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Pulmonary Embolism (PE) Low Risk	→ NO Need to Contact PERT Te	eam
Pulmonary Embolism (PE) Intermediate Risk	See Pages 2 - 3	
Pulmonary Embolism (PE) High Risk	→ See Page 4	
APPENDIX A: Classifications of	f Pulmonary Embolism (PE) Pa	age 5
APPENDIX B: Considerations for	or Pediatric Patients Pa	age 6
APPENDIX C: Criteria for After	r Hours STAT 2D-ECHO Pa	age 7
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INITIAL EVALUATION – INTERMEDIATE RISK¹

TREATMENT



SBP = systolic blood pressure AMS= altered mental status

¹See Appendix A: Classifications of Pulmonary Embolism ² PERT First Responder: On-Call fellow/trainee and attending provider ³See Appendix C: Criteria for After Hours STAT 2D-ECHO ⁴See Appendix D: Contraindications to Anticoagulation Therapy ⁵PESI score calculators:

https://www.mdcalc.com/pulmonary-embolism-severity-index-pesi or https://www.mdapp.co/pulmonary-embolism-severity-index-pesi-score-calculator-118 ^bCriteria to consider for placement of a retrievable filter:

• If temporary/limited time ($\leq 2-3$ months) of contraindication to anticoagulants

- Greater than 6 months survival expected
- Performance Status ≤ 1

⁷Refer to GCC home page (for internal use only)

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Approved by The Executive Committee of the Medical Staff on 04/18/2023

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APPENDIX A: Classifications of Pulmonary Embolism (PE)

Risk Levels	Classifications		
Low Risk	 No hypotension <u>and</u> No RV dysfunction <u>and</u> No myocardial necrosis or strain 		
Low-Intermediate Risk	 RV dysfunction by CT or ECHO <u>or</u> Myocardial necrosis or strain (elevated Troponin T or NT-proBNP) 		
High-Intermediate Risk	 RV dysfunction by CT or ECHO and Myocardial necrosis or strain (elevated Troponin T or NT-proBNP) and/or Absence of signs of hypotension or shock 		
High Risk	 • Sustained hypotension (SBP less than 90 mmHg) at least 15 minutes or • Persistent bradycardia (HR less than 40 bpm) or signs and symptoms of shock or • Need for inotropic support 		

RV = right ventricular

SBP = systolic blood pressure

HR = heart rate

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APPENDIX B: Considerations for Pediatric Patients (< 18 years old)

- PESI score was not validated in pediatric patients. To determine PE risk category, level of care, and management consult general pediatrics. For unstable patients, contact the pediatric intensive care unit provider.
- If heparin is used in the management of pediatric patients, refer to the Pediatric Treatment of VTE with Unfractionated Heparin Infusion order set
- The preferred LMWH in pediatric patients is enoxaparin 1 mg/kg subcutaneous every 12 hours. Doses should be held for platelets < 30 K/microliter
- Dosing of alteplase for pediatrics patients: 0.5 mg/kg/hour IV infusion over 6 hours
- Vital sign considerations for pediatric patients:

Age	Normal awake Heart Rate Beats/minute	Normal Respiratory Rate Breaths/minute	Definition of Hypotension
Newborn (up to 1 month)	100-205	30-53	SBP < 60 (applies to 0 to 28 days)
Infant (1 - 12 months)	100-180	30-53	SBP < 70 (applies to 1 - 12 months)
Toddler (1 - 2 years)	98-140	22-37	SBP $< 70 + (age in years x 2)$ (applies to 1 - 10 years)
Preschooler (3 - 5 years)	80-120	20-28	SBP $< 70 + (age in years x 2)$ (applies to 1 - 10 years)
Child (6 - 11 years)	75-118	18-25	SBP < 70 + (age in years x 2) (applies to 1 - 10 years)
Adolescent (12 - 18 years)	60-100	12-20	SBP < 90 (applies to > 10 years)

LMWH = low molecular weight heparin SBP = systolic blood pressure

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APPENDIX C: Criteria for After Hours STAT 2D-ECHO

Criteria • Patient has to be seen first by a member of the PERT team in order to confirm that none of the other imaging modalities are possible (CT angiogram or ventilation-perfusion (VQ) scan) • Patient is hemodynamically unstable (systolic blood pressure (SBP) < 90 mmHg or receiving vasopressors) • Pulmonary embolism (PE) has to be highly suspected and no other etiology would explain shock (no septic, hemorrhagic or hypovolemic shock)

• PERT team member is to contact and discuss directly the need of the echo with the cardiologist on-call before sonographer is contacted

