ACUTE PULMONARY EMBOLISM- EMPHASIS ON INTERVENTIONAL APPROACH

Dr Anupam Mehrotra

DM Cardiology

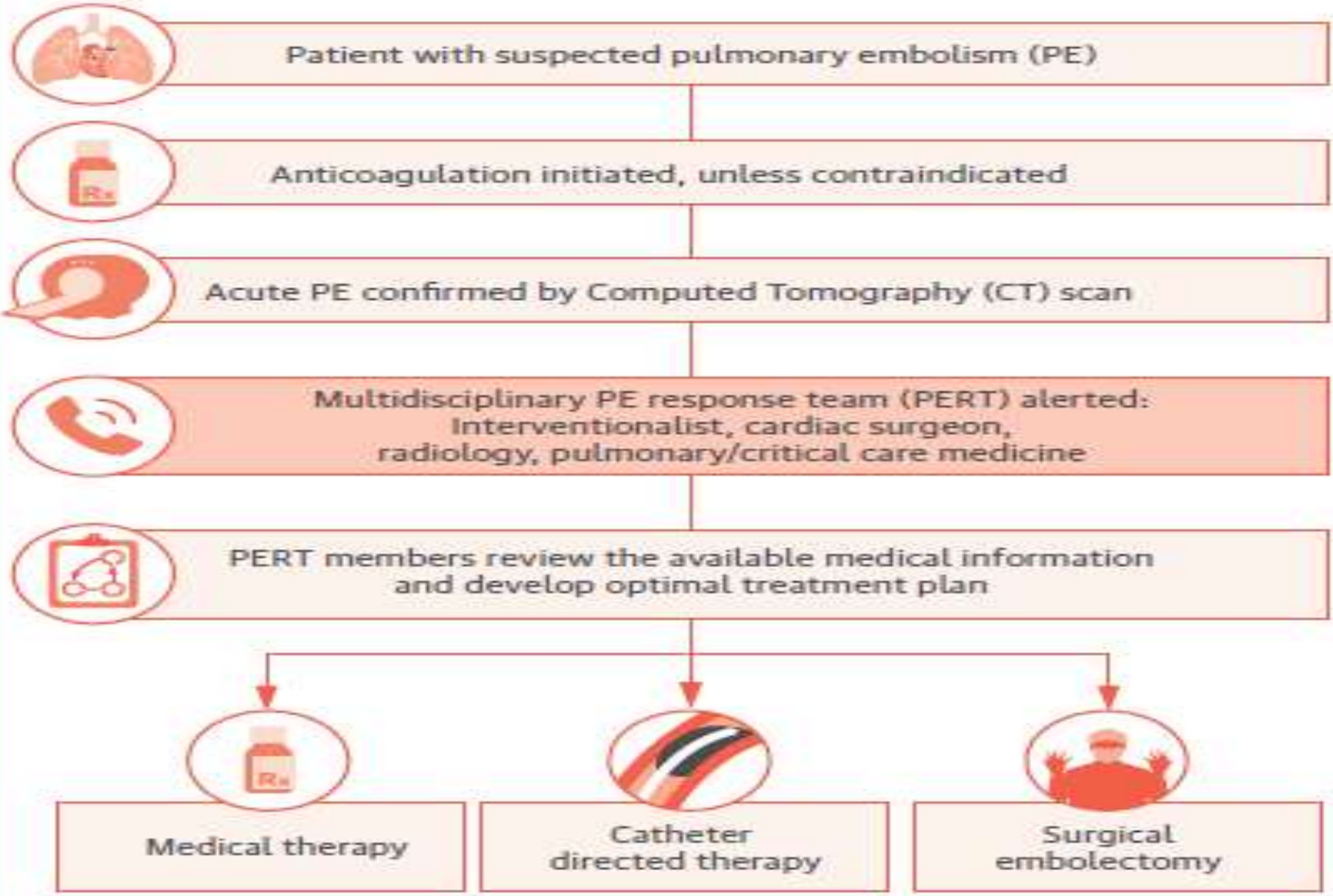
- Compared with recent advances in treatment of serious cardiovascular diseases, such as myocardial infarction and stroke, the treatment and outcome of acute pulmonary embolism (PE) have remained relatively unchanged over the last few decades
- This has prompted several experts to call for the formation of multidisciplinary PE response teams with a more proactive approach to the treatment of PE

BUILDING AN ACUTE PE TEAM AND MANAGEMENT PATHWAY

- Intensive management of acute PE begins with formation of a **PERT**(Pulmonary embolism response team) to engage specialists from different backgrounds to discuss treatment options and provide immediate advice and therapy for patients in the massive and submassive categories
- A PERT may consist of specialists from vascular medicine, pulmonary critical care, emergency medicine, interventional cardiology/ radiology, hematology, vascular surgery, and cardiothoracic surgery

