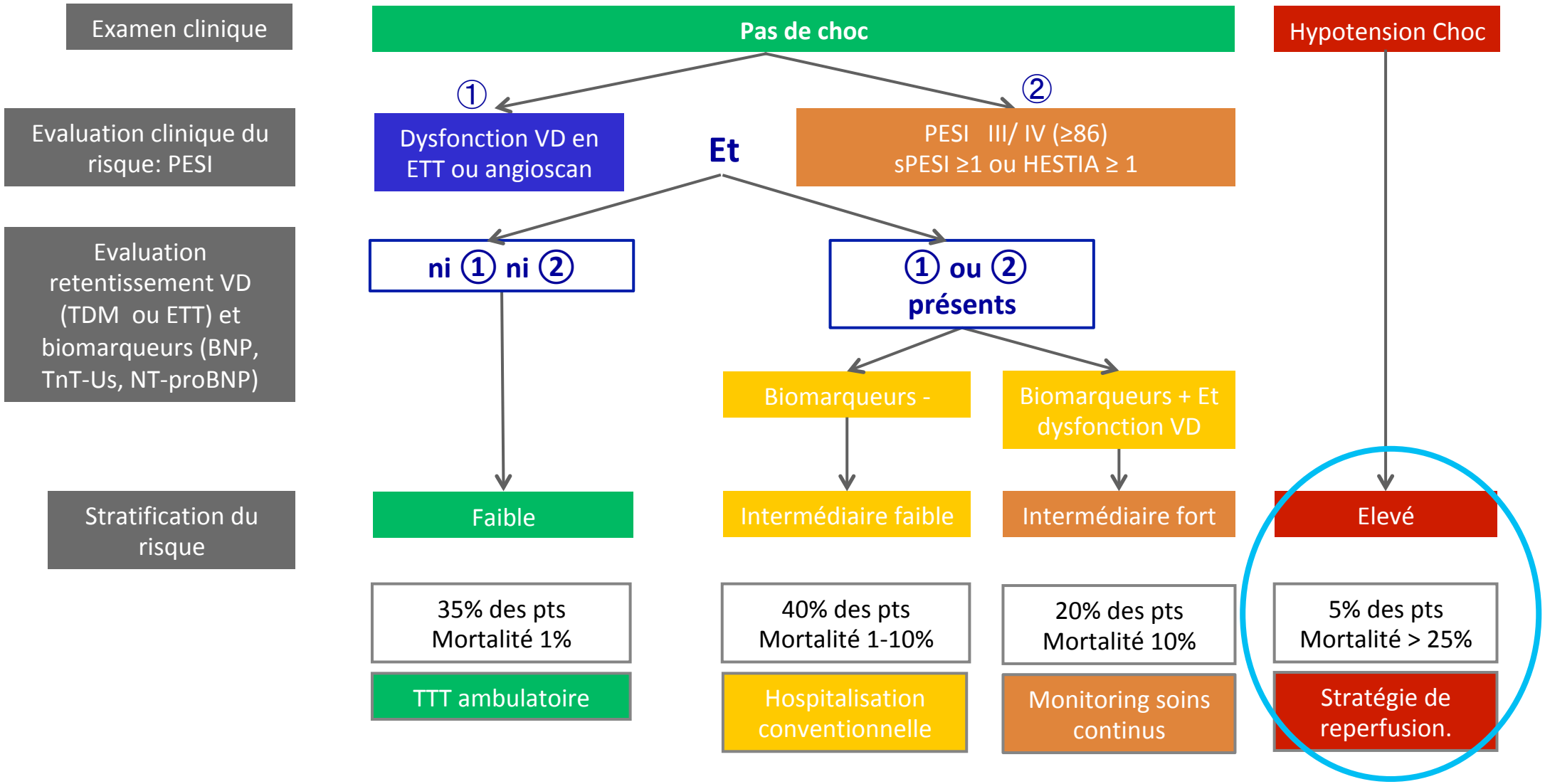
- Bayer HealthCare, Boerhinger, Bristol-Myers Squibb, Pfizer, St Jude medical, Edwards LIfesciences

Scientific Advisory Board

- Bristol-Myers Squibb

Le contenu et/ou les opinions exprimées lors de cette présentation, notamment celui ou celle(s) relatifs à la stratégie thérapeutique ont été réalisés en toute indépendance et sous ma responsabilité. La prescription des produits en France doit se faire dans le cadre de l’AMM et des RCP et être conforme à la stratégie thérapeutique émise par la Haute Autorité de Santé (Avis de la Commission de Transparence) .

