Thrombolytics in Cardiac Arrest

TERREN TROTT

DISCLOSURES

None.

OBJECTIVES

1. Discuss the epidemiology, pathophysiology, and risk stratification of pulmonary embolisms (PE)
2. Review bedside tools and strategies used to narrow the presentation differential
3. Examine treatment options for the management of massive PE

The diagnosis of pulmonary embolism (PE) in the emergency department is challenging due to the lack of clinical diagnostic criteria and imperfect investigations. The presenting symptoms are:

a) symptoms are common and non-specific

b) always include from chest pain and shortness of breath

c) there is a very low false positive rate with non-invasive testing (d-dimer)

d) all of the above

RISK FACTORS FOR PE

- Postoperative states
- Pregnancy
- Malignancies
  Limited mobility
- Previous venous thromboembolism
- Cardiovascular disease
- Estrogen use
- Obesity

Pollack, C.V., et al. J Am Coll Cardiol, 2011. **57**(6): p. 700-6
Anderson, F.A., Jr., et al. Am J Hematol, 2007. **82**(9): p. 777-82.
Raskob, G.E., et al. Arterioscler Thromb Vasc Biol, 2014. **34**(11): p. 2363-71.
Keller, K., et al. Int Angiol, 2016. **35**(2): p. 184-91.

HOW WE DEFINE PULMONARY EMBOLISM

ANATOMIC

VS

PHYSIOLOGIC

Pollack, C.V., et al. J Am Coll Cardiol, 2011. **57**(6): p. 700-6
Morrone, D., et al. Korean Circ J, 2018. **48**(5): p. 365-381.

HOW WE DEFINE PULMONARY EMBOLISM

MASSIVE

VS

SUBMASSIVE

Keller, K., et al. Acta Medica (Hradec Kralove), 2018. **61**(3): p. 93-97
Heit, J.A., et al. Mayo Clin Proc, 2001. **76**(11): p. 1102-10.
Alikhan, R., et al. J Clin Pathol, 2004. **57**(12): p. 1254-7.

MASSIVE

CARDIAC ARREST
SHOCK
SUSTAINED PRESSORS

Bougouin, W., et al. Resuscitation, 2017. **115**: p. 135-140.
Bougouin, W., et al. Circulation, 2016. **134**(25): p. 2125-2127.
Keller, K., et al. Int Angiol, 2016. **35**(2): p. 184-91

