Oral Bleeding Emergency Management

PRESENTATION

Patient presents with oral bleeding[1]

INITIAL EVALUATION

Is the patient in respiratory distress[2] and/or hemodynamic instability[3]?

Yes

Perform resuscitation measures:
- Provide oxygen support[4] and intubate if needed
- Direct tamponade for visualized bleed
- Labs: CBC, CMP, PT with INR, aPTT, d-dimer, fibrinogen, type and screen, lactic acid, POC hemoglobin and hematocrit (if available)
- Establish IV access (2 large bore IV catheters)
- IV fluids
- Blood transfusion[5]
- Reverse coagulopathy[6]
- Rapid history and exam

Is the patient stable?

No

- Continue resuscitation measures (ACLS)
- Initiate a Goal Concordant Care (GCC) conversation[7] with the patient, or if clinically indicated, with the Patient Representative and the Primary Oncologist/Primary Team/ Attending Physician. The Advance Care Planning (ACP) note should be used to document GCC discussion.
- Protect airway
- Consult Anesthesia and/or Head and Neck Surgery for possible surgical airway
- Consider transfer to ICU or higher level of care or palliative unit as clinically indicated and as consistent with the patient's GCC

Yes

No

- Complete history and physical exam
- Direct tamponade of visible bleed
- Labs (including type and screen)
- Chest x-ray
- Initiate a Goal Concordant Care (GCC) conversation[7] with the patient or if clinically indicated, with the Patient Representative and the Primary Oncologist/ Primary Team/Attending Physician. The Advance Care Planning (ACP) note should be used to document GCC discussion.

Assess for the source of the bleed

DISPOSITION

Upper respiratory bleed
- Direct visualization of bleed in the nose or mouth → See Page 2
- Choking, coughing, epistaxis, hematemesis[8]

Lower respiratory bleed
- SOB, coughing, wheezing → See Page 2
- Hemoptysis

Gastrointestinal (GI) bleed
- Hematemesis[8] → See Page 3
- Melena

Unknown source of bleed → Consider consultation from Pulmonary, GI, and Thoracic Surgery as clinically indicated

ACLS = advanced cardiovascular life support
SOB = shortness of breath
DNR = do not resuscitate

[1] Bleeding from the oral cavity, nose, and/or stoma site (*e.g.* tracheostomy or laryngostoma)
[2] Respiratory failure: need > 50% FiO_2 to maintain oxygen saturation of 90%, increased work of breathing, respiration rate > 30 breaths/minute. Acute hypercapnic respiratory failure: $PaCO_2$ > 45 mmHg with pH < 7.35.
[3] Hemodynamic instability: heart rate > 110 beats/minute, systolic blood pressure < 90 mmHg, inability to protect airway, Glasgow Coma Scale (GCS) < 13
[4] Avoid using a face mask if the patient continues to have heavy oral bleed
[5] If the patient is actively bleeding and unstable, obtain untyped and uncrossmatched blood. If vitals are stable and patient is not actively bleeding, wait for hemoglobin and hematocrit results then transfuse for hemoglobin < 7 g/dL.
[6] Consider tranexamic acid 1g (consider topical or inhalation as necessary); fresh frozen plasma (FFP); platelets; cryoprecipitate; specific reversal agents for anticoagulation (see Appendix A). Providers may refer to the Emergency Anticoagulation Reversal Order Set in OneConnect or refer to the Anticoagulation Stewardship: Bleeding Complications page (for internal use only) for additional references. Consult Benign Hematology for treatment of hemostatic defects (see Appendix B).
[7] Refer to GCC home page (for internal use only)
[8] Head and Neck sentinel bleed may present as hematemesis. Hematemesis does not always equal GI bleed for Head and Neck patients.

