

# Acute Pulmonary Embolism

Risk Stratification and Acute Management

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# Case #1

- 55 year old obese male presents to ER with shortness of breath
- CT shows right and left main PA thrombus
- HR 120, SBP 100, 4L/min O2 requirement
- Echo shows RV dilation with moderate dysfunction
- Troponin 2000, pro-BNP 3000



## Case #2

- 28 year old obese female active smoker on oral contraceptives presents to ER with chest pain and shortness of breath.
- HR 140, SBP 80, RR 30, 10 L/min O2 requirement
- CT showing saddle PE, severe RV dilation, contrast reflux into the hepatic vein
- Systemic thrombolysis with TNK and 1 hour later the patient is still requiring 30 mcg/min of norepinephrine

## Case #3

- 85 year old female 8 days post total hip replacement, presenting with shortness of breath
- HR 110, SBP 90, 4L/min O2 requirement
- Multiple segmental and subsegmental filling defects on CT
- RV/LV > 1
- Troponin and pro-BNP mildly elevated



# Pulmonary Embolism

Patient risk stratification (per AHA 2011 guidelines)		
Massive PE	Submassive PE	Minor/Nonmassive PE
High risk	Moderate risk	Low risk
<ul style="list-style-type: none"> <li>• Sustained hypotension (systolic BP &lt;90 mmHg for ≥15 min)</li> <li>• Inotropic support</li> <li>• Pulselessness</li> <li>• Persistent profound bradycardia (HR &lt;40 bpm with</li> </ul>	<ul style="list-style-type: none"> <li>• Systemically normotensive (systolic BP ≥90 mmHg)</li> <li>• <b>RV dysfunction</b></li> <li>• Myocardial necrosis</li> </ul>	<ul style="list-style-type: none"> <li>• Systemically normotensive (systolic BP ≥90 mmHg)</li> <li>• No RV dysfunction</li> <li>• No myocardial necrosis</li> </ul>

30-50% mortality

## RV dysfunction

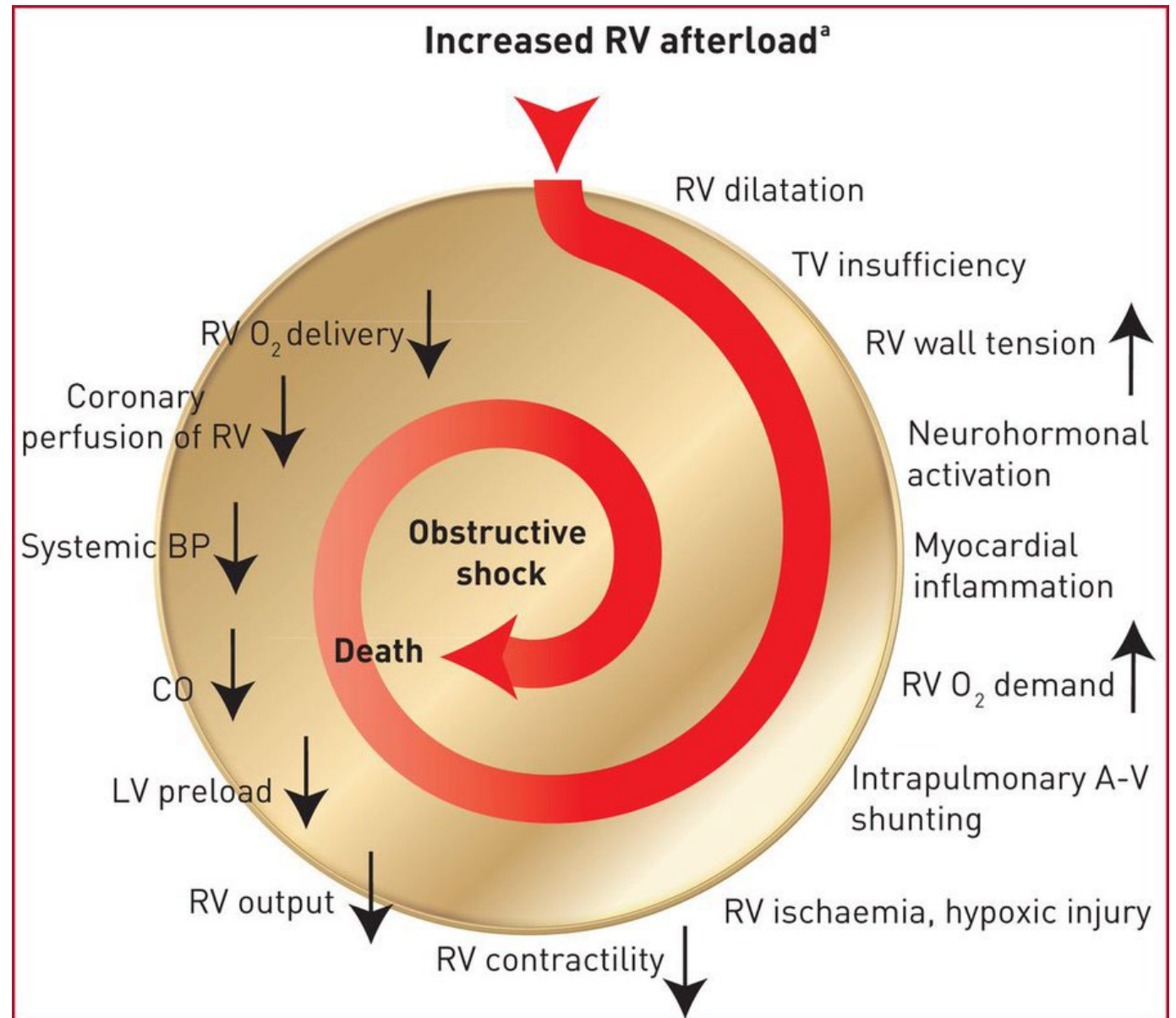
- RV/LV ratio > 0.9 or RV systolic dysfunction on echo
- RV/LV ratio > 0.9 on CT
- Elevation of BNP (>90 pg/mL)
- Elevation of NTpro-BNP (>500 pg/mL)
- ECG changes
  - new complete or incomplete RBBB
  - antero-septal ST elevation or depression
  - antero-septal T-wave inversion

