Protocol # 10 NS

Completed 10/29

Isolated Traumatic Brain Injury Management and ICU utilization

Definitions:

Blunt mechanism only

Mild TBI is characterized as a traumatically induced physiologic disruption that is characterized by brief (<30min LOC), amnesia to events immediately before or after trauma, confusion, disorientation around the time of trauma and GCS of 13-15 after 30 minutes from event.

Mild TBI Patient with Normal Head CT

Reference EAST Mild TBI guidelines

Mild TBI patient with Abnormal Head CT

Defined as findings of intracranial hemorrhage (ICH) or skull fracture on head CT

Moderate TBI is characterized more prolonged neurologic disruption, GCS is 9-12.

Severe TBI is characterized by GCS 8 or less after traumatic injury event.

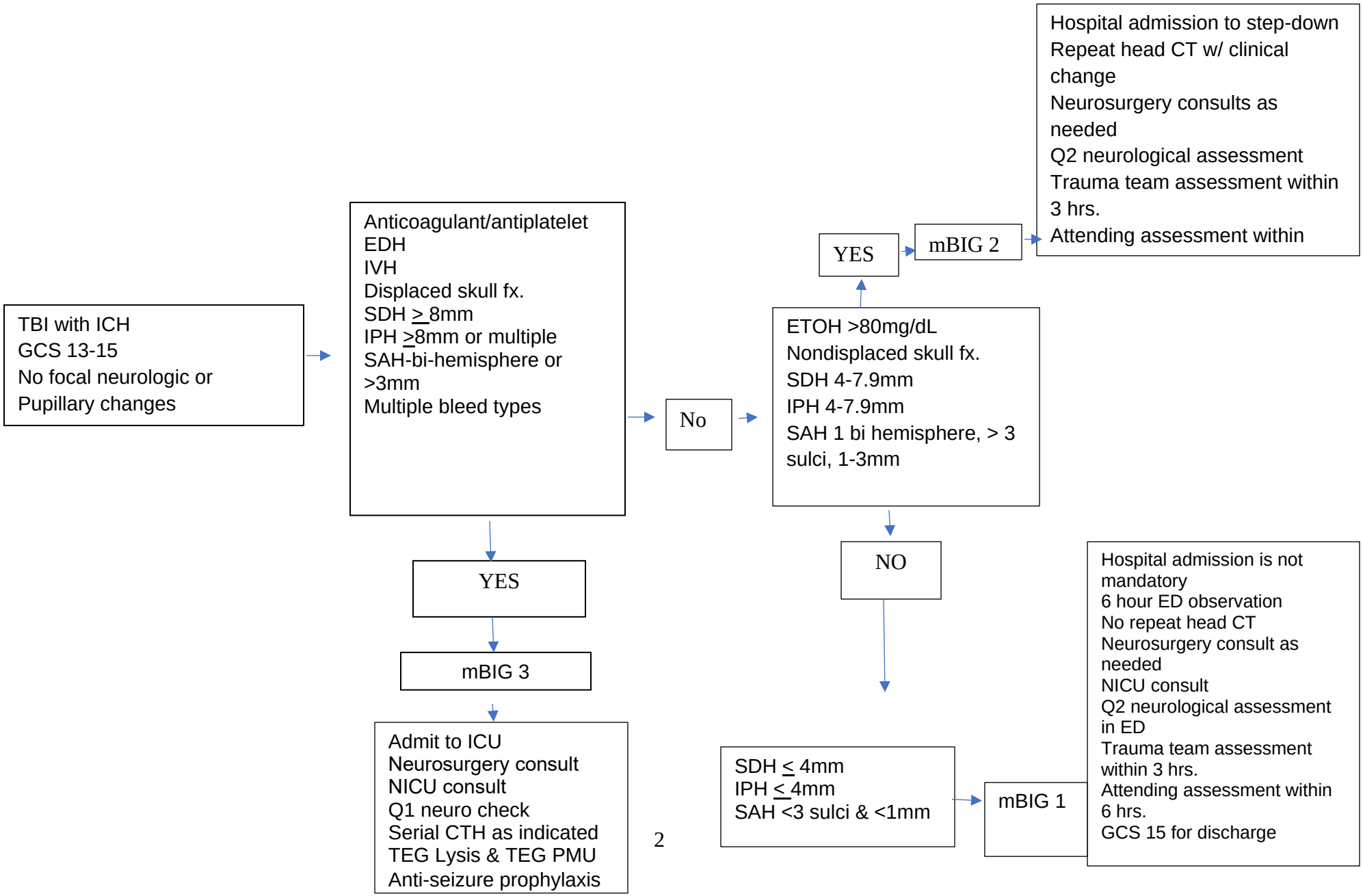
Management of Patients with Traumatic Intracranial Hemorrhage (SDH, EDH, IPH, SAH, IVH) or Skull fracture of head CT