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Oral Bleeding Emergency Management

ASSESSMENT

Respiratory source

- Assess for head and neck tumor
- CTA head and neck with contrast
- Consider risk factors for sentinel bleed (*e.g.,* carotid or innominate):
  - Neck surgery
  - Radiation therapy
  - Tracheostomy
  - Laryngectomy
  - Targeted therapy (*i.e.,* VEGF inhibitors)
  - Anticoagulation therapy
- Assess for lung lesions or chest mass
- CT chest with contrast
- Consider risk factors for hemoptysis:
  - Lung cancer
  - Mediastinal mass
  - Tracheal tumor
  - Anticoagulation therapy
  - Lung metastasis
  - Pulmonary embolism
  - Tuberculosis
  - Fungal pneumonia
  - Radiation therapy to the lung or mediastinal area
- Initiate a Goal Concordant Care (GCC) conversation[1] with the patient or if clinically indicated, with the Patient Representative and the Primary Oncologist/ Primary Team/Attending Physician. The Advance Care Planning (ACP) note should be used to document GCC discussion.

CTA = computed tomography angiography VEGF = vascular endothelial growth factor

TREATMENT

Upper airway

Consult Head and Neck Surgery
- Head and Neck Surgery may consider consulting Interventional Radiology (IR) for possible embolization

Lower airway

Massive hemoptysis[2]?

Yes

- Provide supplemental oxygen[3]
- Intubate if needed
- Place on lateral decubitus with bleeding side down if known
- Tranexamic acid 1g IV for one dose
- Consult Pulmonary Medicine and speak with the pulmonary interventionist on-call
- Consult IR for embolization
- Consult Thoracic Surgery if patient is unstable, intubated, or recommended by Pulmonary Medicine

No

Moderate volume[4] of blood:
- Consult Pulmonary Medicine

Minimal volume[5] of blood:
- Consider an ambulatory referral to Cardiopulmonary Center if the patient is discharged

DISPOSITION

Admit patient to ICU or an acute care floor or palliative care unit as clinically indicated and as consistent with patient's GCC

Admit patient to ICU

Admit patient to an acute care floor

Disposition as clinically indicated

[1] Refer to GCC home page (for internal use only)

[2] Defined by bleeding volume, respiratory failure or hemodynamic instability:
- Volume of blood > 500 mL in 24 hours or > 200 mL in 1 hour
- Respiratory failure: need of > 50% FiO_2 to maintain oxygen saturation of 90%, increased work of breathing, respiration rate > 30 breaths/minute
- Acute hypercapnic respiratory failure: $PaCO_2$ > 45 mmHg with pH < 7.35
- Hemodynamic instability: heart rate > 110 beats/minute, systolic blood pressure < 90 mmHg, inability to protect airway, GCS < 13

[3] Avoid using a face mask if the patient continues to have heavy oral bleed

[4] Moderate volume is between less than massive hemoptysis (> 500 mL in 24 hours or > 200 mL in 1 hour) and more than blood tinged sputum