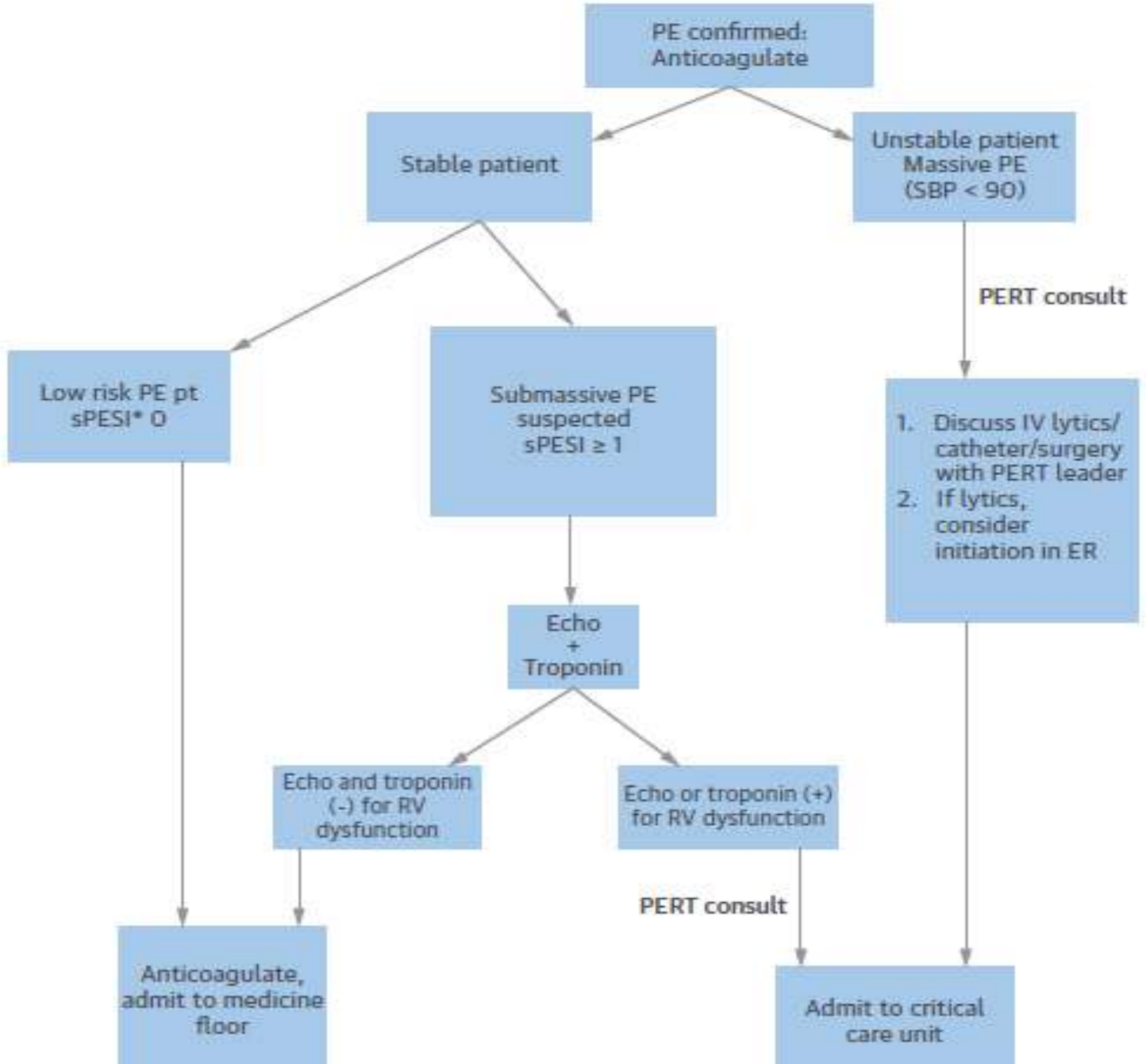
- The PERT's responsibility is to assess each case in a timely manner, examine the patient, review the available data, perform any additional testing, and then (in conjunction with the patient, family members,and care team) develop a consensus regarding the optimal treatment plan.

CENTRAL ILLUSTRATION **PERT Protocol**



Jaber, W.A. et al. J Am Coll Cardiol. 2016; 67(8):991–1002.