Patients will then be stratified by characteristics of their exam, intoxication, antiplatelet/anticoagulation, characteristics of the bleed and skull fracture.

Definitions:

1. Abnormal Neurologic Exam is defined as focal neurologic exam (weakness, sensory loss), abnormal pupillary exam, GCS 12 or less
2. Intoxication is defined as alcohol level that is >80
3. Anticoagulants/Antiplatelets is defined as taking Antiplatelet agents (excluding ASA), Coumadin, Novel Oral Anticoagulants (NOACS)
4. If multiple types of bleeds then classify as mBIG3

Modified Brain Injury Guidelines



DRH Modified Brain Injury Guidelines (BIG)			
Variables	**mBIG1**	**mBIG2**	**mBIG3**
GCS	14-15	13	12 or less
Focal Neurologic Exam	Normal	Normal	Abnormal
Pupillary Exam	Normal	Normal	Abnormal
Antiplatelets/Anticoagulants	No	No	Yes
Intoxication	No	No/Yes	No/Yes
SDH	< 4mm	4-7mm	≥ 8mm
EDH	No	No	Any
IPH	<4mm, 1 location	4-7mm, 2 locations	≥ 8mm, multiple locations
SAH	≤ 3 sulci and <1mm	1 hemisphere, >3 sulci, 1-3mm	Bi-hemispheric or >3mm
IVH	No	No	Yes
Skull Fracture	No	Non-displaced	Displaced
Therapeutic Plan			
Hospitalization	Not mandatory Observed in the ED for -6 hrs.	Step down	ICU
Frequency of Neurological assessment	Q2 neurological assessment	Q2 neurological assessment	Q1 hour
Repeat Head CT at 6 hour	No	Only with clinical change	Yes
TEG Lysis & TEG PMU	No	No	Yes
Discharge GCS	15	15	variable
Anti-epileptic Drug Prophylaxis	No	No	Yes
Neurosurgery consult	As needed	As needed	Yes
NICU consult	Yes	Yes	Yes

*Reversal agent for Head trauma patient refer to the "**DMC Guideline for Management of Anticoagulant Related Bleeding and Reversal in Adults"**

References:

Khan AD, Elseth AJ, Brosius JA, Moskowitz E, Liebscher SC, Anstadt MJ, Dunn JA, McVicker JH, Schroeppel T, Gonzalez RP. Multicenter assessment of the Brain Injury Guidelines and a proposal of guideline modifications. Trauma Surg Acute Care Open. 2020 May 28;5(1):e000483. doi: 10.1136/tsaco-2020-000483. PMID: 32537518; PMCID: PMC7264829.

Ross M, Pang PS, Raslan AM, Selden NR, Cetas JS. External retrospective validation of Brain Injury Guidelines criteria and modified guidelines for improved care value in the management of patients with low-risk neurotrauma. J Neurosurg. 2019 Nov 8:1-6. doi: 10.3171/2019.6.JNS19584. Epub ahead of print. PMID: 31703198.