Stratification du Risque – ESC 2019



Konstantinides SV et al, ESC Scientific Document Group.Eur Heart J.2019;00,1-61.ehz405. https://doi.org/10.1093/eurheartj/ehz405

Systemic thrombolytic therapy for acute high-risk PE

Efficacy outcomes, subgroup analyses

	All studies			Studies including[a] High-risk PE	Intermediate-risk PE	Low and intermediate-risk PE	Group difference
	OR (95% CI)	*P*-value	I^2 (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)	*P*-value
Mortality	0.59 (0.36 to 0.96)	0.034	0	0.48 (0.20 to 1.15)	0.42 (0.17 to 1.03)	0.96 (0.41 to 2.24)	0.36
PE mortality	0.29 (0.14 to 0.60)	<0.001	0	0.15 (0.03 to 0.78)	0.17 (0.05 to 0.67)	0.63 (0.20 to 1.97)	0.23
Death or treatment escalation	0.34 (0.22 to 0.52)	<0.001	0	0.18 (0.04 to 0.79)	0.37 (0.20 to 0.69)	0.35 (0.18 to 0.66)	0.67
PE recurrence	0.50 (0.27 to 0.94)	0.031	0	0.97 (0.31 to 2.98)	0.25 (0.06 to 1.03)	0.46 (0.17 to 1.21)	0.33