[5] Minimal volume is blood tinged sputum

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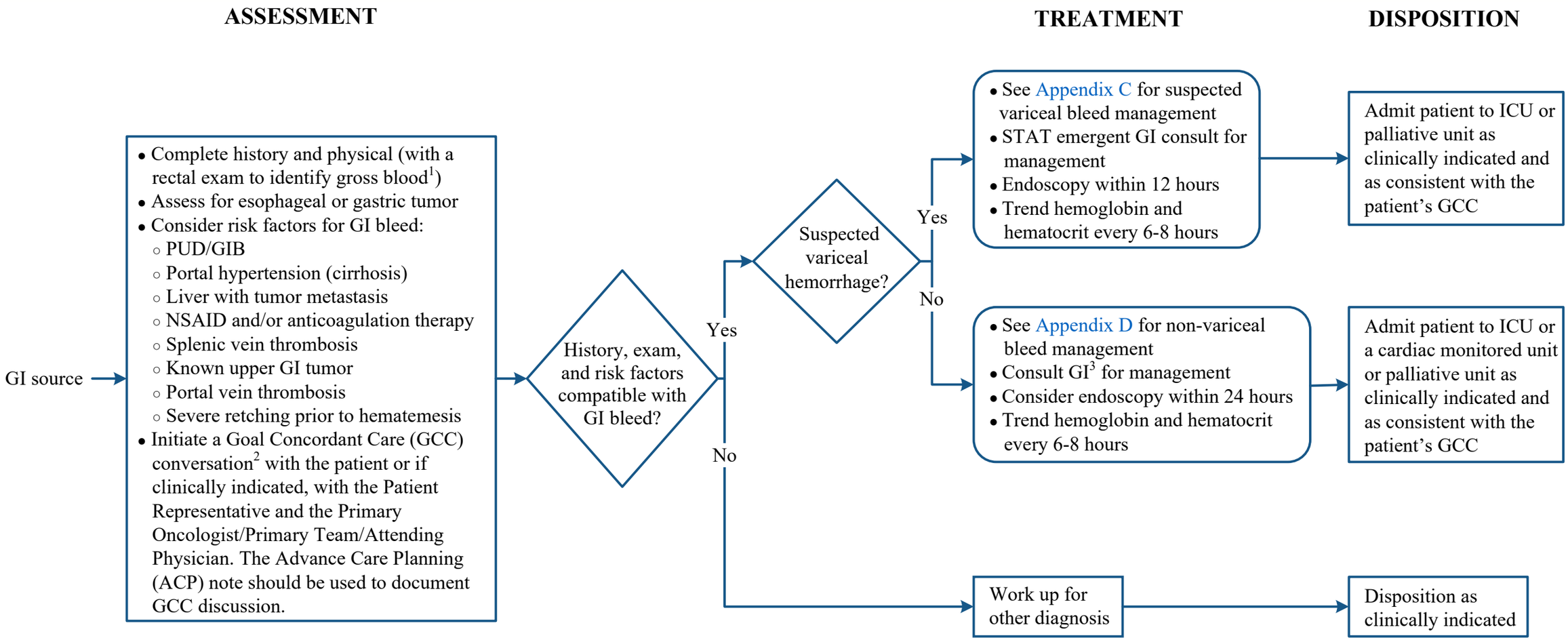
Oral Bleeding Emergency Management

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*



PUD/GIB = peptic ulcer disease/gastrointestinal bleed
NSAID = nonsteroidal anti-inflammatory drug

[1] Fecal occult blood test is not needed for oral bleeding workup
[2] Refer to GCC home page (for internal use only)
[3] If patient is unstable and vomiting blood, place STAT urgent GI consult. If the patient is stable, place routine GI consult after the patient is admitted or at the discretion of the inpatient team.

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Oral Bleeding Emergency Management