SUBMASSIVE

NORMOTENSIVE RV STRAIN

Keller, K., et al. Int Angiol, 2016. **35**(2): p. 184-91

DIAGNOSIS OF MASSIVE PE

DEFINITIVE DIAGNOSIS

DIAGNOSIS OF MASSIVE PE

- EMPIRIC DIAGNOSIS -

PRE-TEST PROBABILITY

RISK FACTORS

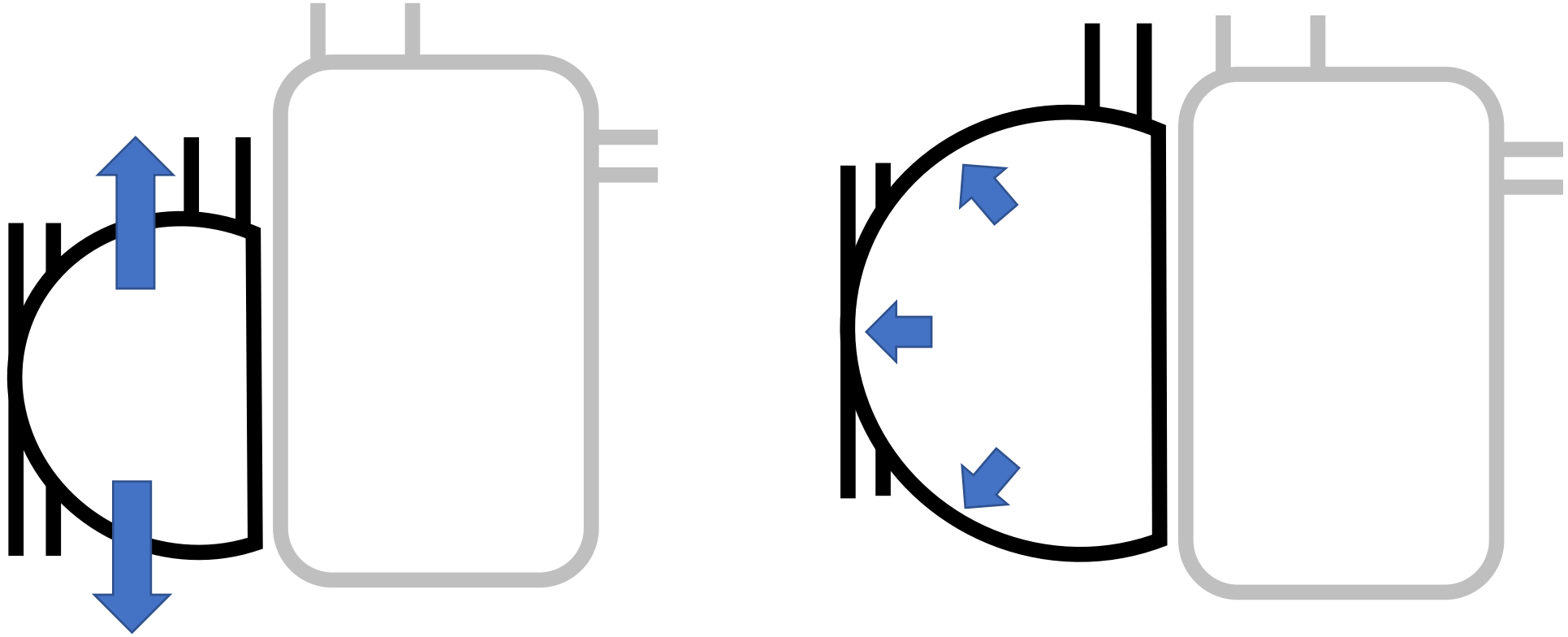
BIOMARKERS

ECG

Duplyakov, D., et al. Eur Heart J Acute Cardiovasc Care, 2015. **4**(4): p. 353-8.
Thomson, D., et al., Postgrad Med J, 2019. **95**(1119): p. 12-17.
Digby, G.C., et al. Ann Noninvasive Electrocardiol, 2015. **20**(3): p. 207-23.
Kline, J.A., et al. J Thromb Haemost, 2008. **6**(5): p. 772-80.
Wolf, S.J., et al. Ann Emerg Med, 2004. **44**(5): p. 503-10
Wells, P.S., et al. Ann Intern Med, 2001. **135**(2): p. 98-107