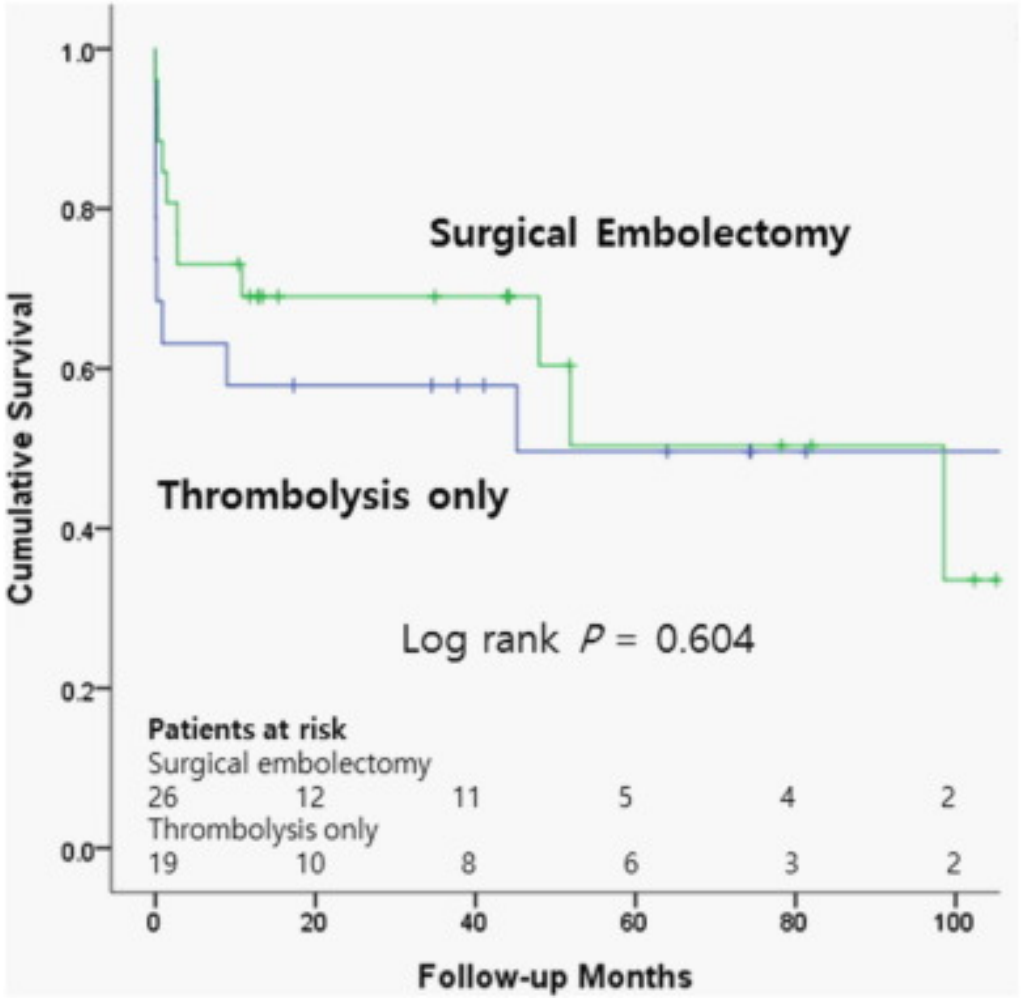
Safety outcomes, subgroup analyses

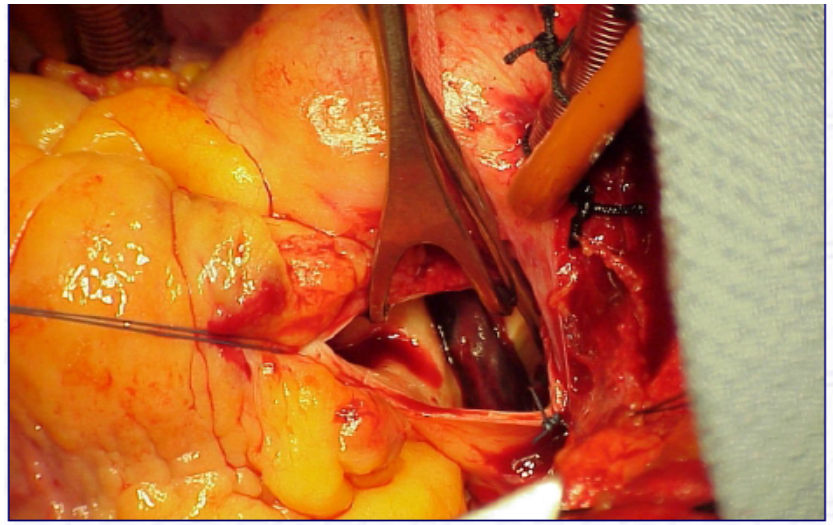
	All studies			Alteplase	Tenecteplase	Other thrombolytics	Group difference
	OR (95% CI)	*P*-value	I^2 (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)	*P*-value
Major bleeding	2.91 (1.95 to 4.36)	<0.001	25	1.07 (0.43 to 2.62)	5.02 (2.72 to 9.26)	2.16 (1.03 to 4.54)	0.02
Fatal/intracranial haemorrhage	3.18 (1.25 to 8.11)	0.008	0	1.09 (0.27 to 4.40)	7.32 (1.64 to 32.63)	NA	0.07

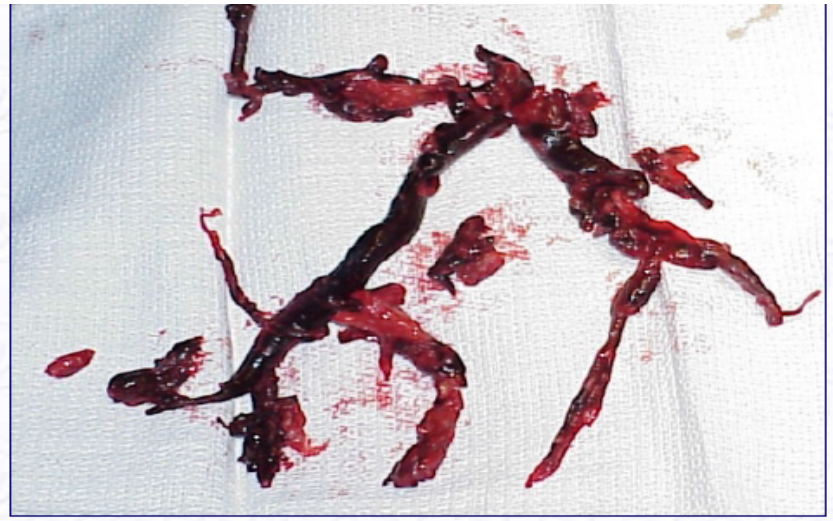
Marti C et al.Eur Heart J.2015;36,605–14