APPENDIX D: Contraindications to Anticoagulation Therapy

 • Major active bleeding (e.g., bleeding requiring ≥ 2 units of packed red blood cells (PRBC) transfusion, decrease in hemoglobin ≥ 2 g/dL, or bleeding in a critical area or organ) • Brain metastases conferring risk of bleeding (renal, choriocarcinoma, melanoma, thyroid • Intracranial or central nervous system (CNS) bleeding within the past 4 weeks • Recent high-risk surgery or bleeding event 	
 Platelet < 25 K/microliter, consult to benign hematology Spinal procedure and/or epidural placement (unless approved by Acute Pain or other appropriate provider) Severe uncontrolled malignant hypertension Active but non-life threatening bleeding Active GI ulceration at high risk of bleeding Platelets < 50 K/microliter, consider consult to benign hematology Patient currently on active protocol that prohibits the use of anticoagulation 	cancer)

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APPENDIX E: Low Molecular Weight Heparin (LMWH)¹ Regimens for Treatment of Cancer Associated Thrombosis

DRUG	DOSE / ROUTE / FREQUENCY		EQUENCY	MONITORING ²	DOSE ADJUSTMENTS
Dalteparin (Fragmin [®])*	Round to nea dose, given s	rest Internati ubcutaneous	onal Units (IU) ly daily	• Baseline: hemoglobin (hgb)/ hematocrit (hct), platelet count,	 <u>Platelets</u>: Consider reducing the daily dose by 2,500 units when platelets are between 50,100 K/microliter and exercise in comparison of the providence of the provi
 *FDA approved for cancer patients • Hold in patients with platelets < 25 K/microliter 	Actual Body Weight (kg) ≤ 56 57-68 69-82 83-98	Month 1 200 IU/kg 10,000 IU 12,500 IU 15,000 IU 18,000 IU	Months 2-6 150 IU/kg 7,500 IU 10,000 IU 12,500 IU 15,000 IU	 Surgical inpatient: hgb/hct and platelet count every 24 hours after starting the LMWH and then every 3 days from day 4-14 unless the LMWH is stopped, or patient is discharged. After day 14, hgb/hct and platelet count at least once weekly. Medical inpatient: hgb/hct and 	 S0-100 K/Interofiter and use with caution in cancer patients when platelets are < 50 K/ microfiter For platelet count < 25 K/microfiter, hold dalteparin <u>Renal</u>: If creatinine clearance (CrCl) < 30 mL/minute: adjust dose to obtain anti-Xa level of 0.5-1.5 IU/mL (4-6 hours after fourth dose). Recommend avoiding if CrCl < 20 mL/minute <u>Weight</u>: Consider obtaining anti-Xa level in patients weighing > 150 kg or < 50 kg, or BMI ≥ 40 kg/m² and adjust dose to obtain anti-Xa level of 0.5-1.5 IU/mL (4-6 hours after fourth dose).
	≥ 99	Consider monitoring anti-Xa levels and adjust dose as needed. Limited data suggests dalteparin 200 IU/kg based on actual body weight (with no dose capping) in one or two divided doses ³ . An alternative option is enoxaparin 1 mg/kg twice daily (see below).			
Enoxaparin (Lovenox [®]) • Hold in patients with platelets < 25 K/microliter	 1 mg/kg subcutaneously every 12 hours Limited data suggest once per day dosing is inferior in cancer patients and may increase risk of bleeding Limited data suggest dose of 0.75-0.85 mg/kg every 12 hours in obese patients (BMI ≥ 40 kg/m²) 			Same as above	 <u>Platelets</u>: Limited data suggest the following enoxaparin dose modification: For platelet count > 50 K/microliter: full-dose, 1 mg/kg twice daily For platelet count 25-50 K/microliter: half-dose, 0.5 mg/kg twice daily For platelet count < 25 K/microliter, hold all anticoagulants Renal: If CrCl < 30 mL/minute: 1mg/kg daily. Recommend avoiding if CrCl < 20 mL/minute Weight: Consider obtaining anti-Xa level in patients weighing > 150 kg or < 50 kg, or BMI ≥ 40 kg/m² For 1 mg/kg every 12 hour dosing regimen: adjust dose to obtain anti-Xa level of 0.6-1 IU/mL (4-6 hours after fourth dose)

¹ Notes:

• Patients who tolerate anticoagulation should be continued on it indefinitely or until active cancer resolves

• Patient should be observed closely for bleeding and signs and symptoms of neurological impairment if therapy is administered during or immediately following diagnostic lumbar puncture, epidural anesthesia, or spinal anesthesia

² If lab results indicate heparin induced thrombocytopenia, follow management guideline per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm

³ Multi-dose vials not recommended for home use

Department of Clinical Effectiveness V4 Approved by The Executive Committee of the Medical Staff on 04/18/2023

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APPENDIX F: Contraindications to Systemic Thrombolysis