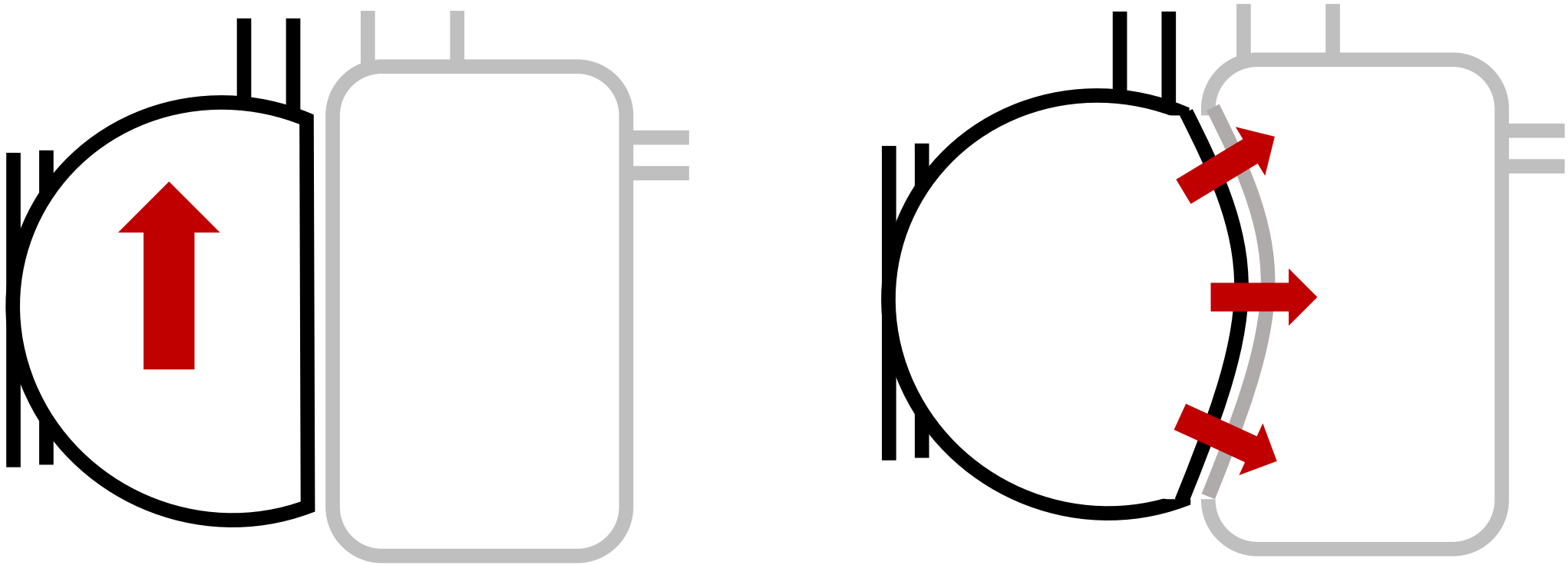
DIAGNOSIS OF MASSIVE PE

RIGHT HEART ULTRASOUND



DIAGNOSIS OF MASSIVE PE

RIGHT HEART ULTRASOUND



DIAGNOSIS OF PULMONARY EMBOLI DURING CARDIAC ARREST

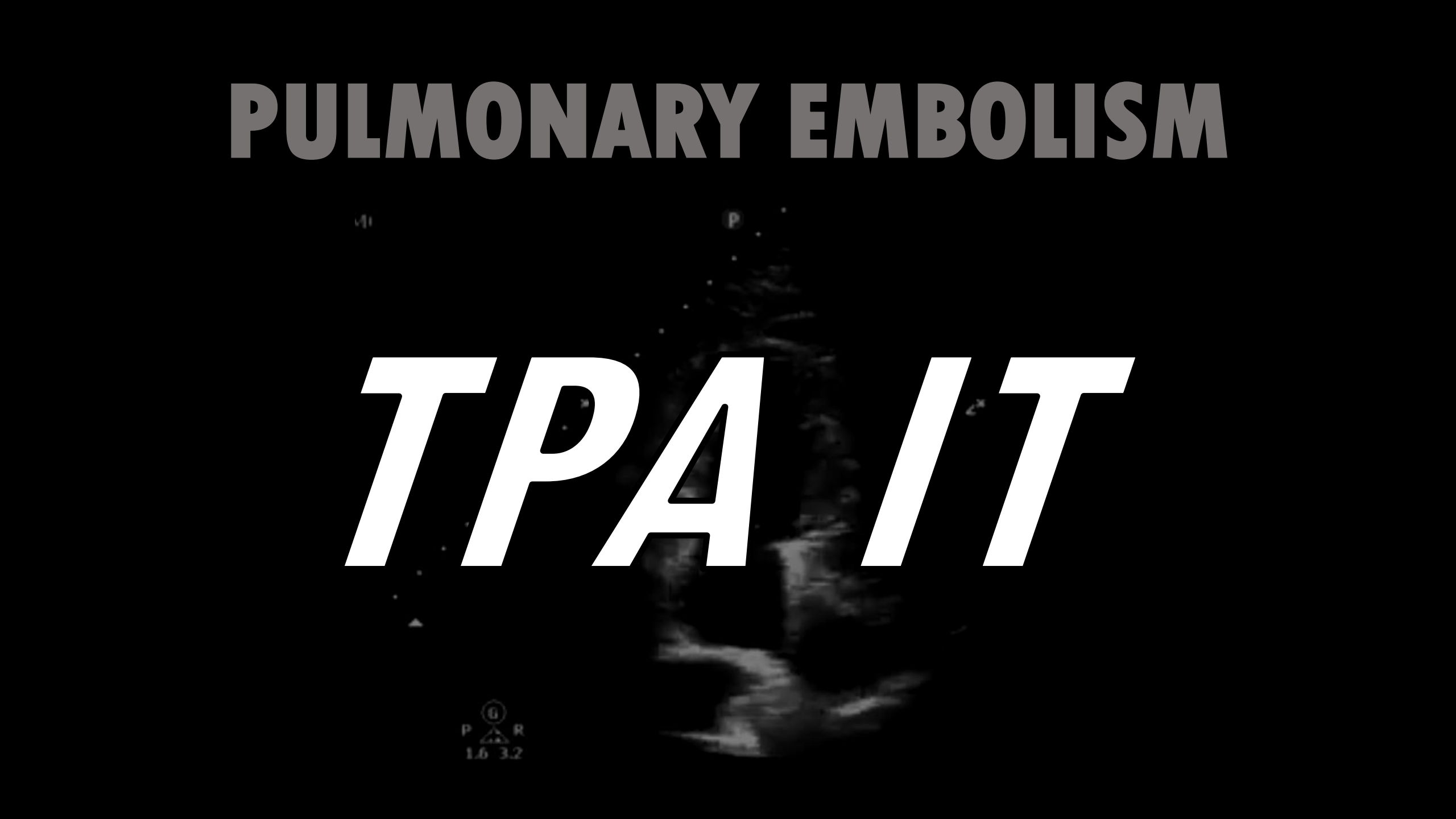
