Who you Gonna Call? Clot Busters! Thrombolytics for Pulmonary Embolism Induced Cardiac Arrest

UTAH SOCIETY OF HEALTH-SYSTEM PHARMACISTS

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Disclosure

- Relevant Financial Conflicts of Interest
  - **CE Presenter, Ashley Jackson, PharmD:**
    - No relevant conflicts of interest
  - **CE mentor, Helen Hou, PharmD, BCPS:**
    - No relevant conflicts of interest
- Off-Label Uses of Medications
  - Alteplase
  - Tenecteplase

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Learning Objectives

- **Pharmacists**:
  1. Explain the pathophysiology of cardiac arrest secondary to pulmonary embolisms (PE)
  2. Describe the role of thrombolytics in cardiac arrest secondary to PEs
  3. Identify patients with contraindications for thrombolytics
  4. Design a patient specific thrombolytic plan
- **Technicians**:
  1. Describe the mechanism of action (MOA) of thrombolytics
  2. Identify brand and generic names for common thrombolytics
  3. Demonstrate appropriate storage and handling requirements for thrombolytics

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Abbreviations

- PE – pulmonary embolism
- CA – Cardiac arrest
- MOA – Mechanism of action
- RA – Rheumatoid arthritis
- APS - Antiphospholipid syndrome
- RV – Right ventricle
- ROSC – Return of spontaneous circulation
- PEA - Pulseless electrical activity
- SWFI - Sterile Water for Injection
- CC – Chief complaint
- SOB – Shortness of breath

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Epidemiology

- Less than 5% of patients with acute PE progress to cardiac arrest
- Cardiac arrest secondary to PEs attributes to 5-13% of unknown CA a year
- 5-6% have been identified as definitive acute PEs in the hospital
- Mortality rate of CA secondary to a PE is 65-95%

Lavonas EJ, Drennan IR, Gabrielli A, et al: Part 10: Special circumstances of resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015; 132:S501–S518

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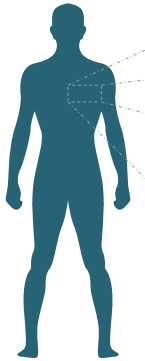
Pathophysiology



1) Increased RV Afterload
2) RV Dilation and Neurohormonal Activation
3) Decreased RV Output / Left Ventricle Preload
4) Decreased Cardiac Output
5) Cardiogenic Shock / Death

Lavonas EJ, Drennan IR, Gabrielli A, et al: Part 10: Special circumstances of resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015; 132:S501–S518
Rech, Megan A., Michelle Horng, Jenna M. Holzhausen, Megan A. Van Berkel, Sarah S. Sokol, Sarah Peppard and Drayton A. Hammond. "International Survey of Thrombolytic Use for Treatment of Cardiac Arrest Due toMassive Pulmonary Embolism." Critical Care Explorations 2, no. 6 (June 2020): e0132. https://do i.org/10.1097/CCE.0000000000000132.

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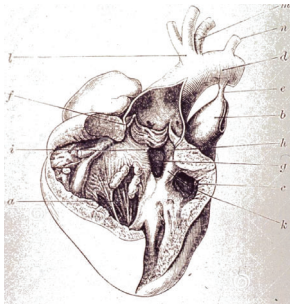
Symptoms of a Pulmonary Embolism

- Dyspnea at rest or with exertion
- Pleuritic pain
- Cough
- Orthopnea
- Calf or thigh pain and/or swelling
- Wheezing
- Hemoptysis
- Transient/persistent arrhythmias
- Syncope
- Hemodynamic instability



Goldhaber, Samuel Z., and Ruth B. Morrison. "Pulmonary Embolism and Deep Vein Thrombosis." *Circulation* 106, no. 12 (September 17, 2002): 1436–38. https://doi.org/10.1161/01.CIR.0000031167.64088.F6.