Joseph B, Friese RS, Sadoun M, Aziz H, Kulvatunyou N, Pandit V, Wynne J, Tang A, O'Keeffe T, Rhee P. The BIG (brain injury guidelines) project: defining the management of traumatic brain injury by acute care surgeons. J Trauma Acute Care Surg. 2014 Apr;76(4):965-9. doi: 10.1097/TA.0000000000000161. PMID: 24662858.

DMC Guideline for Management of Anticoagulant Related Bleeding and Reversal in Adults

NOTE: This guideline is intended for use in reversal and management of anticoagulant related bleeding.

- For perioperative management of anticoagulant please refer to *DMC Guideline for Perioperative Anticoagulation Management for Patients on Chronic Oral Anticoagulation.*
- For Thrombolytic management please refer to the *DMC Guideline for Alteplase Dosing and Reversal Management in Adults*

General considerations for all anticoagulant bleeding and reversal

1. Assessment of Severity (with definitions)

- ***Intracranial Bleeds***: Intracranial hemorrhage including intraparenchymal, subdural, epidural, and subarachnoid hemorrhages
- ***Major Bleed (s):*** Hemodynamic instability, bleeding occurring in a critical site**, hemoglobin drop ≥ 2 gm/dL or ≥ 2 units PRBC
  **Critical site: Other central nervous system hemorrhage (intraocular, intra or extra axial spinal hemorrhages); pericardial tamponade; hemothorax; airway (posterior epistaxis); intra-abdominal bleeding; retroperitoneal hematoma; extremity bleeds (intramuscular and intra-articular bleeding)
- ***Non-major Bleed(s***): All other bleeds not meeting criteria above that require intervention or hospitalization

2. Initial measures and other considerations

- Stop anticoagulant
- Provide mechanical compression, volume resuscitation and hemodynamic support if needed
- Consider source control
- No definitive antidote available (except for dabigatran, heparin and warfarin)
- In most situations, the therapeutic effect will dissipate in 24-48 hours
- Consult to Hematology or Toxicology is strongly encouraged, but should not delay therapy
- Interruption of chronic anticoagulation may lead to increased risk of thromboembolic events

3. In acute overdose scenario

- If ingestion within 2 – 4 hours, give activated charcoal orally and repeat in 6 hours (contraindicated with concurrent GI bleed)

4. For patients at increased risk of bleed or non-major bleed(s) that does not require intervention

- May continue anticoagulant (risk vs. benefit)
- Initiate appropriate measures to control bleeding

5. Dosing considerations for 4-factor prothrombin complex concentrate (4FPCC)* and activated PCC (FEIBA)

- Use total body weight (TBW) or adjusted body weight (AdjBW) if BW >130% IBW (unless fixed-dose regimen is recommended)
  - AdjBW = [(Total body weight - Ideal body weight) x 0.4] + Ideal body weight
- MAX dosing weight = 100kg
- MAX DOSE 5,000 units
- Round to nearest vial size(s)
  - Dose deviation greater than +/- 10% MUST be discussed with prescriber
- 4FPCC dose is based on Factor IX component
- 4FPCC contains small amounts of heparin and should NOT be administered to patients with known or suspected heparin allergy.
- FEIBA™ is drug of choice for patients with heparin allergy, as it does not contain heparin.
- FEIBA™ is the recommended alternative if 4FPCC is not available. Dosing remains the same using the alternative agent.

*4FPCC products include Balfaxar and KCentra. Formulary product may change over time.