FIGURE 1 ER PE Protocol Utilizing PERT Consultation and sPESI Score



SYSTEMIC FIBRINOLYSIS

- A meta-analysis of trials including patients with massive PE showed a reduction in the composite of recurrent PE and death with use of IV fibrinolytic agents, but not in death alone
- Univariate analysis of a large inpatient sample found that among unstable patients with PE, use of IV fibrinolytic therapy was associated with a lower mortality rate, but only 30% of unstable patients received such therapy

- The **MAPPET (Management, Strategies and Prognosis of Pulmonary Embolism)-3 trial** randomized 256 patients with PE and pulmonary hypertension or RV dysfunction to 100 mg of IV alteplase or placebo infused over 2 h plus anticoagulation. IV alteplase was associated with a lower risk of further need to escalate the treatment and with a similar risk of death. Mortality was lower than expected in both groups (3.4% in the alteplase and 2.2% in the placebo group; $p = 0.71$)

- **PEITHO (Pulmonary Embolism Thrombolysis) trial** randomized 1,006 patients with submassive PE (normal blood pressure, RV enlargement, and increased troponin level) to tenecteplase or placebo. The PEITHO trial showed a reduction in the primary endpoint of hemodynamic collapse at 7 days with tenecteplase, but a significant increase in hemorrhagic stroke (most in patients older than 75 years of age), with similar mortality in both groups.

- **MOPETT (Moderate Pulmonary Embolism Treated With Thrombolysis) trial** randomized 121 patients with moderate-risk PE to half-dose alteplase (maximum 50 mg over 2 h)with anticoagulation versus anticoagulation alone. Low-dose alteplase was associated with lower pulmonary pressure at 28 months and no major bleeding.

- Taken together, these studies show that the use of IV fibrinolytic therapy in patients with massive or submassive PE leads to improved hemodynamic stabilization and, possibly, a lower risk of recurrent PE and PE-attributed death.
- However, this benefit comes with an increased risk of severe bleeding and intracranial hemorrhage

CATHETER-BASED THERAPIES

- ***Aim*** to relieve obstruction quickly and restore pulmonary blood flow, thus improving cardiac output and converting a hemodynamically unstable situation into a stable one. This is accomplished with reduced or no doses of fibrinolytic agents. Catheter-directed therapies (CDT) might include clot fragmentation, aspiration, and low-dose fibrinolytic injection
- Guidelines have given advanced therapies a limited recommendation because of a lack of randomized control data

TABLE 1 Catheter-Based Therapies

Device	Size	Mechanism of Action
Pigtail catheter	6- to 8-F	Fragmentation
Peripheral balloon	5 to 10 mm	Fragmentation
Catheter-directed fibrinolysis	4- to 6-F	Direct infusion of fibrinolytic agent
Ultrasound-accelerated thrombolysis	6-F	Direct infusion of fibrinolytic agent plus ultrasound for clot separation. Currently the only catheter-based therapy FDA-approved for PE treatment.
Guide catheter	6- to 10-F	Manual aspiration
Pronto Xl catheter	6- to 14-F	Manual aspiration
Penumbra Indigo system	6- to 8-F	Suction pump aspiration
Inari FlowTriever	22-F sheath	Disruption, retraction, and aspiration of clot
AngioVac	26-F sheath and 18-F cannula	Large-volume aspiration with return of filtered blood utilizing a centrifugal pump

FDA = Food and Drug Administration; PE = pulmonary embolism.

- Simplest and most commonly performed catheter-based therapy is a local, slow infusion of a fibrinolytic agent through low-profile catheters placed in the obstructed pulmonary artery.
- **CDF** is best suited for more stable patients or those who have been hemodynamically stabilized, as thrombus resolution may take several hours.
- For unstable patients who require immediate intervention and/or those with contraindication to fibrinolysis, mechanical thrombus fragmentation, debulking, or aspiration of occlusive thrombi may be attempted.

- ***Potential complications*** of any catheter-based therapy may include pulmonary arterial injury, pericardial tamponade, major bleeding, hemodynamic deterioration, distal embolization and "no-reflow" phenomenon, and access site bleeding.
- A metaanalysis of CDT using ≤10-F low-profile devices reported minor and major procedural complications of 7.9% and 2.4%, respectively .