Embolectomie vs thrombolyse dans l'EP à haut risque

Kaplan-Meier survival curves for all-cause mortality







Cho YH et al.Int J Cardiol.2016;203:579-83

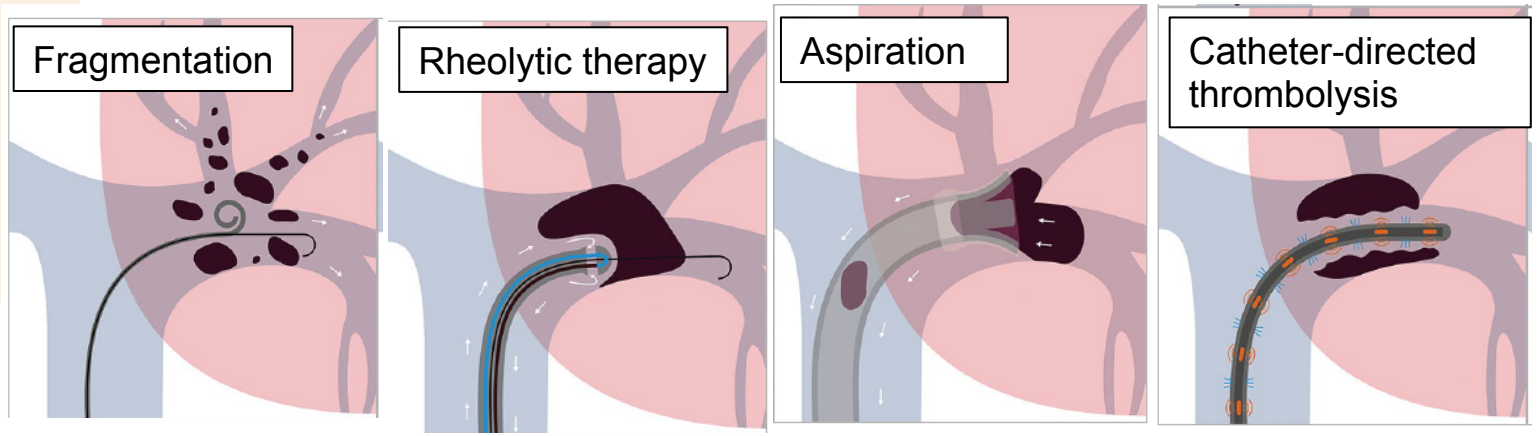
Advantages & potential limitations of catheter-based PE interventions

Advantages

- Rapid initiation of therapy
- Low doses of adjunctive thrombolytic therapy
- Efficacy on surrogate hemodynamic outcomes
- Shorter length of hospital stay
- Safety profile :
  - Low complications rates
  - Major bleeding rates < 6% (very few fatal & intracranial bleeding)

Potential Limitations

- Appropriate expertise & resources
- Expensive procedures
- Learning curve
- No long-term data with regard to recurrent PE, mortality, & CTEPH



Sobieszczyk P et al.Circulation.2012;126:1917-22; Engelberger RP et al.Eur Heart J.2014;35:758-64

Place de l'ECMO dans les EP à haut risque

Signal for lower mortality & more successful weaning when ECMO is combined with surgical embolectomy

Outcome	ECMO + thrombolysis (N=17)	ECMO + surgical thrombectomy (N=17)	ECMO alone (N= 18)	P
30-day all-cause death	13 (76.5%)	**5 (29.4%)**	14 (77.8%)	0.004
90-day all-cause death	13 (76.5%)	**7 (41.2%)**	14 (77.8%)	0.037
90-day major bleeding	7 (41.2%)	9 (52.9%)	4 (22.2%)	0.14
90-day non-major bleeding	9 (52.9%)	9 (52.9%)	5 (29.4%)	0.32
Successful weaning from ECMO	5 (29.4%)	**11 (64.7%)**	3 (17.7%)	0.009
Length of ICU stay	2 [1–9]	**17 [2–21]**	2.5 [2–10]	0.004

