Acute Intracranial Hemorrhage in Adult Cancer Patients

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.*

PRESENTATION/ASSESSMENT

Abrupt onset of neurological signs and symptom(s)[1] without history of trauma

- Brief medical history including history of hypertension, stroke, and use of anticoagulants/antithrombotics
- CT head scan without contrast [MRI or CT angiography if clinical or radiological suspicion of underlying cause such as tumor or arteriovenous malformation (AVM)]
- Laboratory tests (if not already completed): basic metabolic panel, glucose, total bilirubin, CBC, PT/INR, aPTT, fibrinogen, D-Dimer, type and screen, troponin-T
- Neurologic exam using NIHSS[2] and/or GCS[3]

Radiographic evidence of acute intracranial hemorrhage[4]?

MANAGEMENT

Yes

- Notify primary team
- Neurosurgery consult to include discussion with primary team
- Urgent multidisciplinary conference[5] of all teams involved
- Review of available ACP notes
- Discontinue antithrombotic agents, vasoconstrictive agents, and estrogen containing oral contraceptives as clinically indicated[6]
- Transfer to ICU
- Neurological vital signs every hour
- Blood pressure management: discontinue antihypertensives and refer to Appendix C

Further treatment indicated?

Yes (*e.g.,* good baseline performance status, controlled disease with > 1 year life expectancy, and ACP note indicates wish to pursue treatment) → See Page 2 for further treatment

No (*e.g.*, poor baseline performance status, life expectancy < 6 months, refractory thrombocytopenia, massive bleeding with neurological devastation, and/or ACP note indicates patient does not wish to pursue treatment)

- Initiate a GCC conversation[7] with the patient, or if clinically indicated, with the Patient Representative, and the Primary Oncologist/Primary Team/ Attending Physician. The ACP note should be used to document GCC discussion.

Consider:

- Continuation of noninvasive clinical management
- Palliative Care consult
- Comfort measures

No

- Consult Neurology
- Further workup as indicated
- See Management of Acute Ischemic Stroke in Hospitalized Adult Patients algorithm if ischemic stroke is suspected

ACP = advanced care planning GCC = goal concordant care

[1] Neurological signs and symptoms:
- Numbness, tingling, and/or paralysis to face, arm or leg (especially on one side)
- Severe headache
- Difficulty with swallowing or vision
- Loss of balance or coordination
- Difficulty speaking, understanding, reading or writing
- Change in level of consciousness or alertness

[2] See Appendix A: National Institutes of Health Stroke Scale (NIHSS)

[3] See Appendix B: Glasgow Coma Scale (GSC)

[4] Intracranial hemorrhage includes: subarachnoid hemorrhage, subdural hematoma, epidural hemorrhage, intraparenchymal hemorrhage, intraventricular hemorrhage

[5] The objective of this meeting/conference is to discuss the immediate plan of care, including whether surgery is indicated or not. If surgery is not indicated, discuss whether the patient is neurologically devastated and the chances of recovery are very poor justifying further discussion about end of life, do-not-resuscitate status, limitation of life supportive measures (*e.g.*, blood products, ventilation, vasopressors, cardiopulmonary resuscitation) and transition to comfort care.

[6] Antithrombotic agents: anticoagulants, thrombolytics, antiplatelets, NSAIDs
Vasoconstrictive agents (may be associated with reversible cerebral vasoconstrictive syndrome): triptans, selective serotonin reuptake inhibitors (SSRIs), decongestants, stimulants, phentermine, sympathomimetic drugs
Estrogen-containing oral contraceptives (if hemorrhage attributable to central venous sinus thrombosis)

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

Department of Clinical Effectiveness V4
Approved by the Executive Committee of the Medical Staff on 06/20/2023