APPENDIX A: Reversal of Anticoagulants

<table>
<tr><th>Anticoagulant</th><th>Recommended Treatment</th></tr>
<tr><td>Warfarin</td><td>
• Administer prothrombin complex concentrate (Kcentra®) IVPB based on INR and actual body weight:
<table>
<tr><th>INR</th><th>Dosage</th><th>Maximum Dose</th></tr>
<tr><td>2-3.9</td><td>25 units/kg</td><td>2,500 units</td></tr>
<tr><td>4-6</td><td>35 units/kg</td><td>3,500 units</td></tr>
<tr><td>> 6</td><td>50 units/kg</td><td>5,000 units</td></tr>
</table>
• Consider using ideal or adjusted body weight for obese patients
• Add vitamin K 10 mg IV at 1 mg/minute for 1 dose for prolonged reversal of warfarin
• If prothrombin complex concentrate (Kcentra®) is not available or if INR is not supratherapeutic (e.g., ≤ 3), use fresh frozen plasma 15 mL/kg; may use 5-8 mL/kg for urgent reversal
</td></tr>
<tr><td>Dabigatran</td><td>
• Administer activated charcoal 25-50 grams oral or via nasogastric tube for one dose if ingested within the previous 2 hours
• Administer idarucizumab 2.5 grams IV for two doses
• Consider one repeated dose of idarucizumab if absence of specific test to measure dabigatran plasma concentration
• Consider hemodialysis for life-threatening bleeds
</td></tr>
<tr><td>Apixaban or rivaroxaban</td><td>
• Administer activated charcoal 25-50 grams oral or via nasogastric tube for one dose if ingested within the previous 2 hours
• Andexanet alfa: If last dose of apixaban or rivaroxaban was given within 18 hours.
<table>
<tr><th rowspan="2">FXa Inhibitor</th><th rowspan="2">FXa Inhibitor Last Dose</th><th colspan="2">Timing of FXa Inhibitor Last Dose Before Andexanet Alfa Initiation</th></tr>
<tr><th>< 8 hours or unknown</th><th>≥ 8 hours</th></tr>
<tr><td rowspan="2">Apixaban</td><td>≤ 5 mg</td><td>Low dose</td><td rowspan="4">Low dose</td></tr>
<tr><td>> 5 mg/unknown</td><td>High dose</td></tr>
<tr><td rowspan="2">Rivaroxaban</td><td>≤ 10 mg</td><td>Low dose</td></tr>
<tr><td>> 10 mg/unknown</td><td>High dose</td></tr>
</table>
Low dose: 400 mg IV bolus, followed by 4 mg/minute IV infusion for up to 120 minutes
High dose: 800 mg IV bolus, followed by 8 mg/minute IV infusion for up to 120 minutes
• If last dose of apixaban or rivaroxaban given is > 18 hours, andexanet alfa may be given if compelling indication necessitating reversal is present (e.g., acute renal failure or overdose)
• If andexanet alfa is not available, administer prothrombin complex concentrate (Kcentra®) 25 units/kg (maximum dose 2,500 units) to 50 units/kg (maximum dose 5,000 units) IVPB based on actual body weight. Consider using ideal or adjusted body weight for obese patients.
</td></tr>
</table>

Continued on next page

Oral Bleeding Emergency Management

APPENDIX A: Reversal of Anticoagulants - continued

Anticoagulant	Recommended Treatment
Edoxaban[1] or betrixaban[1]	• Administer activated charcoal 25-50 grams oral or via nasogastric tube for one dose if ingested within the previous 2 hours • Administer prothrombin complex concentrate (Kcentra®) 25 units/kg (maximum dose 2,500 units) to 50 units/kg (maximum dose 5,000 units) IVPB based on actual body weight. Consider using ideal or adjusted body weight for obese patients.
Heparin	• Administer 1 mg of protamine IV for every 100 units of IV heparin given over the last 2-2.5 hours • Single doses should not exceed 50 mg • Consider repeat dosing if continued bleeding or a prolonged aPTT
Enoxaparin or dalteparin	• Administer 1 mg of protamine IV for every 100 units of dalteparin or 1 mg of enoxaparin given within the previous 8 hours • Administer 0.5 mg of protamine IV for every 100 units of dalteparin or 1 mg of enoxaparin given in the previous 8 to 12 hours • Single doses of protamine should not exceed 50 mg • Consider coagulation factor VIIa recombinant 20 mcg/kg IV for one dose
Fondaparinux	• Administer prothrombin complex concentrate (Kcentra®) 25 units/kg (maximum dose 2,500 units) to 50 units/kg (maximum dose 5,000 units) IVPB based on actual body weight. Consider using ideal or adjusted body weight for obese patients. • Consider coagulation factor VIIa recombinant 20 mcg/kg IV for one dose

