

MANAGEMENT STRATEGIES OF PATIENTS WITH PE & HIGH BLEEDING RISK

ATEF ELBAHRY, FRCPE(UK), FACA(USA), FICA(USA), FISCPC(CH)

SENIOR CONSULTANT OF CARDIOVASCULAR MEDICINE

VICE PRESIDENT OF THE EGYPTIAN ASSOCIATION OF VASCULAR BIOLOGY & ATHEROSCLEROSIS

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THE PATIENT WITH HIGH BLEEDING RISK

Risk of Bleeding

- Empiric anticoagulation therapy should be considered on a case-by-case basis for patient with moderate or high risk for bleeding.
- 1 risk factor (moderate): 3.2 percent risk of bleeding in the first three months and 1.6 percent per year thereafter
- 2 risk factors (high): 12.8 percent in the first three months and ≥ 6.5 percent per year thereafter

Risk Factors for bleeding	
	Age >65
	Previous bleeding
	Thrombocytopenia
	Antiplatelet therapy
	Recent surgery
	Frequent falls
	Previous stroke
	Diabetes
	Anemia
	Cancer
	Renal failure
	Liver failure
	Alcohol abuse

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RIETE REGISTRY BLEEDING SCORE

- To help guide the estimation of bleeding risk under oral anticoagulant treatment, clinical scores have been developed and validated. The RIETE registry score is one such score that was constructed in a population of almost 20,000 consecutive patients with acute VTE to predict the risk for major bleeding within 3 months of anticoagulant therapy

RIETE Registry Bleeding Score

Risk Factors	Score (Points)
Recent major bleeding	2
Creatinine level > 1.2 mg/dL (110 µmol/L)	1.5
Anemia:	
Men: Hb < 13 g/dL	1.5
Women: < 12 g/dL	
Cancer	1
Clinically overt PE	1
Age > 75 years	1

Thrombosis

Adapted from: Palla G, et al. Thromb Haemostas. 2008;108:28-33

Heart Lung Mindscope CME

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DO NOT USE HAS BLED SCORE IN PE

HAS-BLED Score and Other Predictors of Bleeding in Catheter-Directed Thrombolysis for Pulmonary Embolism

Kara Denby MD and Steven Alexander MD
Vanderbilt University Medical Center

tct2017

Conclusions

- The HAS-BLED score is not predictive of bleeding in CDT
- Traditional bleeding risk factors are not predictive of bleeding outcomes in CDT
- Higher tissue plasminogen activator bolus doses and lack of ultrasound may be associated with higher bleeding risk
- Additional research is needed to further delineate the optimal target population for CDT

tct2017

Bleeding Risk Factors

Bleeding Risk Factors	No Bleeding (n=68)	Bleeding (n=25)	P-value
Hypertension, n (%)	41 (60.3%)	16 (64%)	0.75
Renal disease, n (%)	6 (8.8%)	2 (8%)	0.90
Liver disease, n (%)	5 (7.4%)	1 (5%)	0.56
Stroke, n (%)	6 (8.8%)	3 (12%)	0.65
Cancer history, n (%)	19 (27.9%)	6 (24%)	0.70
Heart failure, n (%)	7 (10.3%)	2 (8%)	0.74
Procedure Details	No Bleeding (n=68)	Bleeding (n=25)	P-value
HAS-BLED Score, mean +/- SD	1.71 +/- 1.08	1.72 +/- 1.1	0.92

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ISTH BLEEDING DEFINITIONS

Factor X_a

ISTH* Bleeding Definitions

■ Major Bleeding – Bleeding...

- with a fall in hemoglobin of ≥ 2 g/dL, or
- with transfusion of ≥ 2 units of PRBC or whole blood, or
- that occurs in a critical location, i.e., intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or
- that causes death

■ Clinically Relevant Non-Major Bleeding – Bleeding...

- that does not meet criteria for major bleeding, and
- that requires any medical or surgical intervention to treat the bleeding