- **Minor** complications included: groin hematomas not requiring transfusion, transient bradyarrhythmia, heart block, hemoglobinuria, mild hemoptysis, temporary renal insufficiency, embolus dislocation , and PA dissection.
- **Major** complications included: groin hematomas requiring transfusion, massive hemoptysis requiring transfusion, renal failure requiring hemodialysis, cardiac tamponade, and death; from bradyarrhythmia and apnea, distal embolization, and cerebral vascular hemorrhage

FRAGMENTATION AND ASPIRATION

- Rotating a pigtail catheter in the PA, the PE can be fragmented. The aim is to reduce the load on the RV by partially relieving the obstruction in the main PA branches. Fragmentation alone may cause distal embolization and potentially worsen distal branch obstruction.
- Fragmentation is frequently combined with local infusion of small-dose fibrinolytic agents (e.g., 4 to 10 mg of tissue-type plasminogen activator [t-PA]), delivered either at the time of the procedure or subsequently via an infusion catheter left in place.
- Fragmentation can also be performed by inflation of an angioplasty balloon

- Concomitant aspiration can reduce the risk of worsening obstruction.
- Aspiration can be attempted using regular 8-F guide catheters or specialized catheters such as-

-10-F Aspirex thrombectomy catheter

-Greenfield embolectomy catheter

-7-F Helix Clot Buster

-8- to 14-F Pronto XL manual extraction catheters

- **Angiojet Rheolytic Thrombectomy System** needs special mention. This 8-F peripheral catheter utilizes the Venturi-Bernoulli effect, using multiple highvelocity saline jets introduced through the distal tip, creating a low-pressure vacuum through small slits in the catheter that can entrain and fragment thrombi.
- A meta-analysis reported higher mortality and morbidity, including massive hemoptysis, renal failure, and death from bradycardia and apnea or from widespread distal embolization , which resulted in a black-box warning from the FDA for use of Angiojet in acute PE

AngioVac thrombectomy device

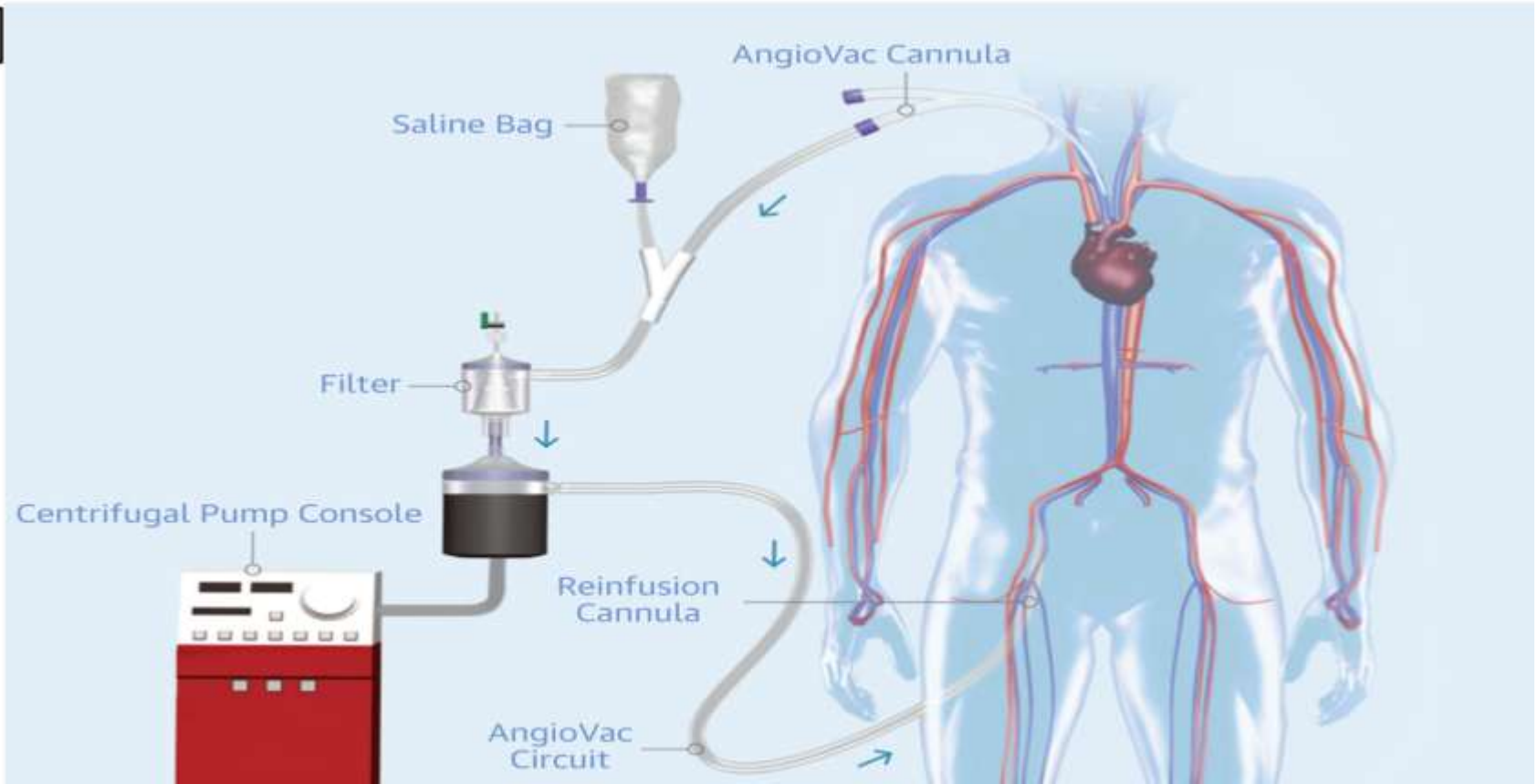
- AngioVac Cannula, a 22-F venous catheter that can remove soft thrombi utilizing the centrifugal pump and venous reinfusion cannula used in cardiopulmonary bypass
- AngioVac catheter consists of a balloon-expandable, funnel-shaped distal tip, which improves removal of large clots en masse