3-15% mortality

1% mortality

# Pathophysiology

- Acute mortality is related to acute RV failure, shock, and/or cardiovascular collapse





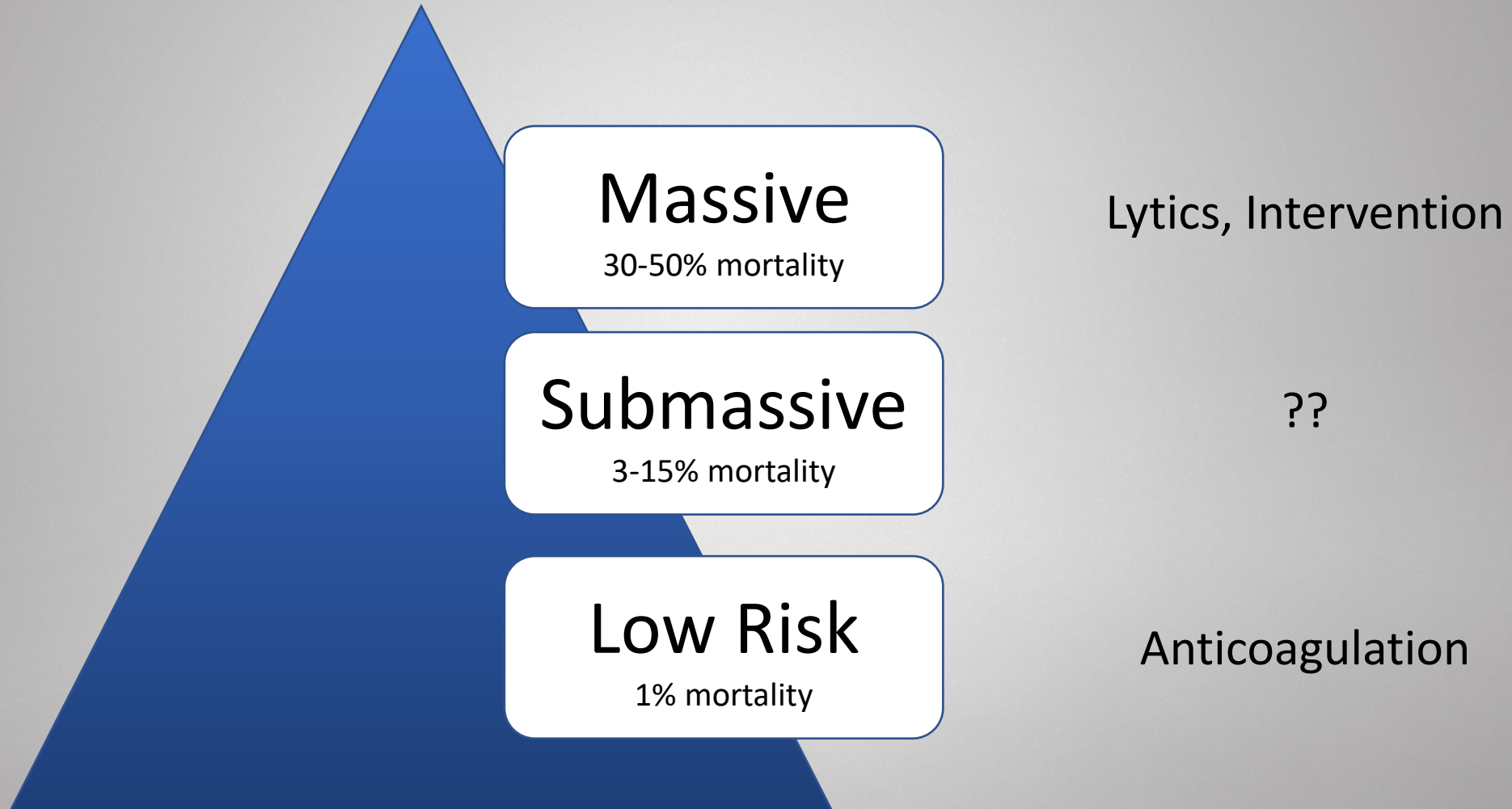
*Massive/Submassive PE is a  
disease of acute right heart failure*