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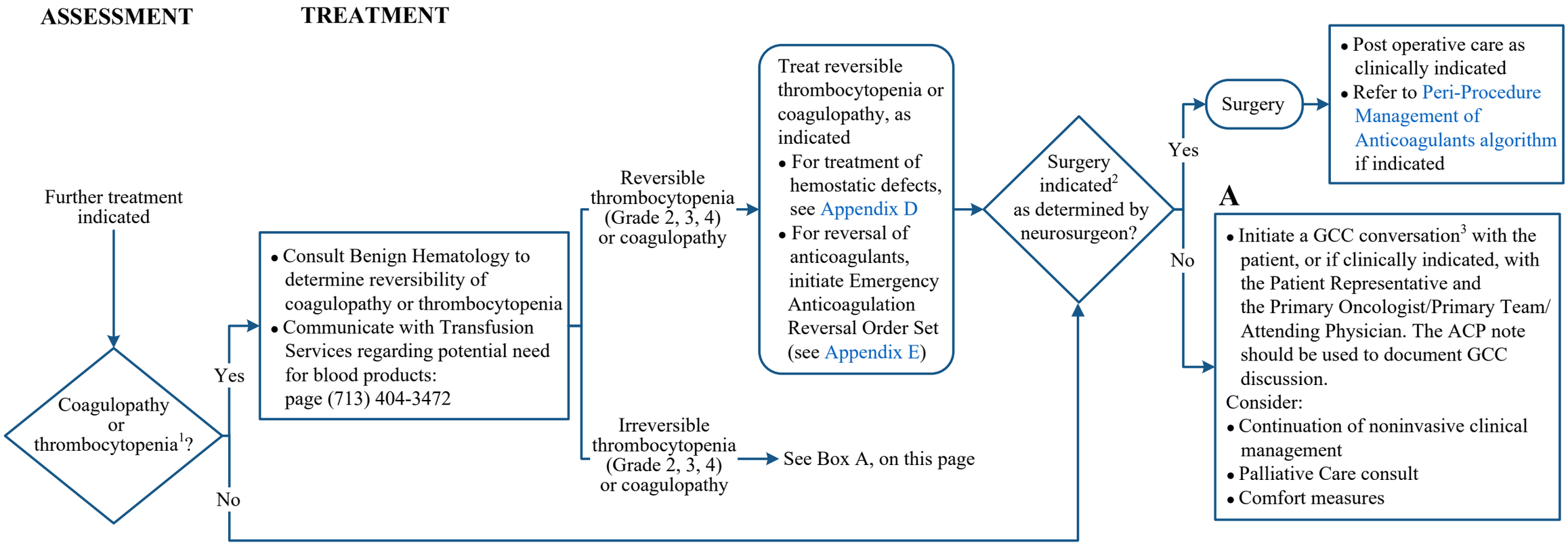

[1] World Health Organization (WHO)/National Cancer Institute (NCI) thrombocytopenia criteria:
- Grade 1: 75 to 150 K/microliter
- Grade 2: 50 to < 75 K/microliter
- Grade 3: 25 to < 50 K/microliter
- Grade 4: < 25 K/microliter

Non-reversible thrombocytopenia (platelet refractory) defined as a one hour post-transfusion platelet increment of < 3,000 K/microliter per unit transfused

[2] Possible surgical indications:
- Intracerebellar hematoma > 30 mm in diameter, hydrocephalus, or brainstem compression
- Supratentorial hematoma 10-20 mL or herniation > 30 mL and within 1 cm of the surface
- Intraventricular hemorrhage with hydrocephalus

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

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APPENDIX A: National Institutes of Health Stroke Scale (NIHSS)

	Title	Responses	Score
1A	Level of consciousness	0 – Alert 1 – Drowsy 2 – Obtunded 3 – Coma/unresponsive	
1B	Orientation questions (2)	0 – Answers both correctly 1 – Answers 1 correctly 2 – Answers neither correctly	
1C	Response to commands (2)	0 – Performs both task correctly 1 – Performs 1 task correctly 2 – Performs neither	
2	Gaze	0 – Normal horizontal movements 1 – Partial gaze palsy 2 – Complete gaze palsy	
3	Visual field	0 – No visual defect 1 – Partial hemianopia 2 – Complete hemianopia 3 – Bilateral hemianopia	
4	Facial movement	0 – Normal 1 – Minor facial weakness 2 – Partial facial weakness 3 – Complete unilateral palsy	
5	Motor function (arm): ◦ Left ◦ Right	0 – No drift 1 – Drift before 10 seconds 2 – Falls before 10 seconds 3 – No effort against gravity 4 – No movement	Left: Right:
6	Motor function (leg): ◦ Left ◦ Right	0 – No drift 1 – Drift before 5 seconds 2 – Falls before 5 seconds 3 – No effort against gravity 4 – No movement	Left: Right:
7	Limb ataxia	0 – No ataxia 1 – Ataxia in 1 limb 2 – Ataxia in 2 limbs	
8	Sensory	0 – No sensory loss 1 – Mild sensory loss 2 – Severe loss	
9	Language	0 – Normal 1 – Mild aphasia 2 – Severe aphasia 3 – Mute or global aphasia	
10	Articulation	0 – Normal 1 – Mild dysarthia 2 – Severe dysarthia	
11	Extinction or inattention	0 – Absent 1 – Mild loss (1 sensory modality lost) 2 – Severe loss (2 modalities lost)	