Non-Major Bleed(s)

- Reversal agents are not recommended in non-major bleeds, with the exception of the need for warfarin reversal
- Medication elimination half-life noted in Table 2 below

Warfarin Reversal

- Warfarin elimination half-life: 48-120 minutes
- Reverse with vitamin K based on INR.
  - Oral is the preferred route for vitamin K for non-major bleeds; Expect reduction of INR within 24-48 hrs and repeat INR 24 hrs post-dose
  - IV route may be considered for rapid reversal; Expect reduction of INR within 6-12 hrs and repeat INR 8-12 hr post-dose

Table 1: Vitamin K Dosing for Warfarin Reversal for Non-Major Bleeds

INR	Vitamin K Dose **(Non-Major Bleeds)**
> Therapeutic but <4.5	Vitamin K not recommended
≥ 4.5 but ≤10	Consider Vitamin K 1-2.5 mg PO x 1
INR >10	Consider Vitamin K 2.5 - 5 mg PO x 1 (May repeat dose in 24-48 hrs)
Rapid reversal required (at any INR)	Vitamin K 2.5-5 mg PO or 1-5 mg IV (May repeat dose in 24 hrs)

Major Bleed(s)/Emergent Reversal, or Intracranial Bleeds

Table 2: Reversal Recommendations

<table>
<tr><th>Anticoagulant</th><th>Major Bleed(s)/
Emergent Reversal</th><th>Intracranial Bleeds</th><th>Anticoagulant Elimination Half-Life /
Additional Comments</th></tr>
<tr><td colspan="4"><u>Factor Xa Inhibitors</u></td></tr>
<tr><td>Apixaban</td><td rowspan="4">– Consider 4FPCC 1,000 units x1
– May repeat 500-1,000 units if patient still exhibiting signs/ symptoms of bleeding, up to a maximum cumulative dose of 5,000 units</td><td rowspan="4">– 4FPCC 50 units/kg (max 5,000 units)
– May give an additional dose, up to a maximum cumulative dose of 5,000 units, if patient still exhibiting signs/symptoms of bleeding, such as expanding hemorrhage</td><td>- Elimination half-life: 12 hrs</td></tr>
<tr><td>Edoxaban</td><td>- Elimination half-life: 9-11 hrs</td></tr>
<tr><td>Rivaroxaban</td><td>- Elimination half-life: 6-9 hrs</td></tr>
<tr><td>Fondaparinux</td><td>- Elimination half-life: 17-21 hrs</td></tr>
<tr><td colspan="4"><u>Enoxaparin</u></td></tr>
<tr><td>Enoxaparin</td><td colspan="2">
<table>
<tr><th>Enoxaparin Administration</th><th>Protamine Dose to Neutralize 1 mg of Enoxaparin</th></tr>
<tr><td>≤ 8 hours after dose</td><td>1 mg</td></tr>
<tr><td>> 8 hours after dose (or second dose of protamine)</td><td>0.5 mg</td></tr>
</table>
- Max single protamine dose is 50mg; may repeat dose after 2-4 hrs
- Infuse protamine over 10 min</td><td>- Elimination half-life: 3-5 hrs
- Protamine will only provide partial neutralization of enoxaparin (~60%)
- Protamine may cause anaphylactic-like reactions
- Excessive doses of protamine (>100 mg) may worsen bleeding by acting as an anticoagulant</td></tr>
</table>