- Limitations include large dual sheaths required for access, leading to a higher likelihood of bleeding complications, and the relatively stiff suction catheter, which is difficult to maneuver into the RV and PA.
- Furthermore, the active participation of an experienced perfusionist is required for AngioVac setup and operation, as there is a learning curve for its use.
- AngioVac has been utilized in PE, although it is more commonly used to retrieve thrombi from the vena cava and right atrium. The rapidity of initiation may limit its use in massive PE situations; future iterations may render it more useful for PE.

A

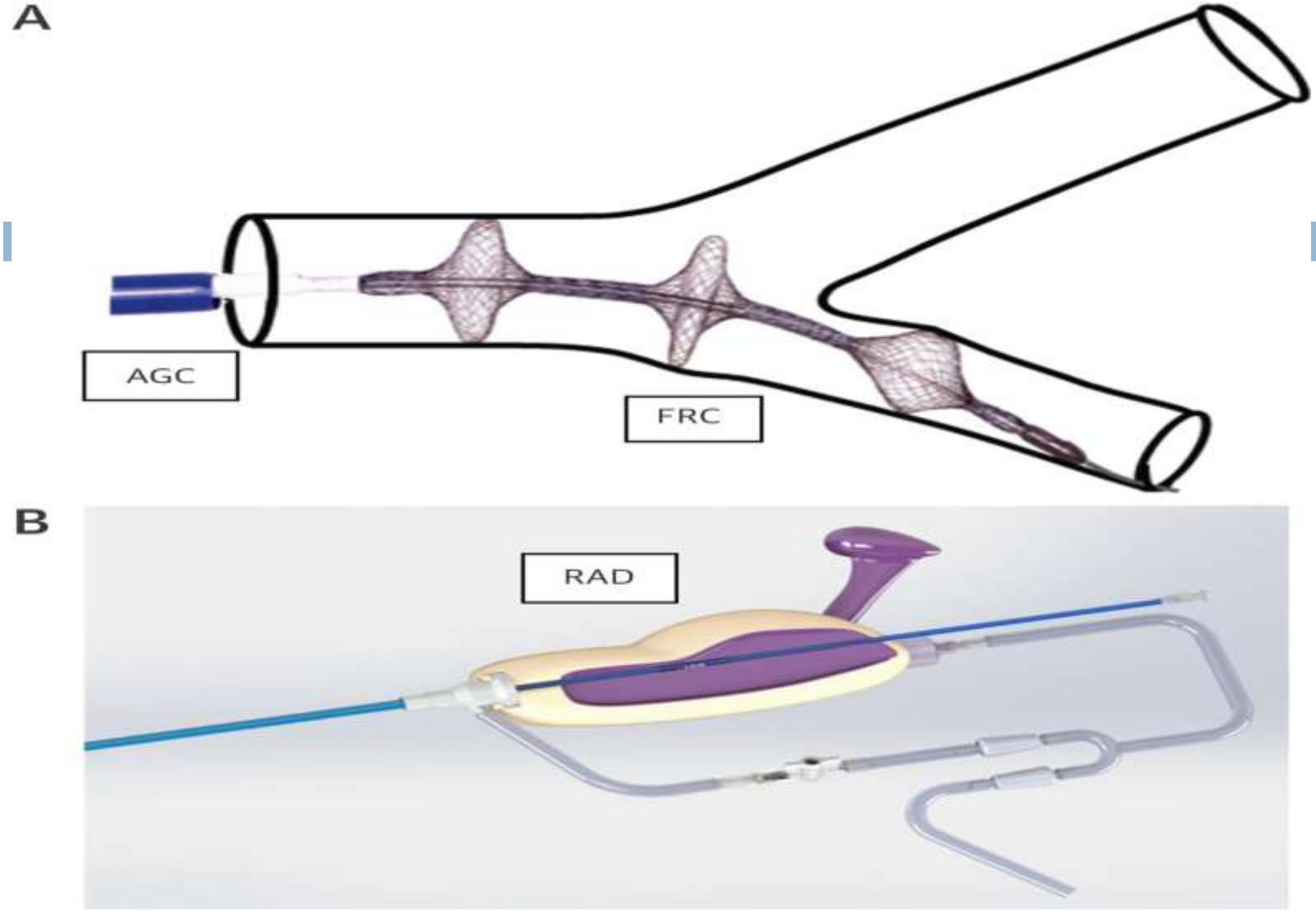
C

B


AngioVac Cannula
Saline Bag
Filter
Centrifugal Pump Console
Reinfusion Cannula
AngioVac Circuit

Flow Triever device

- FlowTriever Infusion Aspiration System requires a 22-F venous sheath and consists of 3 parts: the Flow Restoration Catheter, which is made up of 3 self-expanding nitinol disks; the Aspiration Guide Catheter; and the Retraction Aspirator Device.
- The FlowTriever device is advanced over the wire and into the thrombus, where the expandable disks are deployed using a pin and pull method. The disks and disrupted thrombus are then retracted and removed through the aspiration catheter.
- Set-up is rapid, and there is a modest learning curve for device utilization.
- Limitations include the large size requirement of the access sheath, and manipulation of the large-bore catheter into the PA