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Risk Factors for Pulmonary Embolisms

Transient Risk Factors
Surgery with general anesthesia for > 30 min
Hospitalized with an acute illness
Cesarean section
Estrogen therapy (eg, oral contraceptives, hormone replacement)
Pregnancy and puerperium
Leg injury with decreased mobility for ≥ 3 days

Chronic Risk Factors
Active cancer
Inflammatory bowel disease
Autoimmune disorders (eg, APS, RA)
Chronic infection
Chronic immobility (spinal cord injury)

Ortel et al., "American Society of Hematology 2020 Guidelines for Management of Venous Thromboembolism."

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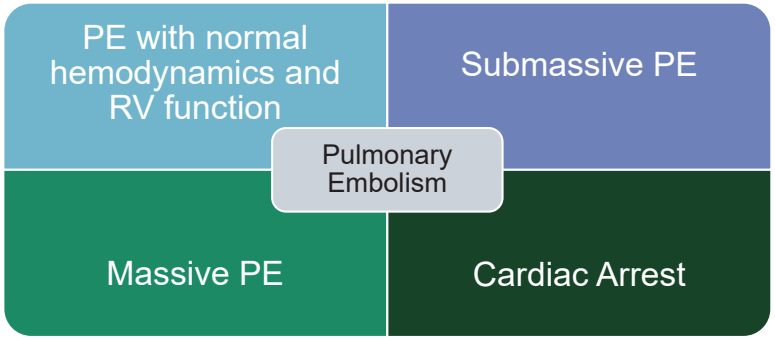
Pulmonary Embolism Stratification



Fengler, Brian T., and William J. Brady. "Fibrinolytic Therapy in Pulmonary Embolism: An Evidence-Based Treatment Algorithm." *The American Journal of Emergency Medicine* 27, no. 1 (January 2009): 84–95. https://doi.org/10.1016/j.ajem.2007.10.021.

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Diagnosing PEs in the setting of CA

- Difficult to diagnose a PE induced CA
  - Other cardiac or pulmonary diseases may cause signs of RV overload or dysfunction
- Use clinical history and assessment
  - Symptoms: dyspnea, pleuritic or substernal chest pain, cough, hemoptysis, syncope and signs of DVT (unilateral lower extremity swelling), past medical history, predisposing factors, and medications
- Capnography
  - Low ETCO2 readings (about 1.7 kPa/13 mmHg) while performing high quality chest compressions may support a diagnosis of PE
- Echocardiography

Lott, Carsten, Anatolij Truhlář, Annette Alfonzo, Alessandro Barelli, Violeta González-Salvado, Jochen Hinkelbein, Jerry P. Nolan, et al. "European Resuscitation Council Guidelines 2021: Cardiac Arrest in Special Circumstances." *Resuscitation* 161 (April 2021): 152–219. https://doi.org/10.1016/j.resuscitation.2021.02.011.

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Echocardiography Diagnostic Criteria for RV Dysfunction

- RV Wall Hypokinesis
- RV Dilatation
- Pulmonary Artery Hypertension
- Other Factors
  - Patent foramen ovale
  - Free-floating night-heat thrombus

Fengler, Brian T., and William J. Brady. "Fibrinolytic Therapy in Pulmonary Embolism: An Evidence-Based Treatment Algorithm." *The American Journal of Emergency Medicine* 27, no. 1 (January 2009): 84–95. https://doi.org/10.1016/j.ajem.2007.10.021.

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Thrombolytics in Pulmonary Embolism Induced Cardiac Arrest

- PE is a potentially reversible cause CA
- Chances for ROSC and survival may be significantly higher if a PE is present and can be treated is not well established
- Overall survival is low

Lott, Carsten, Anatolij Truhlář, Annette Alfonzo, Alessandro Barelli, Violeta González-Salvado, Jochen Hinkelbein, Jerry P. Nolan, et al. "European Resuscitation Council Guidelines 2021: Cardiac Arrest in Special Circumstances." *Resuscitation* 161 (April 2021): 152–219. https://doi.org/10.1016/j.resuscitation.2021.02.011.