PULMONARY EMBOLISM

PULMONARY EMBOLISM

TPA IT

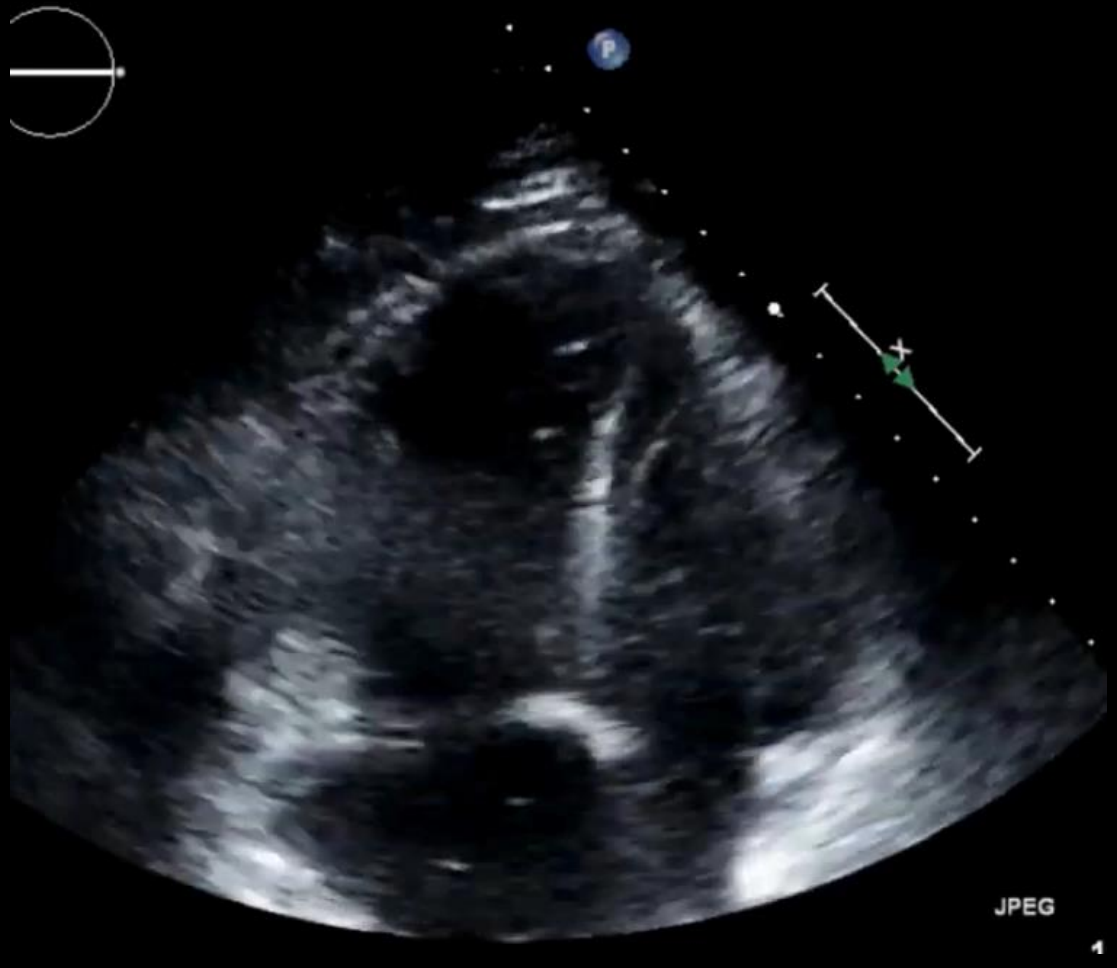
PULMONARY EMBOLISM

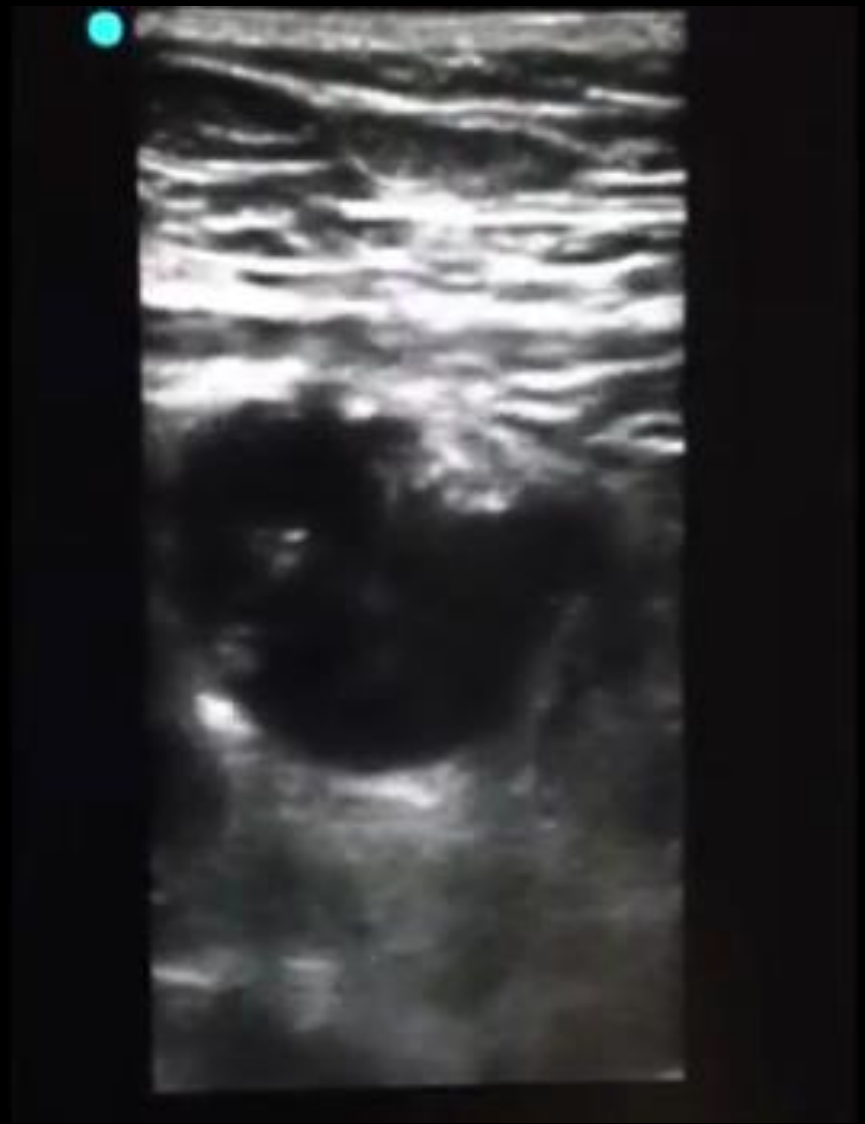
PULMONARY EMBOLISM



TPA IT