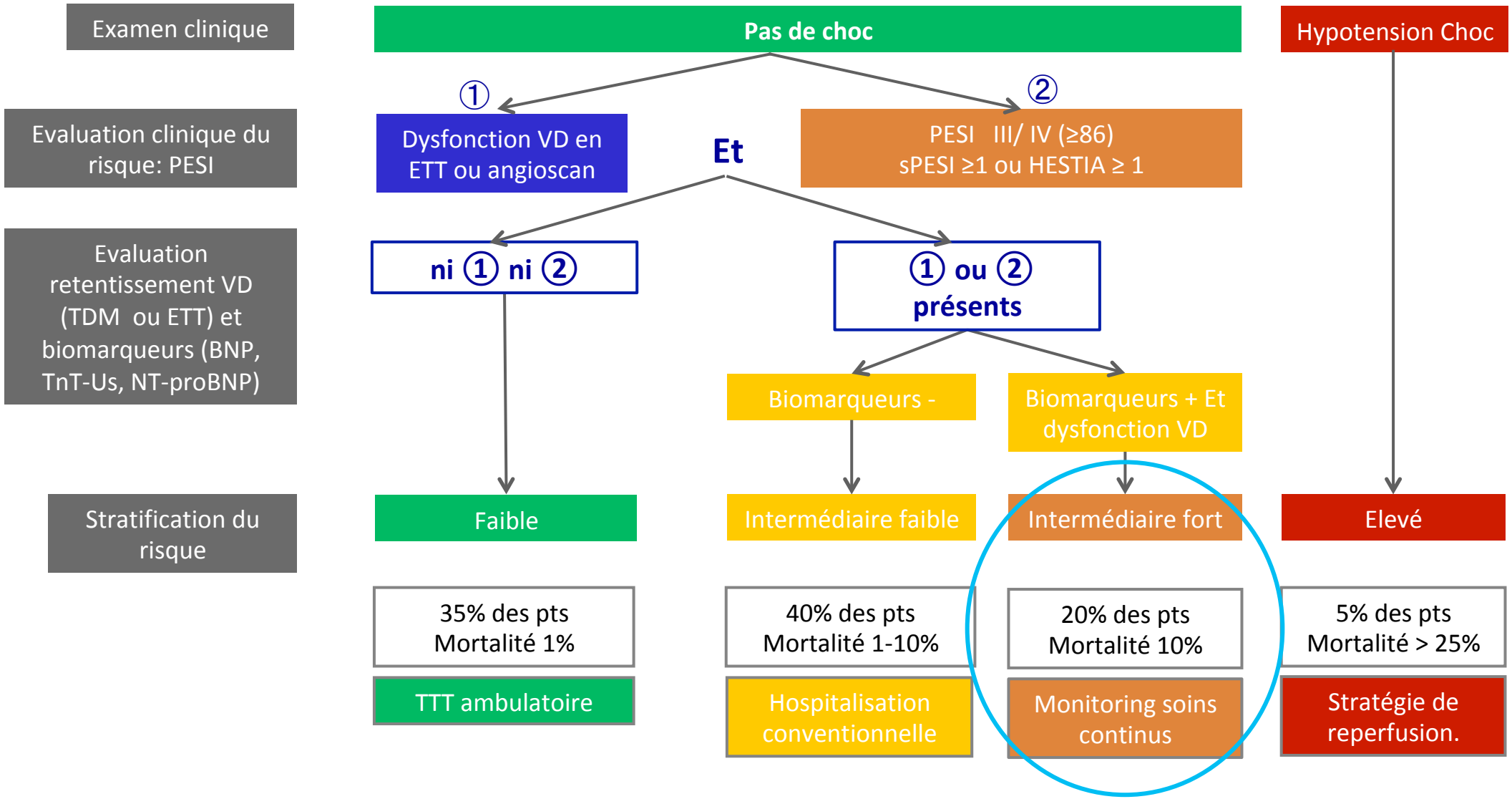
Meneveau N et al.Eur Heart J.2018; 0,1-9

Recommendations for acute-phase treatment of high-risk PE

Recommendations	Class	Level
Systemic thrombolytic therapy is recommended for high- risk PE.	I	B
Surgical pulmonary embolectomy is recommended for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	I	C
ECMO may be considered, in combination with surgical embolectomy or catheter-directed treatment, in patients with PE and refractory circulatory collapse or cardiac arrest.	IIb	C
Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	IIa	C

Konstantinides SV et al, ESC Scientific Document Group.Eur Heart J.2019;00,1-61.ehz405. https://doi.org/10.1093/eurheartj/ehz405

Stratification du Risque – ESC 2019



Konstantinides SV et al, ESC Scientific Document Group.Eur Heart J.2019;00,1-61.ehz405. https://doi.org/10.1093/eurheartj/ehz405

Full dose IV thrombolysis in intermediate-high risk PE

The beneficial effects do not balance the bleeding risk

	Tenecteplase (n=506)		Placebo (n=499)		P value
	n	(%)	n	(%)	
All-cause mortality within 7 days	6	(1.2)	9	(1.8)	0.43
Hemodynamic collapse within 7 days	8	(1.6)	25	(5.0)	0.002
Non-intracranial bleeding					
Major	32	(6.3)	6	(1.5)	<0.001
Minor	165	(33)	43	(8.6)	<0.001
Strokes by day 7	12	(2.4)	1	(0.2)	0.003
Hemorrhagic	10		1		
Ischemic	2		0		

Meyer G et al.N Engl J Med.2014;370:1402-11

Que disent les guidelines 2019 ?