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Adult Advanced Life Support Recommendations

Very Low Certainty Evidence

- Survival with favorable neurological outcome at 30 days
- Survival at 30 days
- Survival to hospital discharge

Treatment Recommendation:

Administer fibrinolytic drugs for cardiac arrest when PE is the suspected cause of cardiac arrest

(weak recommendation, very low-certainty evidence)

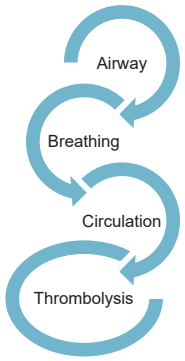
Berg, Katherine M., Jasmeet Soar, Lars W. Andersen, Bernd W. Böttiger, Sofia Cacciola, Clifton W. Callaway, Keith Couper, et al. "Adult Advanced Life Support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations." *Circulation* 142, no. 16_suppl_1 (October 20, 2020). https://doi.org/10.1161/CIR.0000000000000893.

Adult Advanced Life Support Recommendations

Recommendations for Pulmonary Embolism		
COR	**LOE**	**Recommendations**
2a	C-LD	1. In patients with confirmed pulmonary embolism as the precipitant of cardiac arrest, thrombolysis, surgical embolectomy, and mechanical embolectomy are reasonable emergency treatment options.
2b	C-LD	2.Thrombolysis may be considered when cardiac arrest is suspected to be caused by pulmonary embolism.

Magid, David J., Khalid Aziz, Adam Cheng, Mary Fran Hazinski, Amber V. Hoover, Melissa Mahgoub, Ashish R. Panchal, et al. "Part 2: Evidence Evaluation and Guidelines Development: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care." *Circulation* 142, no. 16_suppl_2 (October 20, 2020). https://doi.org/10.1161/CIR.0000000000000898.
Panchal, Ashish R., Jason A. Bartos, José G. Cabañas, Michael W. Donnino, Ian R. Drennan, Karen G. Hirsch, Peter J. Kudenchuk, et al. "Part 3: Adult Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care." *Circulation* 142, no. 16_suppl_2 (October 20, 2020). https://doi.org/10.1161/CIR.0000000000000916.

European Resuscitation Guidelines



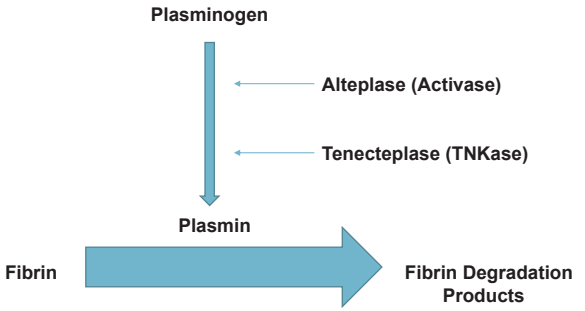
When a PE is the suspected cause of cardiac arrest, thrombolytic drugs should be administered

(weak recommendation, very low certainty of evidence)

Lott, Carsten, Anatolij Truhlář, Annette Alfonzo, Alessandro Barelli, Violeta González-Salvado, Jochen Hinkelbein, Jerry P. Nolan, et al. "European Resuscitation Council Guidelines 2021: Cardiac Arrest in Special Circumstances." *Resuscitation* 161 (April 2021): 152–219. https://doi.org/10.1016/j.resuscitation.2021.02.011.
When PE is the suspected cause of cardiac arrest thrombolytic drugs

MOA of Thrombolytics

- Initiates local fibrinolysis by binding to fibrin in a thrombus (clot) and converts entrapped plasminogen to plasmin



Alteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 5, 2022. Accessed February 4, 2022.
Tenecteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 28, 2022. Accessed February 4, 2022.