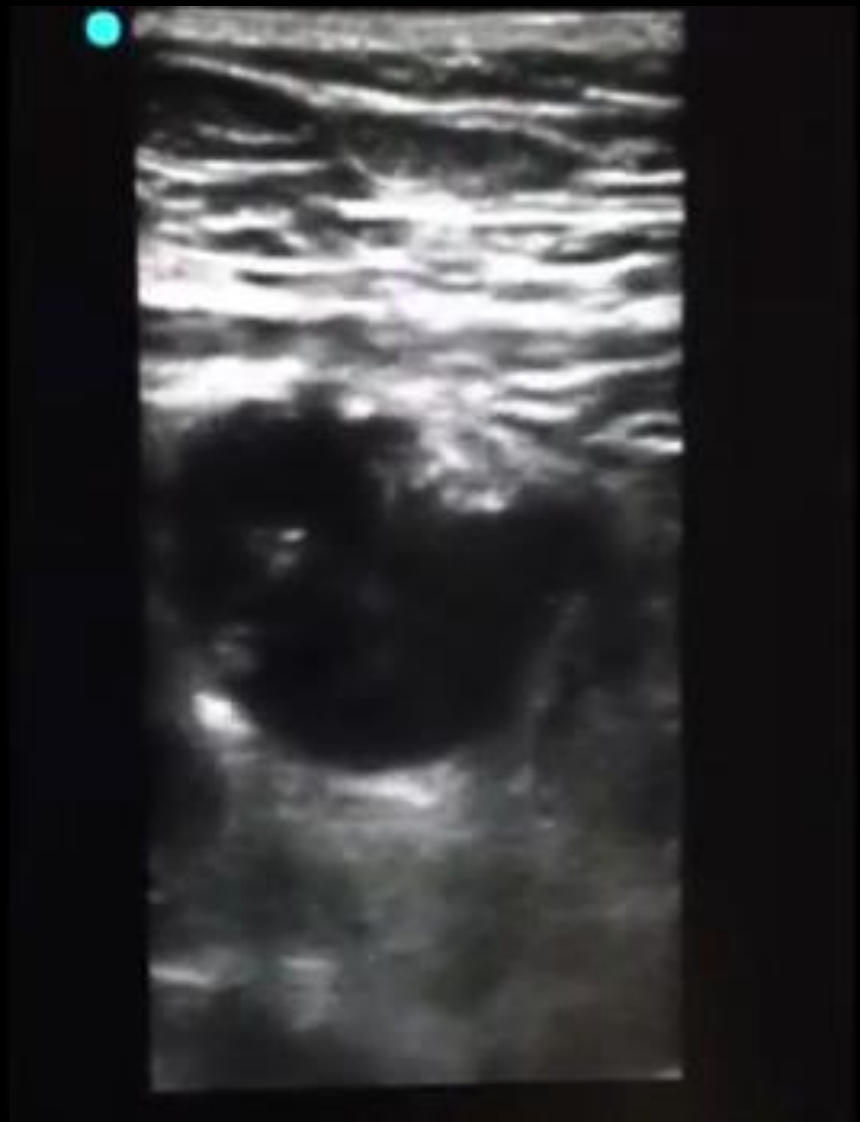
PULMONARY EMBOLISM





PULMONARY EMBOLISM

PULMONARY EMBOLISM



PULMONARY EMBOLISM

TPA IT?

PROB NOT.

PULMONARY EMBOLISM

PULMONARY EMBOLISM

TPA IT?

MAYBE NOT?

CLOT IN TRANSIT

TPA IT.