Score ≥ 25	Very severe neurological impairment
Score 5-24	Mild to severe neurological impairment
Score < 5	Mild impairment

APPENDIX B: Glasgow Coma Scale (GCS)[1]

Item	Description	Score
Eye Opening Response	Spontaneous	4
	To verbal stimuli, command, speech	3
	To pain only (not applied to face)	2
	No response	1
Verbal Response	Oriented	5
	Confused conversation, but able to answer questions	4
	Inappropriate words	3
	Incomprehensible speech	2
	No response	1
Motor Response	Obeys commands for movement	6
	Localizes pain	5
	Withdraws in response to pain	4
	Flexion in response to pain	3
	Extension in response to pain	2
	No response	1

[1] GCS is obtained by adding the score from each item

APPENDIX C: Blood Pressure Management [2,3]

Presenting Blood Pressure	Suggested Management
SBP > 220 mmHg	Consider acute[4] reduction of blood pressure to SBP < 220 mg Hg with continuous IV infusion and frequent monitoring of blood pressure every 5 minutes or continuous intra-arterial pressure monitoring, followed by modest reduction of blood pressure to target of 130-150 mmHg
SBP > 150 and ≤ 220 mmHg **and** no evidence of elevated intracranial pressure	Consider acute reduction of blood pressure[4] to target SBP of 130-150 mmHg using intermittent or continuous intravenous medications to control blood pressure and clinically re-examine the patient every 15 minutes
SBP > 150 and ≤ 220 mmHg **and** possibility of elevated intracranial pressure	Consider monitoring ICP and reducing blood pressure to target SBP of 130-150 mmHg using intermittent or continuous intravenous medications while maintaining a cerebral perfusion pressure of 60 mmHg

ICP = increased intracranial pressure
SBP = systolic blood pressure

[2] The safety and efficacy of intensive blood pressure lowering in patients with large/severe intracranial hemorrhages or those requiring surgical decompression is not known
[3] If clinically indicated, consider target SBP < 180 mmHg for patients with prior history of hypertension or target SBP < 140 mmHg for patients with no history of hypertension
[4] If acute reduction of blood pressure is considered, initiate within 2 hours of intracranial hemorrhage onset and reach target within 1 hour

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APPENDIX D: Hemostatic Defect

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. Use Humate-P® or Alphanate®, begin 40-60 international units/kg.	
Thrombocytopenia	Ideal target platelet count of 100 K/microliter in patients who are not refractory to platelets. Each unit transfused should increase platelet count by 5-10 K/microliter.	

APPENDIX E: 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®) not available, use fresh frozen plasma 15 mL/kg or if INR is not supratherapeutic (e.g., ≤ 3); may use 5-8 mL/kg for urgent reversal
</td></tr>
<tr><td>Dabigatran</td><td>
• Administer activated charcoal 25-50 grams oral or nasogastric tube times one dose if ingested within the previous 2 hours
• Administer idarucizumab 2.5 grams IV times two doses
• Consider repeated dose of idarucizumab if after several hours the patient re-bleeds or has worsening coagulopathy
• Consider hemodialysis for life-threatening bleeds
</td></tr>
<tr><td>Apixaban or rivaroxaban</td><td>
• Administer activated charcoal 25-50 grams oral or nasogastric tube times 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 > 18 hours, andexanet alfa may be given if compelling indication necessitating reversal is present (e.g., acute renal failure or overdose)
• If andexanet alfa 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

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APPENDIX E: Reversal of Anticoagulants - continued

Anticoagulant	Recommended Treatment
Edoxaban[1] or betrixaban[1]	• Administer activated charcoal 25-50 grams oral or nasogastric tube times 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 repeat dosing if continued bleeding
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 times one dose

[1] Non-formulary

SUGGESTED READINGS

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