# Acute Treatment Options

- Anticoagulation alone
- Systemic thrombolysis
- Catheter based thrombolysis
- Surgical/catheter based embolectomy



# Where is the clinical uncertainty?



# The Data

- **TIPES** *J. Thromb Res* March 1, 2010, doi: 10.1016/j.thrombres.2009.09.017
  - Submassive PE, bolus TNK vs placebo, endpoint reduction in RV/LV ratio. Study not powered to evaluate bleeding risk.
- **TOPCOAT** *J Thromb Haemost*, Jan 31 2014, doi: 10.1111/jth.1252
  - Submassive PE, bolus TNK + anticoag vs anticoag alone, endpoint death, recurrent PE, or poor functional outcome.
  - 51% improvement in TNK group, bleeding risk not evaluated.
- **PEITHO** *N Engl J Med* 2014, doi: 10.1056/NEJMoa1302097
  - Submassive PE, TNK + anticoag vs anticoag alone, endpoint death or hemodynamic collapse.
  - 56% reduction in TNK group, but with 10-fold increased rate of ICH (2% vs 0.2%)
- **ULTIMA** *Circulation* 2014, doi: 10.1161/CIRCULATIONAHA.113.005544
  - Submassive PE, Ultrasound assisted catheter directed thrombolytics (USAT) + anticoagulation vs. anticoagulation alone, primary endpoint reduction in RV/LV ratio.
  - Small study, no major bleeds in either group, no difference in minor bleeds



# The Data

- **SEATTLE II** JACC 2015, doi: 10.1016/j.jcin.2015.04.020
  - Submassive PE, USAT + anticoagulation vs. anticoagulation alone, endpoints reduction in RV/LV ratio and mean PA pressures.
  - Increase in bleeding complications, no ICH
- **FLARE** JACC 2019, doi: 10.1016/j.jcin.2018.12.022
  - Submassive PE, single arm study with mechanical embolectomy, endpoint RV/LV ratio
  - “Safe and effective... minimal major bleeding.”
- *To date there are no published studies comparing*
  - *Catheter directed thrombolysis to systemic thrombolysis*
  - *Mechanical thrombectomy to other treatment modalities in submassive PE*
  - *Functional outcomes of any interventional therapy vs. either anticoagulation alone or systemic thrombolysis*