RV FAILURE +

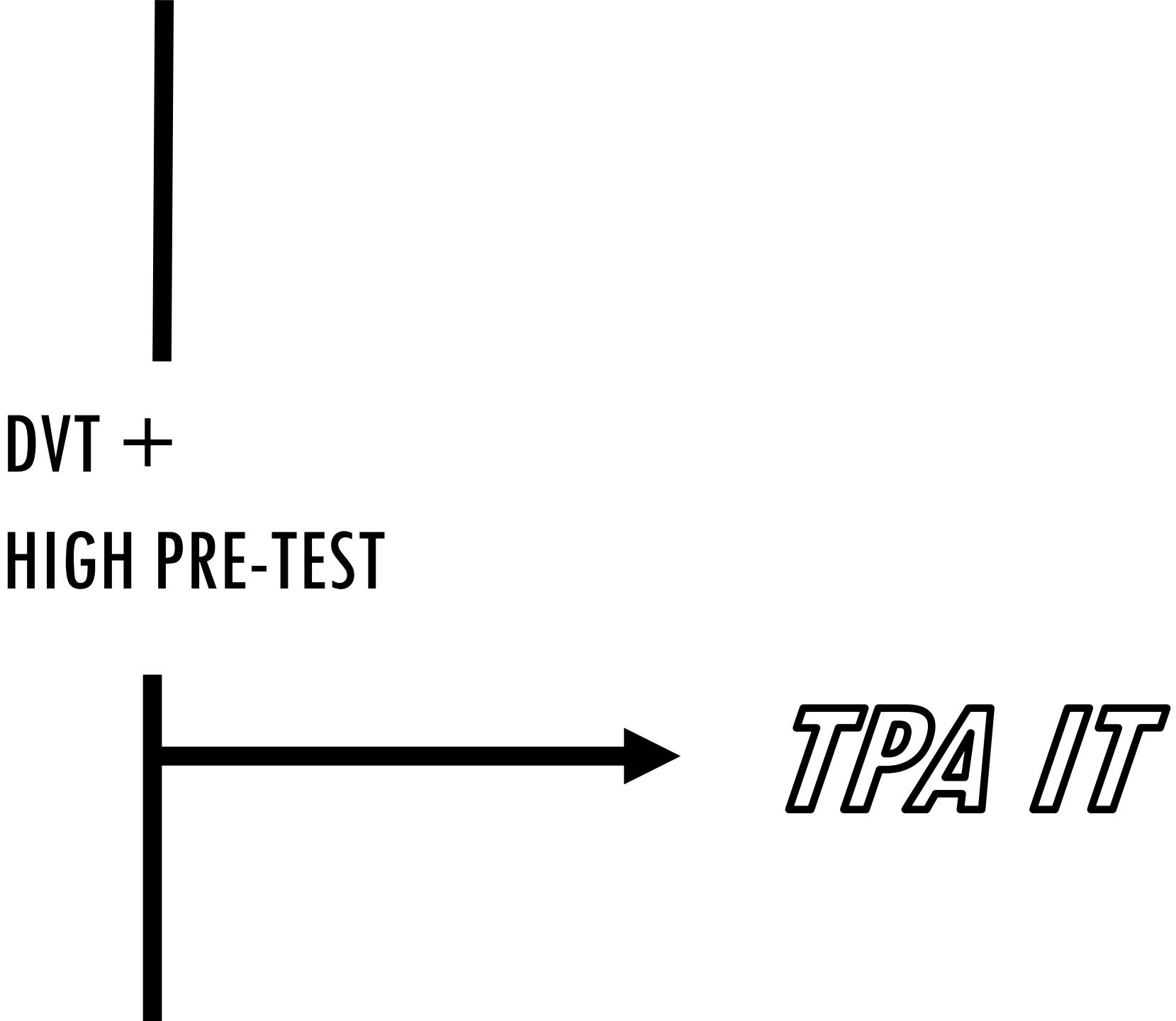
DVT

TPA IT.

RV FAILURE +

HIGH PRE-TEST

TPA IT


DVT +
HIGH PRE-TEST
TPA IT

HIGH PRE-TEST

TPA IT?

TPA IT. > TPA IT > TPA IT?

Which of the following are the common ultrasound features of RV dysfunction in PE:

a) RV wall hypokinesis
b) RV larger than LV in subcostal or apical view
c) free-floating right-heart thrombus
d) All of the above

Use of fibrinolysis in PE is a controversial topic. Which the following are true:

a) most agree that cardiac arrest and hemodyamic instability (SBP $<$ 90mmHg) are indications for thrombolysis.

b) controversy surrounds thrombolysis for stable patients with RV dysfunction on echocardiography

c) the benefit must be weighed against the risk of hemorrhage with thrombolytic therapy

d) thrombolysis has not been shown to improve mortality

MANAGEMENT OF MASSIVE PULMONARY EMBOLI DURING NON-CARDIAC ARREST

Bougouin, W., et al. Resuscitation, 2017. **115**: p. 135-140. 0
Rose, P.S., et. al. Chest, 2002. **121**(3): p. 806-14
Morrone, D, et al. Korean Circ J, 2018. **48**(5): p. 365-381.

MANAGEMENT

ABCS

MANAGEMENT

AIRWAY + BREATHING

HFNC

INTUBATION OF RV FAILURE

ROUGH TRANSITION TO POSITIVE PRESSURE VENTILATION

INTUBATION OF RV FAILURE

RSI VERUS AWAKE

INTUBATION

INTUBATION OF RV FAILURE

RSI VERUS AWAKE

INTUBATION

INTUBATION OF RV FAILURE

TOPICALIZE

AEROSOLIZE

LOW-DOSE KETAMINE

AWAKE INTUBATION

VENTILATION OF RV FAILURE

PRESSURE SUPPORT

INSPIRATORY SUPPORT 5-8

PEEP 0

TITRATE PEEP UP AS TOLERATED

MANAGEMENT

CIRCULATION

NOREPINEPHRINE

+ *VASOPRESSIN/ MILRINONE*

Bougouin, W., et al. Resuscitation, 2017. **115**: p. 135-140.

MANAGEMENT

CIRCULATION

FLUIDS?

WHAT DOSE OF TPA?