[1] Non-formulary

APPENDIX B: Hemostatic Defect

Note: Consult Benign Hematology for an inherited or acquired coagulopathy

Hemostatic Finding	Recommended Treatment	
• Disseminated Intravascular Coagulation (DIC) • Hepatic dysfunction	Fresh frozen plasma (10-15 mL/kg) with ideal recovery would raise factor levels 15-20%	Target INR ≤ 1.3
Vitamin K deficiency	Vitamin K 10 mg IV at 1 mg/minute daily	
Fibrinogen < 150 mg/dL	Cryoprecipitate 1 unit/5 kg up to a total dose of 10 units (target fibrinogen ≥ 150 mg/dL)	
Congenital Factor VII deficiency	Recombinant Factor VII activated 15-30 mcg/kg every 4-6 hours (not recommended for spontaneous intracerebral hemorrhage (ICH) without Factor VII deficiency or oral anticoagulant reversal). Dose ranges from 10-90 mcg/kg based on indication and severity of bleeding.	
Factor VIII deficiency (Hemophilia A)	• Each Factor VIII unit raises plasma Factor VIII levels by 2% [50 units/kg used to raise levels to 100% (80-100 international units/dL)] • Target Factor VIII activity level of 100 international units/dL and maintain level of 50% for 7-10 days (a variety of Factor VIII products are available)	
Factor IX deficiency (Hemophilia B)	• Each Factor IX unit raises plasma Factor IX levels by 1% [100 units/kg used to raise levels to 100% (60-80 international units/dL)] • Target Factor IX activity level of 100 international units/dL and maintain level of 50% for 7-10 days (a variety of Factor VIII products are available)	
Von Willebrand Disease	Target von Willebrand Ristocetin Cofactor (VWF:RCo) and Factor VIII activity levels of 100 international units/dL and maintain levels of 50% for 7-10 days. It is suggested to avoid Factor VIII activity levels of > 200 international units/dL as it is associated with increased risk of venous thrombosis. Use Humate-P® or Alphanate®, begin 40-60 international units VWF:RCo/kg.	
Thrombocytopenia	Ideal target platelet count of 30-50 K/microliter (unless major bleeding) in patients who are not refractory to platelets. Each unit transfused should increase platelet count by 5-10 K/microliter.	

APPENDIX C: Suspected Variceal Bleed Management

Resuscitation
- IV fluids
- Blood product transfusion
  - Transfuse PRBC for a hemoglobin goal of 7 g/dL (over-transfusing can increase intravenous hydrostatic pressure, leading to more bleeding). May consider a higher target if history of cardiac/comorbidities.
  - Transfuse platelet or plasma
  - Avoid over-transfusion due to concern for increasing portal hypertension
- Hold diuretics and beta blockers

Antithrombotic Management
- Consider consulting Benign Hematology
- Hold anticoagulants
- Consider holding anti-platelet agents - weigh thrombotic risk, clinical stability/urgency, and bleeding risk
- Consider continuing aspirin if on dual antiplatelet therapy (DAPT)
- For life-threatening bleeds, consider reversal agents, see Appendix A
- Exercise caution when stopping DAPT with stents, platelet transfusion in patients on anti-platelet agents, and giving vitamin K or reversal agents

Infusions
- Prophylactic antibiotics (*e.g.,* ceftriaxone 1 g IV every 24 hours preferred or fluoroquinolone can be used)
- Octreotide 50 mcg IV for one dose then 50 mcg/hour IV infusion
- Consider pantoprazole 80 mg IV for one dose then 8 mg/hour IV infusion

Procedural Management
- Endoscopy within 12 hours
- Interventional Radiology
- Surgery

Post Procedure Management
- Octreotide/pantoprazole infusion for at least 72 hours
- Prophylactic antibiotic for 7 days

Post Procedure Anticoagulation/Anti-platelet Management
- Reinitiate anticoagulation/anti-platelet once hemostasis achieved and in discussion with prescribing provider

PRBC = packed red blood cells

Oral Bleeding Emergency Management

APPENDIX D: Non-Variceal Bleed Management

Resuscitation
- IV fluids
- Blood product transfusion
  - Transfuse PRBC for a hemoglobin goal of ≥ 7 g/dL. May consider a higher target if history of cardiac/comorbidities.
  - Transfuse platelet or plasma

Antithrombotic Management
- Consider consulting Benign Hematology
- Hold anticoagulants
- Consider holding anti-platelet agents - weigh thrombotic risk, clinical stability/urgency, and bleeding risk
- Consider continuing aspirin if on dual antiplatelet therapy (DAPT)
- For life-threatening bleeds, consider reversal agents, see Appendix A
- Exercise caution when stopping DAPT with stents, platelet transfusion in patients on anti-platelet agents, and giving vitamin K or reversal agents