Pharmacokinetic and Pharmacodynamic Properties

Alteplase (Activase)

- Duration: >50% present in plasma cleared ~5 minutes after infusion terminated,
  - ~80% cleared within 10 minutes; fibrinolytic activity persists for up to 1 hour after infusion terminated
- Half-life elimination: Initial: 5 minutes

Tenecteplase (TNKase)

- Half-life elimination:
  - Biphasic:
    - Initial: 20 to 24 minutes;
    - Terminal: 90 to 130 minutes

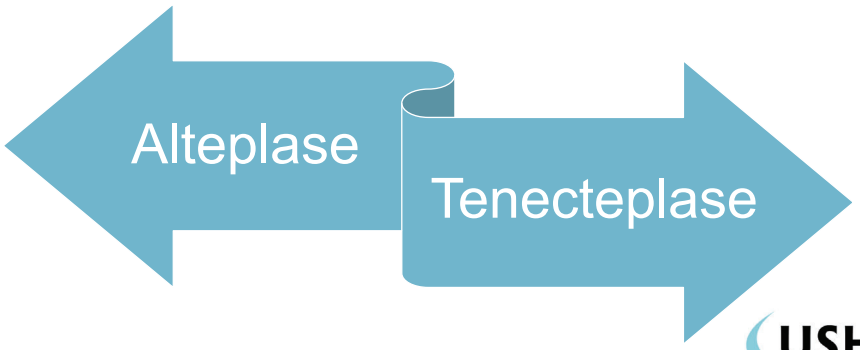
Alteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 5, 2022. Accessed February 4, 2022.
Tenecteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 28, 2022. Accessed February 4, 2022.

Contraindications

- Active internal bleeding (excluding menses)
- History of recent stroke within 3 months (expect when within 4.5 hours)
- Intracranial or intraspinal surgery
- Serious head trauma/facial trauma
- Presence of intracranial conditions that may increase the risk of bleeding (eg, intracranial neoplasm, arteriovenous malformation, aneurysm)
- Known bleeding diathesis
- Severe uncontrolled hypertension
- Suspected aortic dissection

Alteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 5, 2022. Accessed February 4, 2022.
Tenecteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 28, 2022. Accessed February 4, 2022.

Management of PE Induced CA



Pulmonary Embolism associated with cardiac arrest - Off-Label Use

Alteplase (Activase)

Initial: 50 mg bolus over 2 minutes and continue CPR; after 15 minutes, if return of spontaneous circulation is not achieved and medical team decides to continue CPR, repeat 50 mg bolus.

Followed by systemic anticoagulation

Tenecteplase (TNKase)

Administer as a single bolus:

<60 kg: 30 mg

≥60 to <70 kg: 35 mg

≥70 to <80 kg: 40 mg

≥80 to <90 kg: 45 mg

≥90 kg: 50 mg

Followed by systemic anticoagulation

Alteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 5, 2022. Accessed February 4, 2022.
Tenecteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 28, 2022. Accessed February 4, 2022.

Evidence Surrounding the Usage of Thrombolytics in Pulmonary Embolism induced Cardiac Arrest

2003 - Janata et al.

Design	Retrospective cohort study
Population	Patients admitted to the emergency department of a tertiary care university hospital with CA in the course of major pulmonary embolism (n = 67)
Intervention	Alteplase vs no thrombolytic
Purpose	Determine whether (1) thrombolytic treatment increases the risk of bleeding complications, (2) if the risk of bleeding is influenced by the duration of CPR and if (3) thrombolytic therapy improves outcome
Conclusion	• Major bleeding complications appear to occur more frequently in patients treated with thrombolytics (9/36 (25%) vs. 3/30 (10%)) • Intracerebral bleeding, retroperitoneal bleeding, bleeding into a body-cavity, a solid organ and any bleeding complication that required ≥ two transfusions or surgical intervention • ROSC could be achieved more often in patients who received alteplase (24/36 (67%) vs.13/30 (43%) • Survival to discharge was also higher in the thrombolytic group (7/36 (19%) vs. 2/30 (7%)) • Severe bleeding complications tend to occur more frequently in patients receiving thrombolytic, the benefit of this treatment might outweigh the risk of bleeding

Janata, Karin, Michael Holzer, Istepan Kürkciyan, Heidrun Losert, Eva Riedmüller, Branco Pikula, Anton N. Laggner, and Klaus Laczika. "Major Bleeding Complications in Cardiopulmonary Resuscitation: The Place of Thrombolytic Therapy in Cardiac Arrest Due to Massive Pulmonary Embolism." *Resuscitation* 57, no. 1 (April 2003): 49–55. https://doi.org/10.1016/S0300-9572(02)00430-6.