Recommendations in intermediate high-risk PE	Class	Level
Rescue thrombolytic therapy is recommended for patients with haemodynamic deterioration on anticoagulation treatment.	I	B
As an alternative to rescue thrombolytic therapy, surgical embolectomy or percutaneous catheter- directed treatment should be considered for patients with haemodynamic deterioration on anticoagulation treatment.	IIa	C
Routine use of primary systemic thrombolysis is not recommended in patients with intermediate- or low-risk PE.	III	B

Konstantinides SV et al, ESC Scientific Document Group.Eur Heart J.2019;00,1-61.ehz405. https://doi.org/10.1093/eurheartj/ehz405

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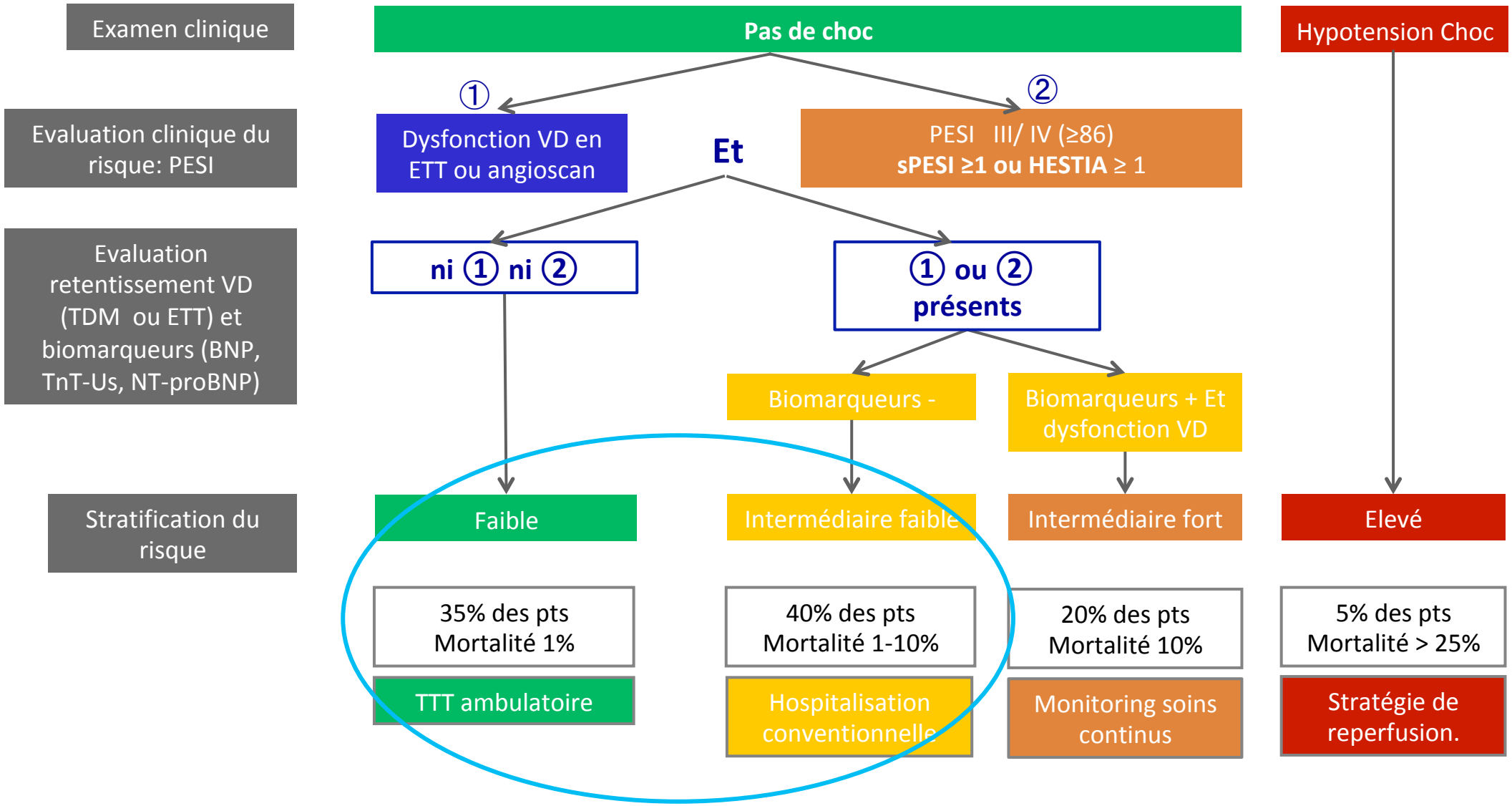