# My Conclusions

- RV dysfunction identifies a group of patients at higher risk for acute mortality
- Systemic thrombolysis probably reduces mortality but increases the rate of ICH
- Catheter directed thrombolysis improves surrogate markers for RV function and therefore has a theoretical survival benefit with a lower bleeding risk.
  - May take 24-48 hours to work
- Mechanical thrombectomy is safe but its effect on mortality is unclear



# Scoring Tools

## PESI/sPESI

- Mortality risk is heavily weighted by baseline patient characteristics

**Table 7** Original and simplified PESI

Parameter	Original version <sup>214</sup>	Simplified version <sup>218</sup>
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110 b.p.m.	+20 points	1 point
Systolic blood pressure <100 mm Hg	+30 points	1 point
Respiratory rate >30 breaths per minute	+20 points	–
Temperature <36 °C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point
	<b>Risk strata<sup>a</sup></b>	
	<b>Class I: ≤65 points</b> very low 30-day mortality risk (0–1.6%) <b>Class II: 66–85 points</b> low mortality risk (1.7–3.5%)  <b>Class III: 86–105 points</b> moderate mortality risk (3.2–7.1%) <b>Class IV: 106–125 points</b> high mortality risk (4.0–11.4%) <b>Class V: &gt;125 points</b> very high mortality risk (10.0–24.5%)	<b>0 points</b> = 30-day mortality risk 1.0% (95% CI 0.0%–2.1%)  <b>≥1 point(s)</b> = 30-day mortality risk 10.9% (95% CI 8.5%–13.2%)

b.p.m. = beats per minute; PESI = Pulmonary embolism severity index.

<sup>a</sup>based on the sum of points.