2016 - Sharifi et al. (PEAPETT Study)

Design	Retrospective, cohort study
Population	Adult patients with PEA and cardiopulmonary arrest due to confirmed massive PE (n = 23)
Intervention	50 mg of alteplase IV push over 1 minute
Purpose	Assess the effects of low dose tissue plasminogen activator on the clinical and echocardiographic outcomes of patients who had presented with PEA and cardiopulmonary arrest due to confirmed PE.
Conclusion	• ROSC occurred in all but one patient • No minor or major bleeding • Two patients died in the hospital, and at 22 ± 3 months of follow-up, 20 patients (87%) were still alive • Rapid administration of 50mg of tPA is safe and effective in ROSC in PEA due to massive PE leading to enhanced survival and a significant reduction in pulmonary artery pressures

Peppard, Sarah R., Ann M. Parks, and Jeffrey Zimmerman. "Characterization of Alteplase Therapy for Presumed or Confirmed Pulmonary Embolism during Cardiac Arrest." *American Journal of Health-System Pharmacy* 75, no. 12 (June 15, 2018): 870–75. https://doi.org/10.2146/ajhp170450.

2018 - Peppard et al.

Design	Multicenter, retrospective, cohort study
Population	Adults who received alteplase during PE-induced cardiac arrest at 16 medical centers (n = 35)
Intervention	Alteplase (bolus only, infusion only, bolus with infusion)
Purpose	Alteplase dosing characteristics, cardiopulmonary resuscitation survival, time to return of spontaneous circulation (ROSC), documented occurrence of major or minor bleeding, intensive care unit and hospital length of stay, and survival to discharge
Conclusion	• Two major bleeding events occurred in patients who received alteplase bolus with infusion and had ROSC • Patients received a cumulative alteplase dose of 100 mg • Three minor bleeding events (bolus only and infusion only category) • 46% of patients received alteplase by a bolus only dosing strategy • Patients receiving alteplase for presumed or confirmed PE during cardiac arrest, the most common treatment was an administration of a single 50-mg bolus of the thrombolytic agent

Peppard, Sarah R., Ann M. Parks, and Jeffrey Zimmerman. "Characterization of Alteplase Therapy for Presumed or Confirmed Pulmonary Embolism during Cardiac Arrest." *American Journal of Health-System Pharmacy* 75, no. 12 (June 15, 2018): 870–75. https://doi.org/10.2146/ajhp170450.

2019 - Javaudin et al.

Design	Retrospective, observational, multicenter study
Population	• Adults managed by a medical intensive care unit, with a diagnosis of pulmonary embolism confirmed on hospital admission (n = 246)
Intervention	• Fibrinolysis vs. no fibrinolysis • 14 (24%) received alteplase, 43 (74%) received tenecteplase, and one (2%) received streptokinase
Purpose	Primary end-point: 30-day survival, irrespective of Glasgow-Pittsburgh Cerebral Performance Categories Secondary-end point: Survival at 24 hours, length of stay in the ICU, and neurologic outcomes
Conclusion	• Thirty-day survival was higher in the thrombolysis group than in the control group (16% vs 6%; P= 0.005) • Good neurologic outcome was not significantly different (10%vs 5%; adjusted relative risk, 1.97; 95% CI, 0.70-5.56).