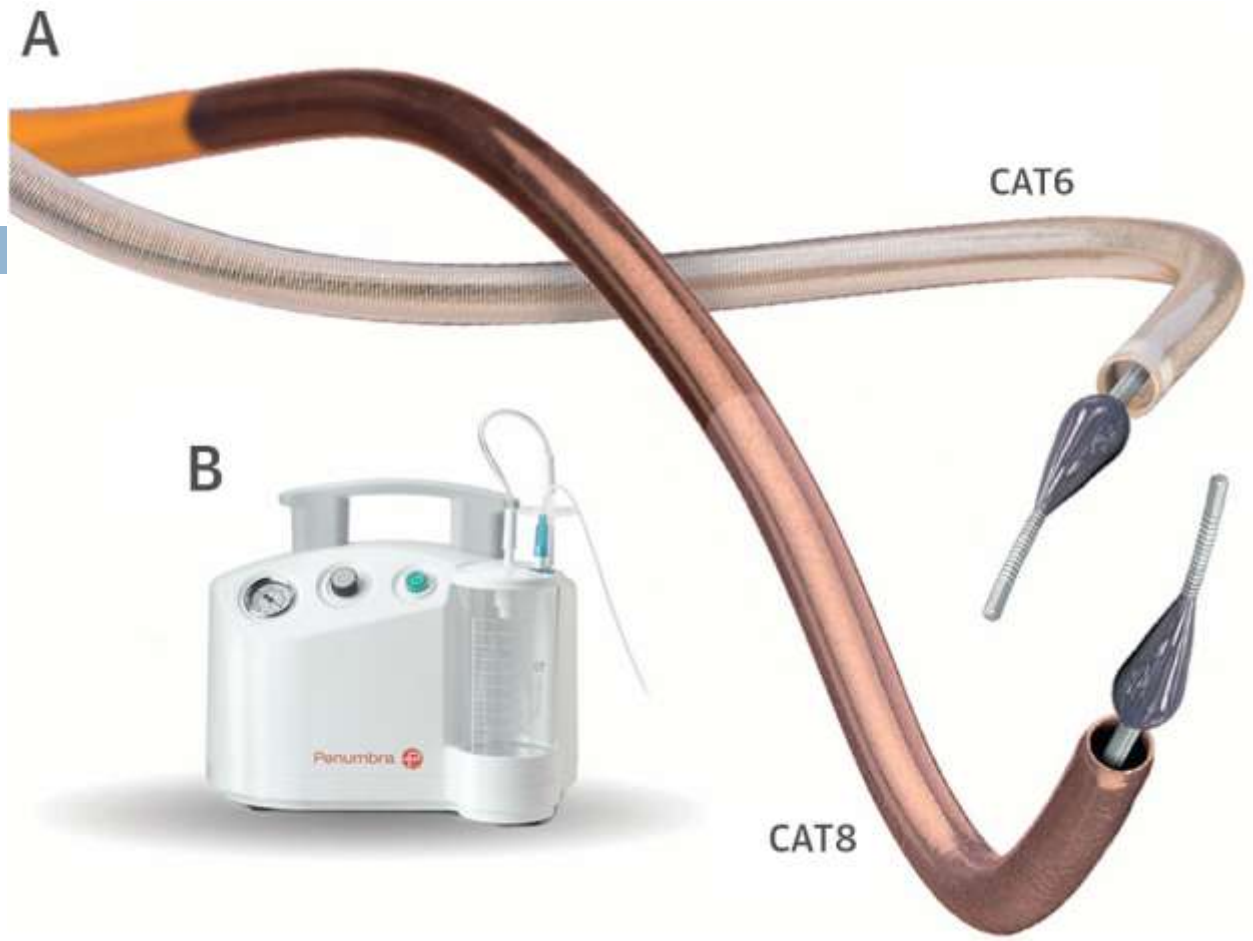
FlowTriever Device

(A) The flow restoration catheter (FRC) is used to enmesh clots and is pulled through the aspiration guide catheter (AGC) utilizing (B) the retraction aspirator device (RAD).

Penumbra Indigo thrombectomy system

- Indigo mechanical thrombectomy system consists of a pump, 6- to 8-F straight or angled catheters, and a Separator device
- It is approved for thrombus removal in both peripheral arterial and venous systems.
- An advantage is that it only requires an 8-F venous sheath and can be placed into the PA system quickly, in an over-the-wire technique. Once placed proximal to the clot, the thrombectomy catheter is advanced while suction is supplied with the ACER pump. The provided Separator wire is used to clear the system of thrombus as the catheter is manipulated inside the artery.

- **A distinct limitation of these last 3 devices is the absence of published data on their overall success and safety.**



(A) The 6- to 8-F straight or angled aspiration catheter (CAT6 or CAT8, respectively) is advanced to the thrombus and aspiration performed with the (B) ACER pump. Separator wires may be inserted into the catheter and utilized in a gentle back and forth motion to clear the catheter of thrombus.