Recombinant tissue plasminogen activator (TPA) (alteplase)	100 mg intravenous over 2 h
Tenecteplase	One bolus of 30 mg to 50 mg (depending on body weight) over 5 s to 10 s
Reteplase	Two boluses of 10 U at a 30 min interval
Streptokinase	1.5 million IU over 2 h in continuous infusion
Urokinase	3 million IU over 2 h in continuous infusion

Sors, et al. *CHEST.* 1994; 106: 712-717.
Le Conte, et al. *Am J Emerg Med*. 2003; 21: 438-440.
Wang, et al. *Chest.* 2010; 137(2): 254-262

WHAT DOSE OF TPA?

Study	Publication Year	N	Low-Dose tPA Dosing Regimen	Comparator Regimen
Sors et al	1994	53	0.6 mg/kg (Max = 50 mg) IV over 15 min	100 mg IV tPA over 2 hours
Le Conte et al	2003	21	0.6 mg/kg (Max = 50 mg) IV over 15 min	None
Wang et al	2010	118	50 mg IV over 2 hours	100 mg IV tPA over 2 hours

Sors, et al. *CHEST.* 1994; 106: 712-717.
Le Conte, et al. *Am J Emerg Med*. 2003; 21: 438-440.
Wang, et al. *Chest.* 2010; 137(2): 254-262.

WHAT DOSE OF TPA?

Reference	Lytic Regimen	ROSC, n/N (%) Lytic	ROSC, n/N (%) Control	Survival 24 hours, n/N (%) Lytic	Survival 24 hours, n/N (%) Control	Survival to Discharge, n/N (%) Lytic	Survival to Discharge, n/N (%) Control
Kurkciyan (2000)	50 mg bolus x 2 **OR** 15 mg bolus + 85 mg infusion over 90 min	17/21 (81)*	9/21 (43)	NR	NR	2/21 (10%)	1/21 (5%)
Lederer (2001)	15 mg bolus → 50 mg over 30 min → 35 mg over 60 min	76/108 (70.4)*	110/214 (51.0)	52/108 (48.1)*	71/214 (32.9)	27/108 (25)*	33/214 (15.3)
Ruiz-Bailen (2001)	50 mg bolus (2-3 min) then 50 mg bolus (5 min) after 30 min	NR	--	NR	--	4/6 (66.7)	--
Janata (2002)	0.6 – 1.0 mg/kg (max of 100 mg)	24/36 (67)	13/30 (43)	19/36 (53)*	7/30 (23)	7/36 (19)	2/30 (7)

Kurkciyan I, et al. *Arch Intern Med.* 2000; 160: 1529-1535.
Ruiz-Bailen M, et al. *Resuscitation.* 2001; 51: 97-101.
Lederer W, et al. *Resuscitation.* 2001; 50: 71-76.
Janata K, et al. *Resuscitation.* 2003; 57: 49-55.

SALVAGE THERAPY

ECMO

SURGICAL THROMBECTOMY

CDT

CONCLUSION

REFERENCES

- 1. Pollack, C.V., et al., *Clinical characteristics, management, and outcomes of patients diagnosed with acute pulmonary embolism in the emergency department: initial report of EMPEROR (Multicenter Emergency Medicine Pulmonary Embolism in the Real World Registry).* J Am Coll Cardiol, 2011. **57**(6): p. 700-6.
- 2. Anderson, F.A., Jr., et al., *Estimated annual numbers of US acute-care hospital patients at risk for venous thromboembolism.* Am J Hematol, 2007. **82**(9): p. 777-82.
- 3. Raskob, G.E., et al., *Thrombosis: a major contributor to global disease burden.* Arterioscler Thromb Vasc Biol, 2014. **34**(11): p. 2363-71.
- 4. Heit, J.A., et al., *Incidence of venous thromboembolism in hospitalized patients vs community residents.* Mayo Clin Proc, 2001. **76**(11): p. 1102-10.
- 5. Alikhan, R., et al., *Fatal pulmonary embolism in hospitalised patients: a necropsy review.* J Clin Pathol, 2004. **57**(12): p. 1254-7.
- 6. van Langevelde, K., et al., *Finding the origin of pulmonary emboli with a total-body magnetic resonance direct thrombus imaging technique.* Haematologica, 2013. **98**(2): p. 309-15.
- 7. van Dam, L.F., et al., *Clinical and computed tomography characteristics of COVID-19 associated acute pulmonary embolism: A different phenotype of thrombotic disease?*Thromb Res, 2020. **193**: p. 86-89.
- 8. Rose, P.S., N.M. Punjabi, and D.B. Pearse, *Treatment of right heart thromboemboli.* Chest, 2002. **121**(3): p. 806-14.
- 9. Morrone, D. and V. Morrone, *Acute Pulmonary Embolism: Focus on the Clinical Picture.* Korean Circ J, 2018. **48**(5): p. 365-381.
- 10. Bougouin, W., et al., *Pulmonary embolism related sudden cardiac arrest admitted alive at hospital: Management and outcomes.* Resuscitation, 2017. **115**: p. 135-140.
- 11. Bougouin, W., et al., *Factors Associated With Pulmonary Embolism-Related Sudden Cardiac Arrest.* Circulation, 2016. **134**(25): p. 2125-2127.
- 12. Keller, K., et al., *Typical symptoms for prediction of outcome and risk stratification in acute pulmonary embolism.* Int Angiol, 2016. **35**(2): p. 184-91.
- 13. Keller, K., et al., *Evaluation of Risk Stratification Markers and Models in Acute Pulmonary Embolism: Rationale and Design of the MARS-PE (Mainz Retrospective Study of Pulmonary Embolism) Study Programme.* Acta Medica (Hradec Kralove), 2018. **61**(3): p. 93-97.