Javaudin, François, Jean-Baptiste Lascarrou, Quentin Le Bastard, Quentin Bourry, Chloé Latour, Hugo De Carvalho, Philippe Le Conte, et al. "Thrombolysis During Resuscitation for Out-of-Hospital Cardiac Arrest Caused by Pulmonary Embolism Increases 30-Day Survival." *Chest* 156, no. 6 (December 2019): 1167–75. https://doi.org/10.1016/j.chest.2019.07.015.
Patel, Jayshil J., and Paul A. Bergl. "Confirm, Don't Conform Toward Thrombolysis in Acute Pulmonary Embolism in Out-of-Hospital Cardiac Arrest." *Chest* 157, no. 5 (May 2020): 1396–97. https://doi.org/10.1016/j.chest.2019.12.045.

2021 - Kataria et al.

Design	Multicenter, retrospective, chart review
Population	Adults with suspected or confirmed PE who experienced a cardiac arrest (n = 27)
Intervention	Alteplase or tenecteplase
Purpose	Primary end-point: Survival to discharge Secondary end-point: Evaluated attainment of ROSC, dosing strategies utilized, and the incidence of major bleeding events
Conclusion	• Among the 11 patients (41%) with ROSC, two (7%) survived to hospital discharge • Confirmed PE, an initial presenting rhythm of pulseless electrical activity, and administration of alteplase within 5 minutes of cardiac arrest • Thrombolysis may have facilitated ROSC, but survival to hospital discharge was low

Kataria, Vivek, Kelsey Kohman, Ronald Jensen, and Adan Mora. "Usefulness of Thrombolysis in Cardiac Arrest Secondary to Suspected or Confirmed Pulmonary Embolism." *Baylor University Medical Center Proceedings* 34, no. 4 (July 4, 2021): 442–45. https://doi.org/10.1080/08998280.2021.1911494.

2021 - De Paz et al.

Design	Retrospective observational study
Population	Adults with confirmed or highly suspected PE as the primary cause of the CA and who had received with or without emergency thrombolysis (n = 16)
Intervention	Alteplase
Purpose	Compare the outcomes after cardiopulmonary-cerebral resuscitation (CCPR) with and without thrombolytic therapy (TT) in patients with CA secondary to PE
Conclusion	• ROSC occurred in 100% of patients who received TT and in 88% of non-thrombolysed patients • Mortality rate of patients who received TT and non-thrombolysed patients at 24 hours was 25% and 50% • At the time of hospital discharge, the mortality was the same in both groups (62%) • Intra-arrest thrombolysis resulted in a higher likelihood of ROSC and a higher 24-hour survival in adults with CA secondary to acute PE

De Paz, David, Julio Diez, Fredy Ariza, Diego Fernando Scarpetta, Jaime A Quintero, and Sandra Milena Carvajal. "Emergency Thrombolysis During Cardiac Arrest Due to Pulmonary Thromboembolism: Our Experience Over 6 Years." *Open Access Emergency Medicine* Volume 13 (February 2021): 67–73. https://doi.org/10.2147/OAEM.S275767.
Ewy, Gordon A. "Cardiocerebral and Cardiopulmonary Resuscitation - 2017 Update." *Acute Medicine & Surgery* 4, no. 3 (July 2017): 227–34. https://doi.org/10.1002/ams2.281.

2021 - Bakkum et al.

Design	Systematic review
Population	A search in PubMed was conducted for clinical studies evaluating thrombolytic therapy for PE or circulatory arrest
Intervention	Accelerated alteplase regimen of 0.6 mg/kg (max 50 mg) rtPA in 15 min vs 100 mg/ 2hours
Purpose	Define a regimen that is compatible with CPR (understanding the change in pharmacodynamics)
Conclusion	• A strong rationale is provided that the accelerated protocol is the regimen of choice for patients with PE-induced circulatory arrest

Bakkum, M.J., V.L. Schouten, Y.M. Smulders, E.J. Nossent, M.A. van Agtmael, and P.R. Tuinman. "Accelerated Treatment with RtPA for Pulmonary Embolism Induced Circulatory Arrest." *Thrombosis Research* 203 (July 2021): 74–80. https://doi.org/10.1016/j.thromres.2021.04.023..