Infusions
- Pantoprazole 80 mg IV for one dose then 8 mg/hour IV infusion
- Consider octreotide 50 mcg IV for one dose then 50 mcg/hour IV infusion if uncertain about possibility of variceal bleeding

Procedural Management
- Endoscopy within 24 hours
- Interventional Radiology
- Surgery

Post Procedure Management
- Continue high dose IV proton pump inhibitor (PPI) for 72 hours in PUD with high risk stigmata
- Transition to oral PPI in PUD with low risk stigmata
- Consider the need for PPI long term

Post Procedure Anticoagulation/Anti-platelet Management
- Reinitiate anticoagulation/anti-platelet once hemostasis achieved
- Discuss anticoagulation/anti-platelet agents with prescribing provider for high risk of rebleeding or other concerns
- Resume anticoagulation within first week or consider bridge with short acting agent
- Discuss anticoagulant/anti-platelet timing with prescribing provider

PRBC = packed red blood cells

SUGGESTED READINGS

David, K. & Shojaee, S. (2020). Managing massive hemoptysis. *CHEST, 157*(1), 77-88. doi:10.1016/j.chest.2019.07.012

Franchini, M. (2008). Surgical prophylaxis in von Willebrand's disease: A difficult balance to manage. *Blood Transfusion, 6*(Supple 2), s33-s38. doi:10.2450/2008.0035-08

Garcia-Tsao, G., Abraldes, J. G., Berzigotti, A., & Bosh, J. (2017). Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology, 65*(10), 310-335. doi:10.1002/hep.28906

Gershman, E, Guthrie, R., Swiatek, K., & Shojaee, S. (2019). Management of hemoptysis in patients with lung cancer. *Annals of Translational Medicine, 7*(15), 1-12. doi:10.21037/atm.2019.04.91

Gralnek, I. M., Dumonceau, J.-M., Kuipers, E. J., Lanas, A., Sanders, D., Kurien, M., … Hassan, C. (2015). Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy, 47*(10). A1-a46. doi:10.1055/s-0034-1393172

Kathuria, H., Hollingsworth, H. M., Vilvendhan, R., & Reardon, C. (2020). Management of life-threatening hemoptysis. *Journal of Intensive Care, 8*(23). doi:10.1186/s40560-020-00441-8

Kinoshita, T., Ohbe, H., Matsui, H., Fushimi, K., Ogura, H., & Yasunaga, H. (2019). Effect of tranexamic acid on mortality in patients with hemoptysis: A nationwide study. *Critical Care, 23*(347). doi:10.1186/s13054-019-2620-5

MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy
Advance Care Planning (ACP) Conversation Workflow (ATT1925)

Mujtaba, S., Chawla, S., & Massaad, J. F. (2020). Diagnosis and management of non-variceal gastrointestinal hemorrhage: A review of current guidelines and future perspectives. *Journal of Clinical Medicine, 9*(2), 402. doi:10.3390/jcm9020402

Olsen, K. M., Manouchehr-Pour, S., Donnelly, E. F., Henry, T. S., Berry, M. F., Boiselle, P. M., … Kanne, J. P. (2020). ACR appropriateness criteria hemoptysis. *Journal of the American College of Radiology, 17*(5S), S148-S159. doi:10.1016/j.jacr.2020.01.043

Richards, D. M., & Ross, W. A. (2019). Gastrointestinal bleeding in critically ill cancer patients. In *Oncologic Critical Care.* (pp. 857-867). Springer International Publishing. doi:10.1007/978-3-319-74588-6_72

Richards, D. M., Thekkel, S., & Ross, W. A. (2019). Endoscopic and pharmacologic management of upper GI bleeding. In *Oncologic Critical Care* (pp. 869-883). Springer International Publishing. doi:10.1007/978-3-319-74588-6_176

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