Absolute Contraindications:	Relative Contraindications:
 Active bleeding History of hemorrhagic stroke or stroke of unknown origin Intracranial tumor Ischemic stroke in previous 3 months (if ischemic stroke onset within 4.5 hours, see Management of Acute Ischemic Stroke in Hospitalized Adult Patients algorithm) Recent brain or spinal surgery¹ and/or head or facial trauma Suspected or confirmed aortic dissection Platelet count below 100 K/microliter 	 Age > 75 years old Pregnancy or first post-partum week Non-compressible puncture sites Traumatic cardiopulmonary resuscitation Recent major surgery, invasive procedure, and/or trauma (within 1 month) Refractory hypertension (SBP > 180 mmHg, DBP > 110 mmHg) Known bleeding diathesis or acquired coagulopathy Significant non-intracranial bleeding within 1 month Life expectancy ≤ 6 months

SBP = systolic blood pressure

DBP = diastolic blood pressure

¹ Discussion with neurosurgery for recent brain or spinal surgery

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SUGGESTED READINGS

- Aujesky, D., Obrosky, D. S., Stone, R. A., Auble, T. E., Perrier, A., Cornuz, J., ... Fine, M. J. (2005). Derivation and validation of a prognostic model for pulmonary embolism. American Journal of Respiratory and Critical Care Medicine, 172(8), 1041-1046. doi: 10.1164/rccm.200506-862OC
- Chan, C. M., Woods, C., & Shorr, A. F. (2010). The validation and reproducibility of the pulmonary embolism severity index. Journal of Thrombosis and Haemostasis, 8(7), 1509-1514. doi:10.1111/j.1538-7836.2010.03888.x
- Douketis, J. D., Spyropoulos, A. C., Spencer, F. A., Mayr, M., Jaffer, A. K., Eckman, M. H., ... Kunz, R. (2012). Perioperative management of antithrombotic therapy. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, 141(2 suppl), e326S-e350S. doi:10.1378/chest.11-2298
- Kabrhel, C., Jaff, M. R., Channick, R. N., Baker, J. N., & Rosenfield, K. (2013). A multidisciplinary pulmonary embolism response team. Chest, 144(5), 1738-1739. doi:10.1378/chest.13-1562
- Konstantinides, S. V., Torbicki, A., Agnelli, G., Danchin, N., Fitzmaurice, D., Galiè, N., ... Spyropoulos, A. C. (2014). 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism: The task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). European Heart Journal, 35(43), 3033-3080. doi:1093/eurheartj/ehu283
- Kucher, N., Boekstegers, P., Müller, O. J., Kupatt, C., Beyer-Westendorf, J., Heitzer, T., ... Baumgartner, I. (2013). Randomized, controlled trial of ultrasound-assisted catheterdirected thrombolysis for acute intermediate-risk pulmonary embolism. Circulation, 129(4), 479-486. doi:10.1161/CIRCULATIONAHA.113.005544
- MDApp. (2017). Pulmonary embolism severity index (PESI) score. Retrieved from https://www.mdapp.co/pulmonary-embolism-severity-index-pesi-score-calculator-118/
- MD+CALC. (n.d.). Pulmonary embolism severity index (PESI). Retrieved from https://www.mdcalc.com/pulmonary-embolism-severity-index-pesi
- National Comprehensive Cancer Network. (2022). Cancer-associated venous thromboembolic disease (NCCN Guideline Version 1.2022). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf
- Piazza, G., Hohlfelder, B., Jaff, M. R., Ouriel, K., Engelhardt, T. C., Sterling, K. M., ... Goldhaber, S. Z. (2015). A prospective, single-arm, multicenter trial of ultrasoundfacilitated, catheter-directed, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: The SEATTLE II study. JACC: Cardiovascular Interventions, 8(10), 1382-1392. doi:10.1016/j.jcin.2015.04.020
- Piran, S., Le Gal, G., Wells, P. S., Gandara, E., Righini, M., Rodger, M. A., & Carrier, M. (2013). Outpatient treatment of symptomatic pulmonary embolism: A systematic review and meta-analysis. Thrombosis Research, 132(5), 515-519. doi:10.1016/j.thromres.2013.08.012
- Quintana, D., Salsamendi, J., Fourzali, R., & Narayanan, G. (2014). Ultrasound-assisted thrombolysis in submassive and massive pulmonary embolism: Assessment of lung obstruction before and after catheter-directed therapy. Cardiovascular and Interventional Radiology, 37(2), 420-426. doi:10.1007/s00270-013-0696-x
- Rivera-Lebron, B., McDaniel, M., Ahrar, K., Alrifai, A., Dudzinski, D. M., Fanola, C., ... Channick, R. (2019). Diagnosis, treatment and follow up of acute pulmonary embolism: Consensus practice from the PERT Consortium. Clinical and Applied Thrombosis/Hemostasis, 25, 1-16. doi:10.1177/1076029619853037

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This practice consensus statement is based on majority expert opinion of the PERT work group at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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