# Scoring Tools

## Bova

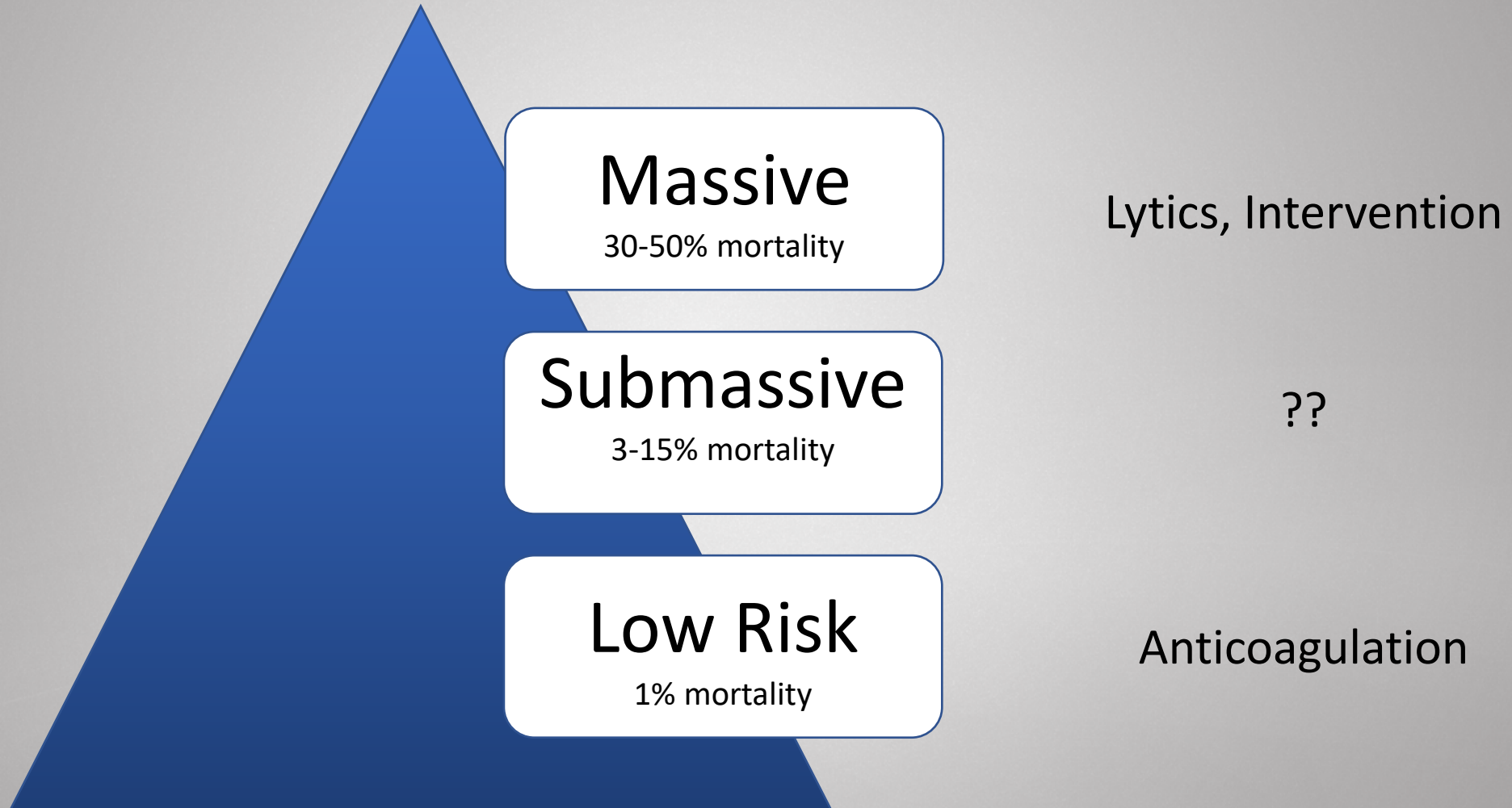
**Table 1.** *Modified Bova score*

Predictor variable	Points
Systolic blood pressure < 100 mmHg	2
Cardiac troponin I > 0.04 ng/ml	2
Right ventricular dysfunction	2
Heart rate $\geq$ 110 beats/min	1

- Based more on the acute physiology
- > 4 predicts a high mortality risk



# What do the guidelines say?



AHA SCIENTIFIC STATEMENT

**Management of Massive and Submassive Pulmonary Embolism, Iliofemoral Deep Vein Thrombosis, and Chronic Thromboembolic Pulmonary Hypertension**

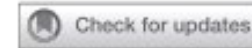
A Scientific Statement From the American Heart Association

- Fibrinolysis may be considered for patients with submassive acute PE judged to have clinical evidence of adverse prognosis ... and low risk of bleeding complications.
- Embolectomy is reasonable for patients with massive PE and contraindications to fibrinolysis.
- Embolectomy is reasonable for patients with massive PE who remain unstable after receiving fibrinolysis.
- Embolectomy may be considered for patients with submassive acute PE judged to have clinical evidence of adverse prognosis.
- Embolectomy is not recommended for patients with low-risk PE or submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and no clinical worsening.



## Antithrombotic Therapy for VTE Disease

### Second Update of the CHEST Guideline and Expert Panel Report



- In patients with acute PE associated with hypotension (SBP < 90) who do not have a high bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy.
- In selected patients with acute PE who deteriorate after starting anticoagulant therapy but have yet to develop hypotension and who have an acceptable bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy.
- We suggest systemic thrombolytic therapy using a peripheral vein over catheter-directed thrombolysis.

## Antithrombotic Therapy for VTE Disease

### Second Update of the CHEST Guideline and Expert Panel Report



- In patients with acute PE associated with hypotension who also have (i) a high bleeding risk, (ii) failed systemic thrombolysis, or (iii) shock that is likely to cause death before systemic thrombolysis can take effect (eg, within hours), we suggest catheter- assisted thrombus removal over no such intervention.