CATHETER-DIRECTED FIBRINOLYSIS

- Full-dose systemic fibrinolysis is helpful in stabilizing high-risk PE patients and reducing pulmonary pressure, but at the cost of increased systemic bleeding, interest has risen in local delivery of low-dose fibrinolytics close to or into the PA thrombus
- One small trial randomized 34 patients with angiographically large PE to IV- or catheter-based infusion of t-PA at a dose of 50 mg over 2 h, and showed similar safety and angiographic and hemodynamic results by both techniques.

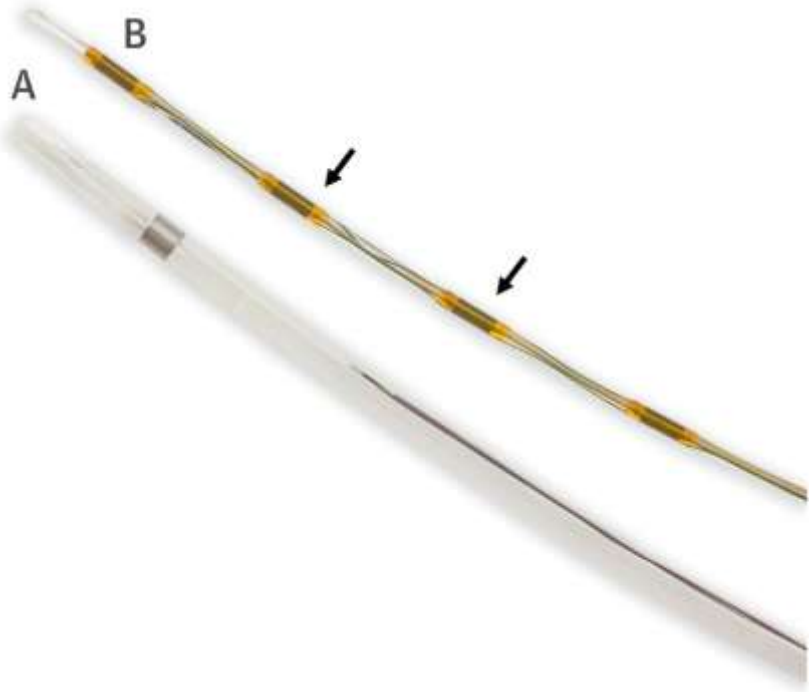
- In a more recent prospective registry of 101 massive and submassive PE patients treated with catheter-based therapy (mostly local fibrinolysis), there was a significant decrease in PA pressure and improvement in RV function, with no reported major complications, major bleeding, or strokes.
- It is reasonable to consider CDF in patients with already stabilized massive PE who have contraindications to systemic fibrinolysis and in patients with intermediate-high–risk PE ,particularly those deemed at increased bleeding risk with full-dose systemic fibrinolysis
- More prominent hemodynamic benefit was obtained in patients with **symptom duration <14 days**