What Dose Should We Use? Review of Current Literature

Dosing

Janata et al.
- Alteplase
  - Bolus of 0.6-1.0 mg/kg; 100 mg max

PEAPETT
- 50 mg of alteplase IV push over 1 minute

Peppard et al.
- Alteplase (one of the following):
  - 50 mg bolus only
  - 100 mg infusion only over 2 hours
  - 50 mg bolus with 50 mg infusion over 2 hours

Javaudin et al.
- Tenecteplase
  - Median dose, 45 mg
- Alteplase
  - Median dose, 50 mg

Dosing

Kataria et al.
- Five received alteplase 100 mg (bolus)
- Five received alteplase 50 mg (bolus)
- Tenecteplase dosing was unknown

De Paz et al.
- Alteplase
  - Dosing strategy is unknown

Bakkum et al.
- Alteplase
  - 0.6 mg/kg (max 50 mg) rtPA in 15 mins

Operational Considerations

Preparation

Alteplase

50 mg vial:

- Using aseptic technique, use a large-bore needle and syringe to withdraw 50 ml of SWIFI
- Insert the syringe into the stopper on the 50-mg vial of Activase and inject the contents, directing the stream into the lyophilized cake. DO NOT USE IF VACUUM IS NOT PRESENT.
- Mix the solution with a gentle swirl

Reconstituting guidelines for Activase® (alteplase). activase. https://www.activase.com/ais/dosing-and-administration/reconstituting.html. Accessed February 10, 2022.

Preparation

Alteplase

100 mg vial:

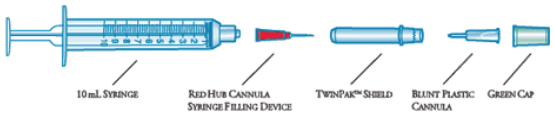
- Reconstitute alteplase (Activase) immediately before administration, using SWFI, U.S. Pharmacopeia (USP) and the transfer device.
- Mix by gentle swirling; <u>final concentration: 1 mg/mL.</u>

Reconstituting guidelines for Activase® (alteplase). activase. https://www.activase.com/ais/dosing-and-administration/reconstituting.html. Accessed February 10, 2022.

Preparation

Tenecteplase

- Remove the shield assembly from the supplied B-D 10 mL syringe with TwinPak™ Dual Cannula Device.
- Aseptically WITHDRAW 10 mL of Sterile Water for Injection, USP, using the B-D 10 mL syringe with TwinPak™ Dual Cannula Device included in the kit.
- INJECT entire contents (10 mL) into the TNKase vial, directing the diluent into the powder.
- GENTLY SWIRL until contents are completely dissolved.
- <u>Final concentration is 5 mg/mL</u>



TNKase® dosing, administration, and reconstitution. tnkase. https://www.tnkase.com/dosing-and-administration/dosing-administration-and-reconstitution.html#reconstitution-tnkase. Accessed February 11, 2022.

Avoid Medication Errors

- Do not use the abbreviation “TPA”
- Refer to all three tissue plasminogen activators by their brand names, generic names or both in communication
- Do not use “TNK” as an abbreviation for TNKase
- Remove the abbreviation “TPA” and “TNK” from all standardized order sets
- State the indication on prescription orders to help ensure the correct drug is ordered and dispensed
- Consider the use of alerts for TNKase in electronic prescriber order entry systems and/or automatic dispensing cabinets (e.g., “Warning: Frequently confused with Activase [alteplase], verify the correct drug for the appropriate indication”)

FDA advise-err: Avoid using the error-prone abbreviation, TPA. Institute For Safe Medication Practices. https://www.ismp.org/alerts/fda-advise-err-avoid-using-error-prone-abbreviation-tpa. Published September 24, 2015. Accessed February 6, 2022.
ISMP List of High-Alert Medications in Acute Care Settings. 2018. https://www.ismp.org/sites/default/files/attachments/2018-08/highAlert2018-Acute-Final.pdf