# My Conclusions

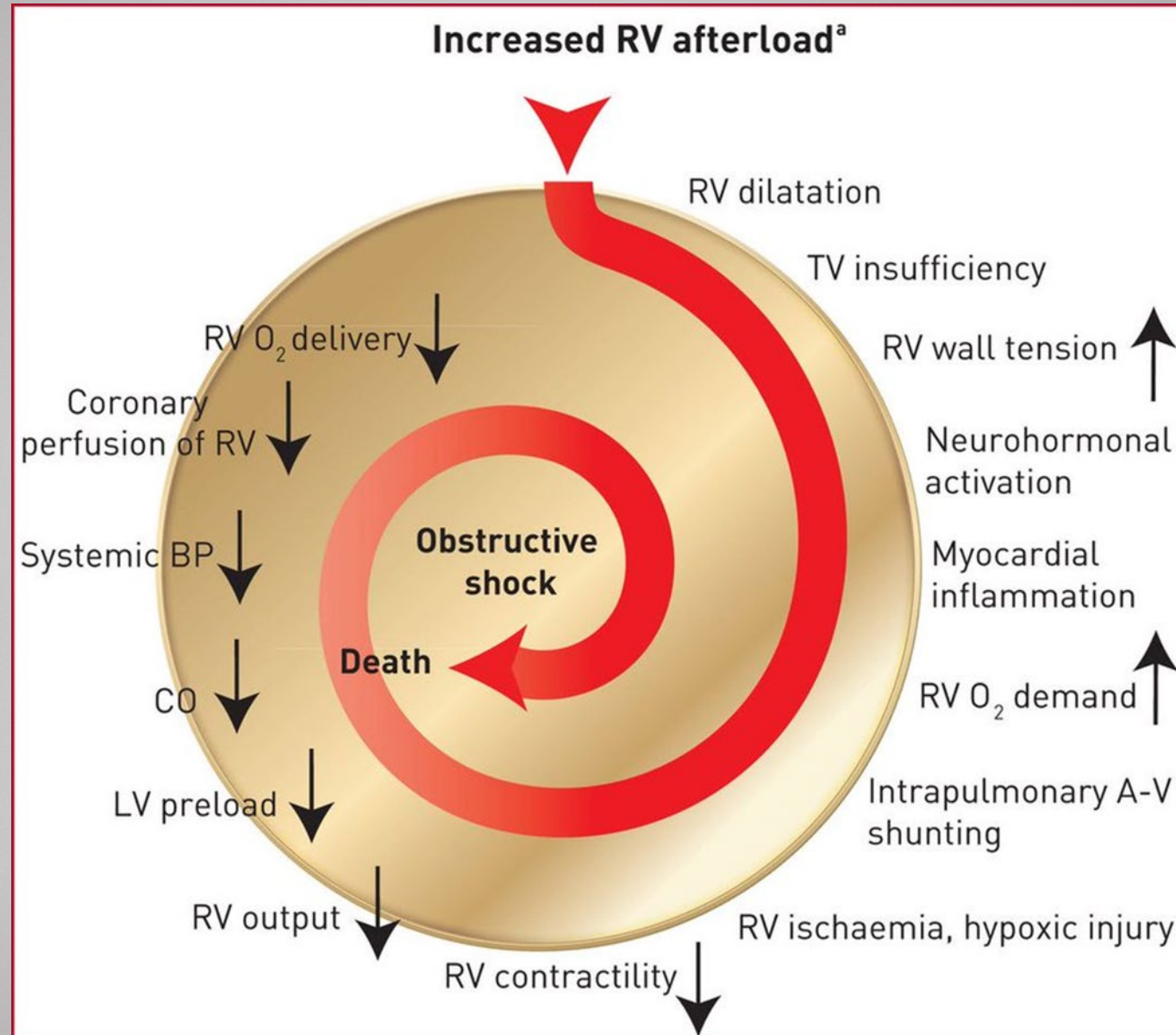
- Mortality in acute PE is directly correlated with the degree of right heart dysfunction, and clinical decision making should be based on the presence and severity of acute cor pulmonale.
- All intermediate and high-risk patients should receive anticoagulation without delay, preferably with LMWH.
- High risk patients without contraindications should receive systemic thrombolytic therapy.
- Revascularization therapy should be considered for all intermediate and high-risk patients, with the type of therapy dictated by patient characteristics and local resources.
- At this point, interventional therapies have no proven outcome benefit over medical therapies for most patients.



# Additional Thoughts

- Hypoxemia is rarely a factor in clinical decision making for acute pulmonary embolism.
- “Clot burden” on CT angiography has a poor correlation with clinical severity and should not drive clinical decision making.
- Volume loading should only be done if there is clear clinical evidence that hypovolemia is contributing to the patient’s shock.
- Positive pressure ventilation can exacerbate acute cor pulmonale and should be avoided if at all possible.





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