*ISTH – International Society of Thrombosis and Haemostasis

CLINICAL CLASSIFICATIONS OF PE

Low Risk PE

- Normotensive
- No RV dysfunction
- Normal biomarkers

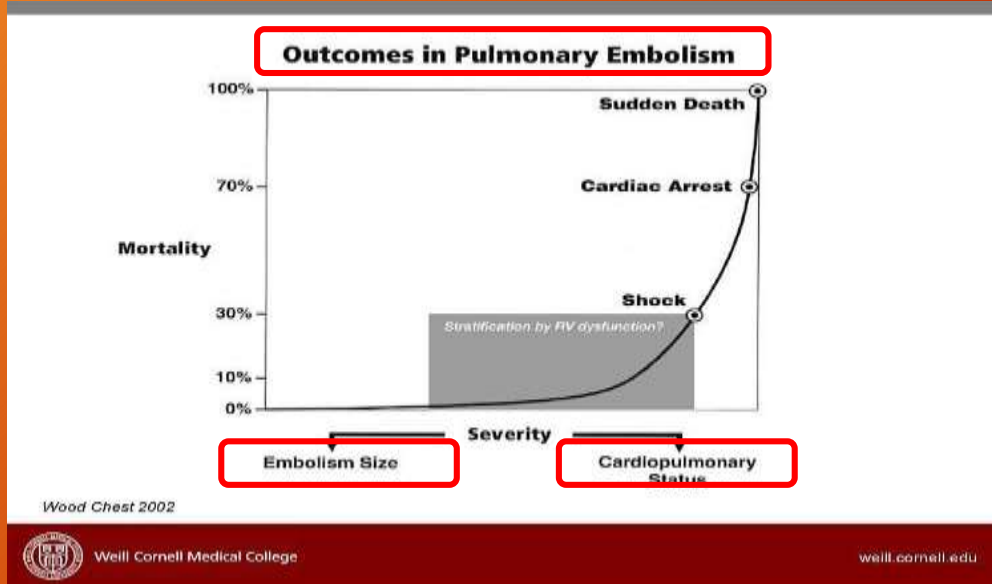
Intermediate Risk PE (Submassive)

- Normotensive
- **RV dysfunction/ RV dilation**
 - BNP > 90 pg/mL
 - pro-BNP > 500 pg/mL
- **Myocardial necrosis**
 - Trop I > 0.4 ng/mL
 - Trop T > 0.1 ng/mL

High Risk PE (Massive)

- **Hypotension** (SBP < 90 for > 15 min) or **Shock**
- **Pulselessness**
- **Profound bradycardia** (HR < 40)

Zambrano. Europ Heart J 2014
Jan, Dec 2011



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Pulmonary Embolism

Scope of the Problem



PE is the third most common cause of CV death in the US after MI and stroke



The incidence of PE is increasing, whereas the incidence of stroke has stabilized and the incidence of MI is falling



Treatment options:
anticoagulation or interventional approaches

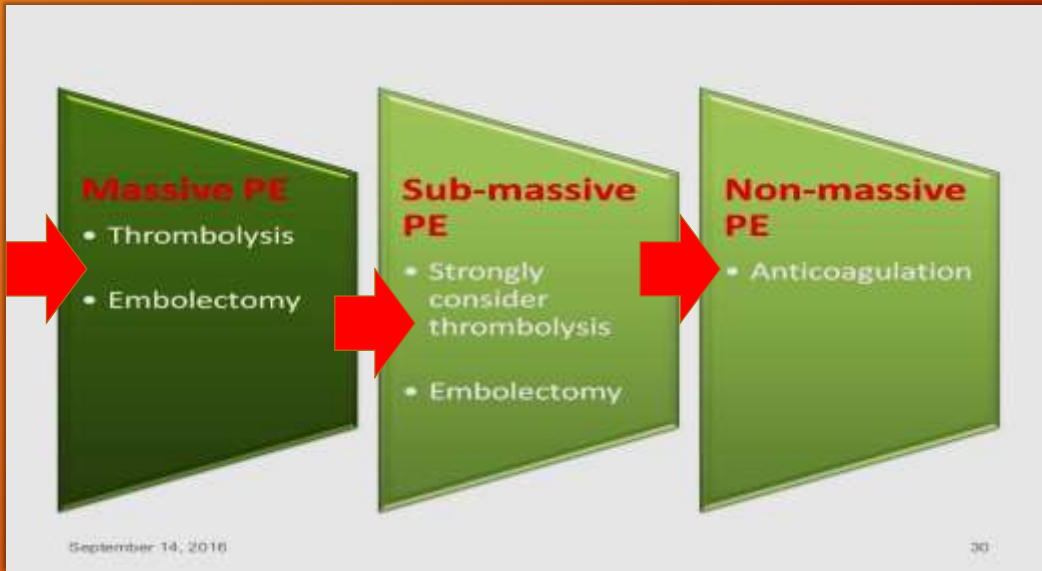


The Surgeon General estimates that there are at least 100,000 to 180,000 deaths per year resulting from PE in the United States alone



US Department of Health and Human Services. The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism.