Storage

	Alteplase	Tenecteplase
Intact Vials: Room Temperature (not to exceed 30°C [86°F])	✔	✔
Intact Vials: Refrigeration (2°C to 8°C (36°F to 46°F))	✔	✔
Protect from Light	✔	✕
Reconstituted Vials	2°C to 30°C (36°F to 86°F) Use within 8 hours	Store in refrigerator immediately Use within 8 hours
Solutions	0.5 mg/mL, 1 mg/mL, and 2 mg/mL in SWI retained ≥94% of fibrinolytic activity at 48 hours when stored at 2°C in plastic syringes	✕

Alteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 5, 2022. Accessed February 4, 2022.
Tenecteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 28, 2022. Accessed February 4, 2022.
Alteplase [package insert]. San Francisco, CA: Genentech, Inc.; 2015.
Tenecteplase [package insert]. San Francisco, CA: Genentech, Inc.; 2018

Storage

Time Sensitive Medication

	Alteplase	Tenecteplase
Intact Vials: Room Temperature (not to exceed 30°C [86°F])	✔	✔
Intact Vials: Refrigeration (2°C to 8°C (36°F to 46°F))	✔	✔
Protect from Light	✔	✕
Reconstituted Vials	Use within 8 hours	Use within 8 hours
Solutions	0.5 mg/mL, 1 mg/mL, and 2 mg/mL in SWI retained ≥94% of fibrinolytic activity at 48 hours when stored at 2°C in plastic syringes	✕

Alteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 5, 2022. Accessed February 4, 2022.
Tenecteplase. Lexi-Drugs. Hudson, OH: Lexicomp, 2015. http://online.lexi.com/. Updated January 28, 2022. Accessed February 4, 2022.
Alteplase [package insert]. San Francisco, CA: Genentech, Inc.; 2015.
Tenecteplase [package insert]. San Francisco, CA: Genentech, Inc.; 2018

Spoilage

- Genentech Spoilage Replacement Program for alteplase and tenecteplase
  - Prescribed and prepared for a labeled indication, but not administered due to unforeseen patient clinical circumstances
- Retain all labeled syringes/bag and packaging
- Must complete Spoilage replacement Program Form

Replacement will not be shipped for following reasons:

Used for an off-label indication

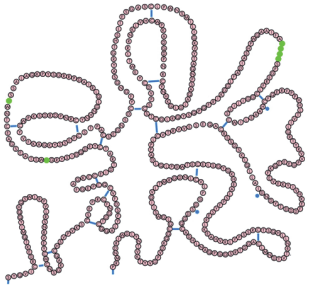
ANY portion used

Product return and replacement: Activase® (alteplase). activase. https://www.activase.com/ais/dosing-and-administration/product-return.html. Accessed February 12, 2022.

Handling

Pneumonic System Do Not Tube List

- Cost
- Drug Alteration
  - Purified glycoproteins
    - Tube system may denature protein



Pneumatic Tube Exceptions. Published March, 13, 2020. https://pulse.utah.edu/site/dirc/Documents/Help-Book/help-book-pneumatic-tube-exceptions.pdf#search=pneumatic%20system
https://www.researchgate.net/figure/The-molecular-structure-of-alteplase-56_fig5_259268866

Limitations

- Literature surrounding PE induced CA consists of small sample sizes
- Researches rarely provided definitions for IV bolus in their studies

Barriers to Care

- CA induced PE requires timely diagnostics and retrieval of drug
  - Requires a physician diagnosis
  - Thrombolytics are not stored in crash carts
  - Pharmacists will often leave a code to acquire drug and compound at the bedside
    - Timely administration requires close communication between the physician and the pharmacist
  - Shortages
    - Monitor for drug shortages using the Drug Information Center and Pharmacy Purchasing team

Summary

A pulmonary embolism is a potentially reversible cause of cardiac arrest

Thrombolytics may be administered in patients with PE induced CA

Use a patient's clinical history and assessment to diagnosis a PE

Thrombolytics may facilitate ROSC and improve patient outcomes

Pharmacists and pharmacy technicians play a key role in patient care

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