Konstantinides SV et al, ESC Scientific Document Group.Eur Heart J.2019;00,1-61.ehz405. https://doi.org/10.1093/eurheartj/ehz405

Recommendations for acute-phase treatment of intermediate- or low- risk PE

Recommendations	Class	Level
Oral anticoagulants		
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.	I	A
When patients are treated with a VKA, overlapping with parenteral anticoagulation is recommended until an INR of 2.5 (range 2.0–3.0) is reached.	I	A
NOACs are not recommended in patients with severe renal impairment, during pregnancy and lactation, and in patients with the antiphospholipid antibody syndrome.	III	C

Konstantinides SV et al, ESC Scientific Document Group.Eur Heart J.2019;00,1-61.ehz405. https://doi.org/10.1093/eurheartj/ehz405

Home treatment in PE patients: the Hot-PE study

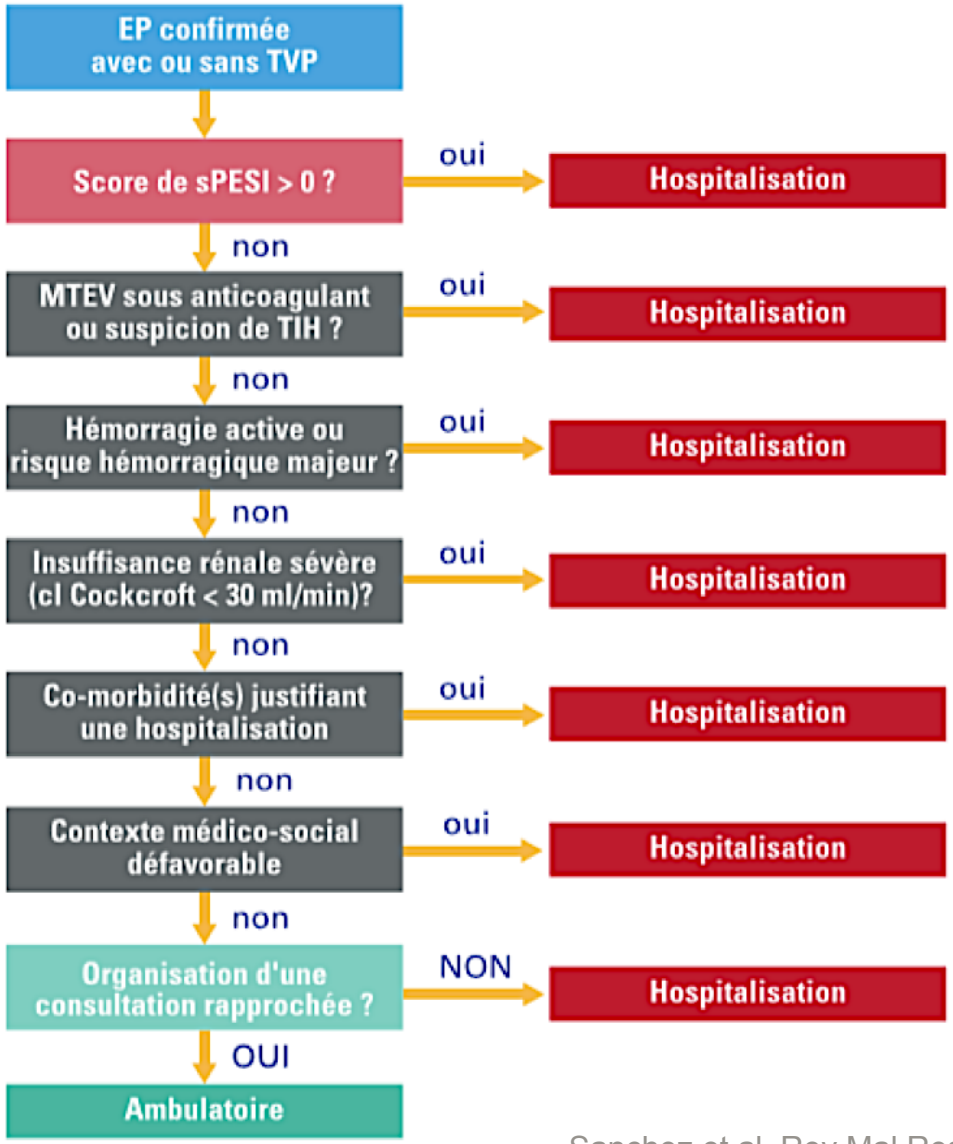
Outcomes	
Primary efficacy outcome: recurrent VTE or fatal PE, n/N (%; one-sided upper 99.6% CI)	3/525 (0.6; 0–2.1)
Recurrent PE, n/N (%; two-sided 95% CI)	3/525 (0.6; 0.1–1.7)
Recurrent deep vein thrombosis, n	0
Death related to PE, n	0
Safety outcomes, n/N (%; two-sided 95% CI)	
ISTH major bleeding	6/519 (1.2; 0.4–2.5)
Clinically relevant bleeding	31/519 (6.0; 4.1–8.4)
At least one serious adverse event	58/519 (11.2; 8.6–14.2)