REFERENCES

- 14. Duplyakov, D., et al., *Value of syncope in patients with high-to-intermediate risk pulmonary artery embolism.* Eur Heart J Acute Cardiovasc Care, 2015. **4**(4): p. 353-8.
- 15. Thomson, D., et al., *ECG in suspected pulmonary embolism.* Postgrad Med J, 2019. **95**(1119): p. 12-17.
- 16. Ferrari, E., et al., *The ECG in pulmonary embolism. Predictive value of negative T waves in precordial leads--80 case reports.* Chest, 1997. **111**(3): p. 537-43.
- 17. Digby, G.C., et al., *The value of electrocardiographic abnormalities in the prognosis of pulmonary embolism: a consensus paper.* Ann Noninvasive Electrocardiol, 2015. **20**(3): p. 207-23.
- 18. Kline, J.A., et al., *Prospective multicenter evaluation of the pulmonary embolism rule-out criteria.* J Thromb Haemost, 2008. **6**(5): p. 772-80.
- 19. Kline, J.A., et al., *Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism.* J Thromb Haemost, 2004. **2**(8): p. 1247-55.
- 20. Wolf, S.J., et al., *Prospective validation of Wells Criteria in the evaluation of patients with suspected pulmonary embolism.* Ann Emerg Med, 2004. **44**(5): p. 503-10.
- 21. Wells, P.S., et al., *Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer.* Ann Intern Med, 2001. **135**(2): p. 98-107.
- 22. Schouten, H.J., et al., *Diagnostic accuracy of conventional or age adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis.* BMJ, 2013. **346**: p. f2492.
- 23. Righini, M., et al., *Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study.* JAMA, 2014. **311**(11): p. 1117-24.
- 24. Sharp, A.L., et al., *An Age-Adjusted D-dimer Threshold for Emergency Department Patients With Suspected Pulmonary Embolus: Accuracy and Clinical Implications.* Ann Emerg Med, 2016. **67**(2): p. 249-57.
- 25. van der Hulle, T., et al., *Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study.* Lancet, 2017. **390**(10091): p. 289-297.

REFERENCES

- 26. Kabrhel, C., et al., *Multicenter Evaluation of the YEARS Criteria in Emergency Department Patients Evaluated for Pulmonary Embolism.* Acad Emerg Med, 2018. **25**(9): p. 987-994.
- 27. Rudski, L.G., et al., *Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography.* J Am Soc Echocardiogr,
- 2010. **23**(7): p. 685-713; quiz 786-8.
- 28. Kopecna, D., et al., *Interobserver reliability of echocardiography for prognostication of normotensive patients with pulmonary embolism.* Cardiovasc Ultrasound, 2014. **12**: p. 29.
- 29. Paczynska, M., et al., *Tricuspid annulus plane systolic excursion (TAPSE) has superior predictive value compared to right ventricular to left ventricular ratio in normotensive patients with acute pulmonary embolism.* Arch Med Sci, 2016. **12**(5): p. 1008-1014.
- 30. Daley, J., et al., *Emergency physician performed tricuspid annular plane systolic excursion in the evaluation of suspected pulmonary embolism.* Am J Emerg Med, 2017. **35**(1): p. 106-111.
- 31. Lobo, J.L., et al., *Prognostic significance of tricuspid annular displacement in normotensive patients with acute symptomatic pulmonary embolism.* J Thromb Haemost, 2014. **12**(7): p. 1020-7.
- 32. Alerhand, S. and S.M. Hickey, *Tricuspid Annular Plane Systolic Excursion (TAPSE) for Risk Stratification and Prognostication of Patients with Pulmonary Embolism.* J Emerg Med, 2020. **58**(3): p. 449-456.
- 33. McConnell, M.V., et al., *Regional right ventricular dysfunction detected by echocardiography in acute pulmonary embolism.* Am J Cardiol, 1996. **78**(4): p. 469-73.
- 34. Dwyer, K.H., J.S. Rempell, and M.B. Stone, *Diagnosing centrally located pulmonary embolisms in the emergency department using point-of-care ultrasound.* Am J Emerg Med, 2018. **36**(7): p. 1145-1150.
- 35. Kooiman, J., et al., *Randomised trial of no hydration vs. sodium bicarbonate hydration in patients with chronic kidney disease undergoing acute computed tomography-pulmonary angiography.* J Thromb Haemost, 2014. **12**(10): p. 1658-66.
- 36. Kooiman, J., et al., *No increase in Kidney Injury Molecule-1 and Neutrophil Gelatinase-Associated Lipocalin excretion following intravenous contrast enhanced-CT.* Eur Radiol, 2015. **25**(7): p. 1926-34.