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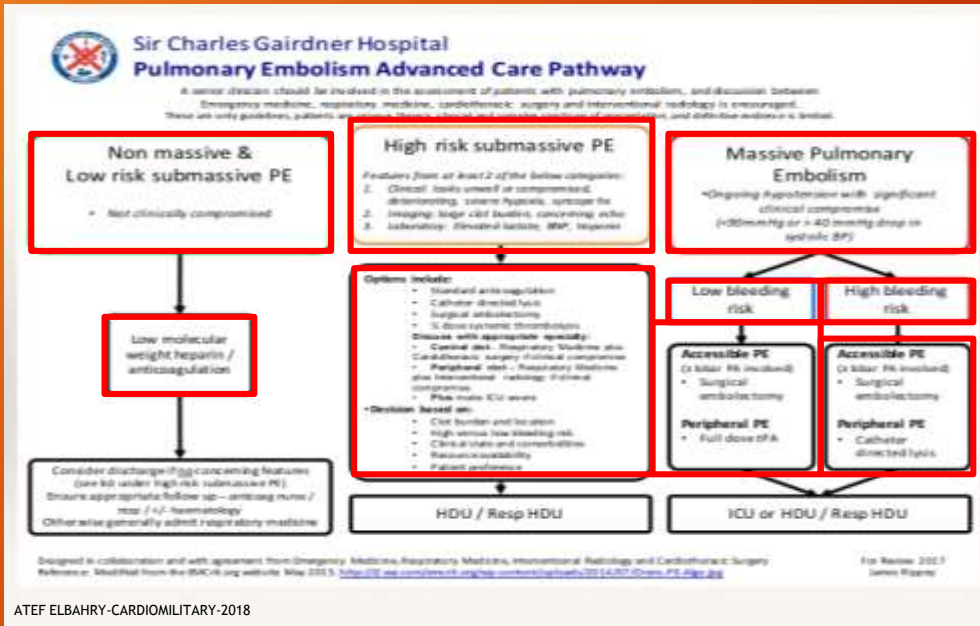
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OREN ALGORITHM FOR MANAGEMENT STRATEGIES IN PE IN HIGH RISK BLEEDING PATIENTS



*Looks Clinically Unstable, Poor Clinical Course, Worrisome Echo, Severe hypoxia, Syncope, Elevated lactate, BNP/ Trop elevation, Large residual thrombus ATEF ELBAHRY-CARDIOMILITARY-2018

Scott Weingart. Podcast 128 - Pulmonary Embolism Treatment Options and the PEAC Team with Oren Friedman. *EMCrit Blog*. Published on July 14, 2014. Accessed on December 29th 2017



Thrombolysis

• Pros:

- Less long-term pulmonary hypertension (MOPETT trial)
- Clots resolve faster
- Patients appear to improve faster clinically
- Decreased death or haemodynamic instability (PEITHO trial)

• Cons:

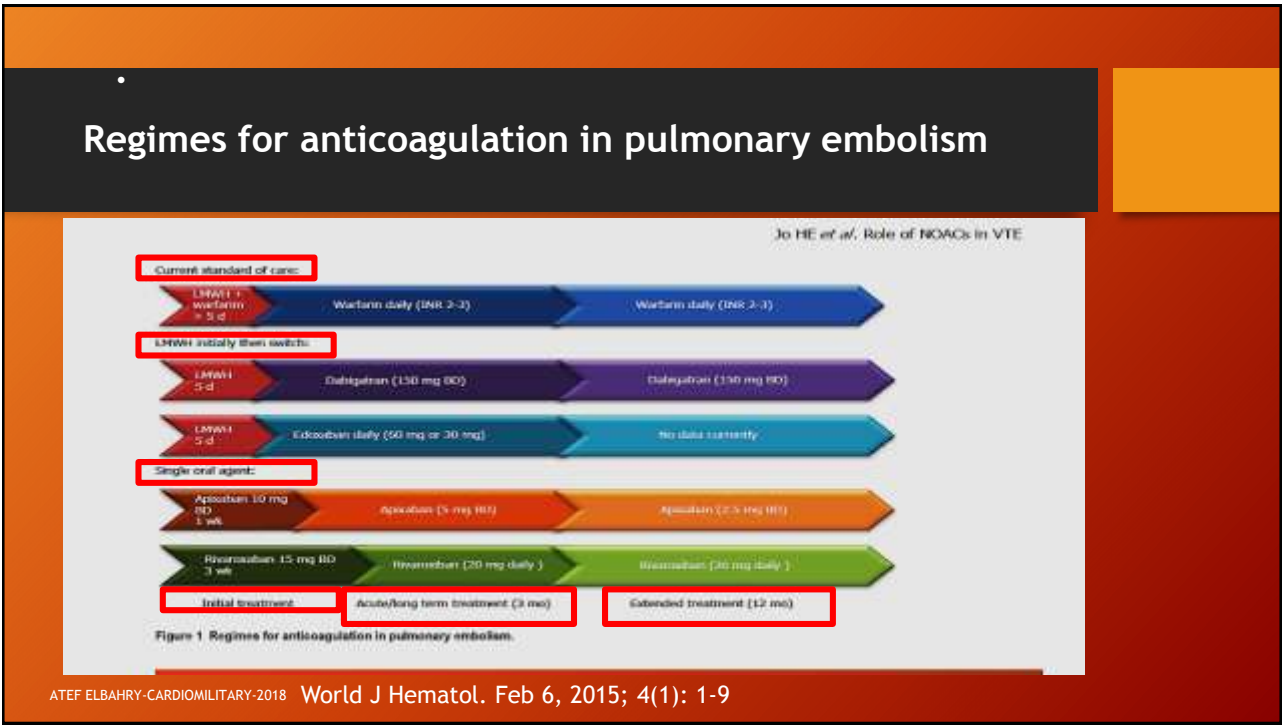
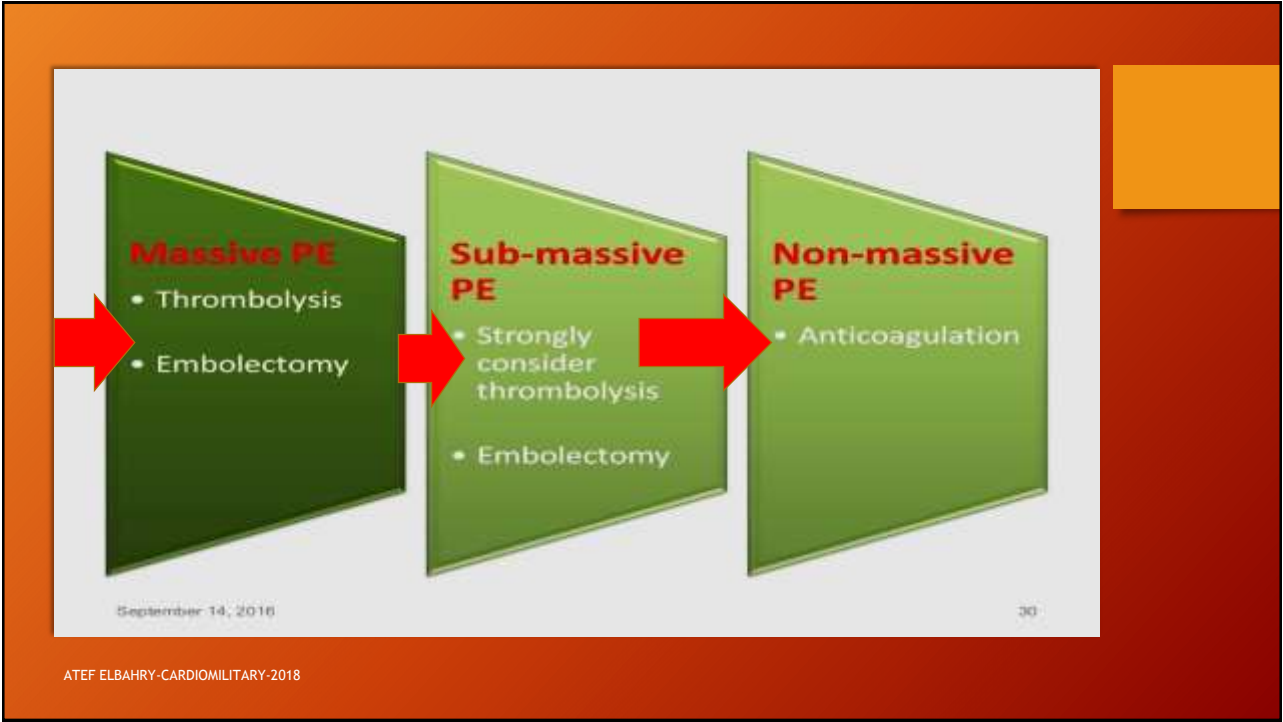
- Risk of ICH (2% in >75yo in PEITHO)
- Risk of other haemorrhage (~6% in PEITHO)
- similar improvement at 7 days overall (~6% reduction in size of total defect regardless of whether thrombolysed or ant coagulated)



Intra-Arterial Thrombolysis

- Potential for same benefits as systemic thrombolysis with lower bleeding risk
- Wire passed through embolus followed by an infusion catheter with multiple openings - thrombolytic is then infused to the clot
- Evidence is lacking - SEATTLE-II trial 2015