Early discharge and home treatment with rivaroxaban is effective and safe in carefully selected patients with acute low-risk PE

Barco S et al.Eur Heart J.2019;ehz367: doi:10.1093/eurheartj/ehz367

Proposition d'algorithme pour une hospitalisation ou prise en charge ambulatoire d'une EP

Recos SPLF 2019



- R116 - Chez les pts ayant une EP objectivement confirmée, il est recommandé d'évaluer, aux urgences et/ou après une hospitalisation très courte (< 48 heures), la possibilité d'une prise en charge ambulatoire (Grade 1+).
- R117 - Il est suggéré d'utiliser soit la règle HESTIA (= 0), soit le score PESI (≤ 85), soit le score PESI simplifié (= 0), associé aux critères pragmatiques pour sélectionner les pts éligibles au traitement ambulatoire (Grade 2+).
- R118 - En cas d'EP non grave, si une prise en charge ambulatoire est envisagée, il est recommandé d'évaluer le risque hémorragique incluant la fonction rénale, le contexte médical et social, les souhaits et les possibilités de suivi du pt (Grade 1+).
- R119 - Il est recommandé, aux centres souhaitant traiter en ambulatoire des pts ayant une EP non grave, de mettre en place une filière spécifique à la prise en charge de ces pts (Grade 1+).
- R120 - Il est suggéré de réaliser une consultation spécialisée précoce, pendant le passage initial ou dans les tous premiers jours suivant la sortie, afin de valider le diagnostic et le traitement initial, d'informer les personnes impliquées et d'organiser le suivi ultérieur en lien avec le médecin référent (Grade 2+).

Sanchez et al. Rev Mal Respir. 2019 Feb;36(2):249-283.

Supporting evidence from RDZ trials using NOACs for treatment of cancer-associated VTE

HOKUSAÏ-VTE-Cancer,[1] n (%)	Edoxaban (n = 522)	Dalteparin (n = 524)	HR (95% CI)
Recurrent VTE or major bleeding	67 (12.8)	71 (13.5)	0.97 (0.70–1.36)
Recurrent VTE	41 (7.9)	59 (11.3)	0.71 (0.48–1.06)
Major bleeding	36 (6.9)	21 (4.0)	1.77 (1.03–3.04)

SELECT-D,[2] n (%)	Rivaroxaban (n = 208)	Dalteparin (n = 203)	HR (95% CI)
Recurrent VTE	8 (4*)	18 (11*)	0.43 (0.19–0.99)
Major bleeding	11 (6*)	6 (4*)	1.83 (0.68–4.96)
Clinically relevant non major bleeding	8 (4)	26 (13)	3.76 (1.63- 8.69)

CARAVAGGIO,[3] n (%)	Apixaban (n = 576)	Dalteparin (n = 579)	HR (95% CI)
Recurrent VTE	32 (5.6)	46 (7.9)	0.63 (0.37–1.07)
Major bleeding	22 (3.8)	24 (3.0)	0.82 (0.40–1.69)
Major gastrointestinal bleeding	11 (1.9)	10 (1.7)	1.05 (0.44- 2.50)

1. Raskob GE et al.N Engl J Med.2018;378:615-24; 2. Young A et al.J Clin Oncol.2018;10:2017-23. 3. Agnelli G et al. N Engl J Med; 2020; 382:1599-607.

*Cumulative incidence

Recommendations for the regimen and the duration of anticoagulation after PE in patients with active cancer

Recommendations	Class	Level
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs.	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.	IIa	B
Rivaroxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.	IIa	C
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months) should be considered for an indefinite period or until the cancer is cured.	IIa	B

Konstantinides SV et al,ESC Scientific Document Group.Eur Heart J.2019;00,1-61.ehz405. https://doi.org/10.1093/eurheartj/ehz405

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