- A commonly used t-PA dose is 0.5 to 1.0 mg/h per catheter. The total t-PA dose is typically between 12 and 24 mg, delivered over 6 to 24 h. Lowdose, weight-adjusted heparin infusion is usually continued during t-PA infusion, with a target partial thromboplastin time on the low end of the therapeutic range (e.g., 40 to 60 s).
- **Risk of intracranial hemorrhage is <0.2%**

Ultrasound accelerated fibrinolysis

- **Eko- Sonic catheter** consists of a 5.2-F conventional infusion catheter with an inner cable that transmits high-frequency, low-power ultrasound signals, designed to loosen the fibrin strands and enhance thrombus penetration of the fibrinolytic agent, hence theoretically achieving a faster thrombus breakdown
- It is uncertain whether this treatment is suitable for patients who are hemodynamically unstable and need faster resolution of the PE or if there is long-term benefit of the prolonged treatment in prevention of future pulmonary hypertension, underscoring the need for more evidence.

EkoSonic Endovascular Device



The 5.2-F infusion catheter (A), which contains 3 lumens: 1 each for the inner ultrasound cable, drug infusion, and normal saline as a coolant. The inner cable (B) is shown with ultrasound crystals (arrows). Ultrasound energy separates fibrin strands, allowing for enhanced thrombus penetration of fibrinolytic agent.

EXTRACORPOREAL MECHANICAL OXYGENATION AND RV ASSIST DEVICES

- ECMO placement has been described in case reports of patients with massive PE, as it has the potential to unload the RV and, importantly, provides oxygenation during massive PE to allow for RV recovery
- Percutaneous RV assist device (Impella RP) may one day be considered for use in massive PE, either as a bridge to definitive therapy, or to support RV recovery after thrombus removal

SURGICAL EMBOLECTOMY

- Currently, surgical therapy is considered a last resort for acute PE and is offered only to patients in extremis.
- This concept is on the basis of data from the 1960s, when the surgical pulmonary embolectomy mortality rate was in excess of 50%
- Significant advances in cardiac surgical techniques have led to an impressive reduction in operative mortality, which is as low as 6% in the current era
- In a 2013 report on 27 consecutive surgical pulmonary embolectomy patients, there was no in-hospital mortality and a 10-year actuarial survival rate of 93%; both late mortalities were unrelated to PE or related therapy

VENA CAVA FILTER

- Placement of an inferior vena cava (IVC) filter is indicated in patients with acute PE who have absolute contraindications to anticoagulation or in patients who have recurrent PE, despite adequate anticoagulation
- The position of the filter below or above the renal veins depends on the absence or presence of renal vein thrombus, respectively. Retrievable filters are preferable because they are associated with lower complication rates
- Both the American and the European guidelines do not recommend routine use of IVC filters in patients with PE

- **PREPIC 2 trial**, a randomized, open-label, blinded endpoint trial with a 6-month follow-up, was more recently published.Hospitalized patients with acute, symptomatic PE associated with lower-limb vein thrombosis and at least 1 criterion for severity were assigned to retrievable inferior vena cava filter implantation plus anticoagulation (n 200) or anticoagulation alone with no filter implantation (n 199).
- Anticoagulant treatment was not interrupted during filter placement, and access site hematomas were observed in only 2.6% of the patients.
- By 3 months, recurrent PE had occurred in 6 patients (3.0%; all events fatal) in the filter group and in 3 patients (1.5%; 2 fatal) in the control group (RR with filter: 2.0) results were similar at 6 months

- However, 3 large analyses, including a U.S. nationwide hospital sample and a study from Japan, suggest that IVC filters may result in better outcomes in patients with massive or intermediate high– risk PE.
- In the International Cooperative Pulmonary Embolism registry, IVC filter use in patients with massive PE was associated with reduced rates of recurrent PE and mortality at 90 days

CONCLUSIONS

- At this time, there is not enough evidence to strongly support routine utilization of any of the previously discussed techniques in the management of submassive or massive PE, beyond anticoagulation
- Currently, CDF with use of the EKOS catheter is the only FDA-approved catheter-based therapy for use in treatment of acute PE, although adequate comparative studies are lacking

- Although some centers have reported favorable outcomes with surgical embolectomy as a first-line management of intermediate high– and high-risk PE, it is reasonable to reserve it for patients with massive PE and shock, who have contraindications to fibrinolysis, who have failed other treatments, or who have concomitant intracardiac thrombus or paradoxical embolus

THANK YOU