2014 ESC Guidelines Treatment of Acute PE

• Class I; Level B

- In parallel to parenteral anticoagulation, treatment with a VKA is recommended; targeting an INR of 2.0 to 3.0
- Replace combination of parenteral anticoagulation and VKA with anticoagulation with
 - Rivaroxaban (15 mg twice daily for 3 wk, followed by 20 mg daily)
 - OR apixaban (10 mg twice daily for 7 d, followed by 5 mg twice daily)
- Following acute-phase parenteral anticoagulation, replace VKA treatment with
 - Dabigatran (150 mg twice daily, or 110 mg twice daily for patients aged > 80 years)
 - OR edoxaban (60 mg once daily or 30 mg once daily if creatinine clearance 30 to 50 mL/min or body weight < 60 kg)

Konstantinides SV, et al. *Eur Heart J*. 2014;35:3033-3069, 3069a-3069k.

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NOACs: VTE Acute Treatment Trials

Trial and Drug	Recurrent VTE	NOAC vs Conventional Therapy Major Bleeding or CRNM Bleeding	Major Bleeding
Hokusai-VTE ^(a) Edoxaban	3.2% vs 3.5% HR, 0.89 (CI, 0.70-1.13) P < .001 (noninferiority)	8.5% vs 10.3% HR, 0.81 (CI, 0.71-0.94) P = .004	1.4% vs 1.6% HR, 0.84 (CI, 0.59-1.21) P = .35
AMPLIFY ^(b) Apixaban	2.3% vs 2.7% RR, 0.84 (CI, 0.60-1.18) P < .001 (noninferiority)	4.3% vs 9.7% RR, 0.44 (CI, 0.36-0.55) P < .001	0.6% vs 1.8% RR, 0.31 (CI, 0.17-0.55) P < .001
EINSTEIN-DVT ^(c) Rivaroxaban	2.1% vs 3.0% HR, 0.68 (CI, 0.44-1.04) P < .001 (noninferiority)	8.1% vs 8.1% HR, 0.97 (CI, 0.76-1.22) P = .77	0.8% vs 1.2% HR, 0.65 (CI, 0.33-1.30) P = .21
EINSTEIN-PE ^(d) Rivaroxaban	2.1% vs 1.8% HR, 1.12 (CI, 0.75-1.68) P = .003 (noninferiority)	10.3% vs 11.4% HR, 0.90 (CI, 0.76-1.07) P = .23	1.1% vs 2.2% HR, 0.49 (CI, 0.31-0.79) P = .003
RE-COVER II ^(e) Dabigatran	2.4% vs 2.1% HR, 1.10 (CI, 0.65-1.84) P < .001 (noninferiority)	5.6% vs 8.8% HR, 0.63 (CI, 0.47-0.84) P = .002	1.6% vs 1.9% HR, 0.82 (CI, 0.45-1.48) P = .38
RE-COVER II ^(f) Dabigatran	2.3% vs 2.2% HR, 1.08 (CI, 0.64-1.80) P < .001 (noninferiority)	5.0% vs 7.9% HR, 0.62 (CI, 0.45-0.84)	1.2% vs 1.7% HR, 0.69 (CI, 0.36-1.32)

a. Hokusai-VTE Investigators, et al. *N Engl J Med*. 2013;369:1406-1415; b. Agnelli G, et al. *N Engl J Med*. 2013;369:799-808; c. EINSTEIN Investigators, et al. *N Engl J Med*. 2010;363:2499-2510; d. EINSTEIN Investigators, et al. *N Engl J Med*. 2012;366:1287-1297; e. Schulman S, et al. *N Engl J Med*. 2009;361:2342-2352; f. Schulman S, et al. *Circulation*. 2014;129:764-772.

Clinically relevant non-major (CRNM) bleeding was defined as overt bleeding not meeting criteria for major bleeding but requiring medical intervention, hospitalization, temporary interruption or delayed dosing of anticoagulation, pain, or impairment of daily activities.

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TAKE HOME MESSAGE

1. ESTIMATION OF BLEEDING RISK IN PE IS MANDATORY IN MASSIVE & SUBMASSIVE CASES USING THROMBOLYSIS
2. HIGH BLEEDING RISK RIETE SCORE IS BETTER THAN HAS BLED SCORE IN PE PATIENTS
3. USING NOACs CAN REDUCE BLEEDING RISK COMPARING IT VKA OR UFMH

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THANKS FOR YOUR KIND ATTENTION

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