<table>
<tr><th>Anticoagulant</th><th>Major Bleed(s)/
Emergent Reversal</th><th>Intracranial Hemorrhage</th><th>Anticoagulant Elimination Half-Life /
Additional Comments</th></tr>
<tr><td colspan="4"><u>Heparin</u></td></tr>
<tr><td>Intravenous Heparin</td><td colspan="2"><table><tr><th>Time Elapsed Since Infusion</th><th>Protamine Dose to Neutralize 100 units of Heparin</th></tr><tr><td>Immediate (< 30 min)</td><td>1 mg</td></tr><tr><td>30 min to < 2 hours</td><td>0.5 mg</td></tr><tr><td>≥ 2 hours</td><td>0.25 - 0.375 mg</td></tr></table>Protamine:
– Dose calculation: use total amount of heparin given within the past 3 hours prior to reversal
– Max single protamine dose is 50 mg; may repeat dose after 2 hrs
– Infuse protamine over 10 min</td><td>– Elimination half-life: 60-90 minutes
- Check aPTT ~5-15 min after protamine (onset of reversal ~5 min after dose, duration of reversal ~2 hours)
- Protamine may cause anaphylactic-like reactions
- Heparin rebound with bleeding may occur up to 18 hrs post dose
- Excessive doses of protamine (>100 mg) may worsen bleeding by acting as an anticoagulant</td></tr>
<tr><td>Subcutaneous Heparin</td><td colspan="2">Protamine
– Dose: Give 1-1.5 mg of protamine per 100 units of heparin</td><td>– Elimination half-life: 30-90 minutes
– Administer bolus of 25 mg over 10 min and infuse remaining dose over 8 hours</td></tr>
<tr><td colspan="4"><u>Direct Thrombin Inhibitors</u></td></tr>
<tr><td>Dabigatran</td><td>– Idarucizumab (Praxbind) 5 gm IV x 1 (administered as 2 separate doses of 2.5 gm IV (50 mL) no more than 15 minutes apart)
– If idarucizumab not available, consider 4FPCC 1,000 units x1 (May repeat 500-1,000 units if patient still exhibiting signs/symptoms of bleeding, up to a maximum cumulative dose of 5,000 units)</td><td>– Idarucizumab (Praxbind) 5 gm IV x 1 (administered as 2 separate doses of 2.5 gm IV (50 mL) no more than 15 minutes apart)
○ Consider re-dosing with an additional 5 gm of idarucizumab if coagulation parameters (aPTT) still elevated at 6-12 hours after first dose
– If idarucizumab not available, consider 4FPCC 50 units/kg (max 5,000 units). May give an additional dose, up to a maximum cumulative dose of 5,000 units, if patient still exhibiting signs/symptoms of bleeding, such as expanding hemorrhage</td><td>Elimination half-life:<table><tr><th>CrCl</th><th>Half-Life</th></tr><tr><td>> 50 ml/min</td><td>12-17 hrs</td></tr><tr><td>30-50 mL/min</td><td>15-18 hrs</td></tr><tr><td><30 mL/min</td><td>28-34 hrs</td></tr></table>- Give idarucizumab only if dabigatran was administered within a period of 3-5 half-lives (half-lives are longer in renal insufficiency)
- Dabigatran has protein binding and is removed by hemodialysis (fraction removed by 2 hrs of HD is ~62% and 4 hrs of HD is ~68%)</td></tr>
<tr><td>Argatroban

Bivalirudin</td><td colspan="2">No reversal agent. Use supportive measures and volume replacement</td><td>Elimination half-life:<table><tr><td>Argatroban</td><td>40-50 min</td></tr><tr><td>Bivalirudin</td><td>25 min</td></tr></table>- Factor VIIa is NOT recommended (has theoretical benefits in-vivo only; case reports showed thromboembolic complications)</td></tr>
</table>

<table>
<tr><th>Anticoagulant</th><th>Major Bleed(s)/
Emergent Reversal</th><th>Intracranial Hemorrhage</th><th>Anticoagulant Elimination Half-Life /
Additional Comments</th></tr>
<tr><td colspan="4"><u>Vitamin K Antagonist</u></td></tr>
<tr><td rowspan="3">Warfarin</td><td rowspan="3">1. Vitamin K 10 mg IVPB x 1 dose
AND
2. May also consider 4FPCC 1,000 units x1 (May repeat 500-1,000 units after 30 minutes if patient still exhibiting signs/symptoms of bleeding)</td><td>1. Vitamin K 10 mg IVPB x 1 dose
AND
2. 4FPCC
INITIAL Dose:<table><tr><th>INR</th><th>INITIAL Dose</th><th>Max Dose</th></tr><tr><td>2-4</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>– If INR not available, may initiate with 2,500 units x1
– Note: 4FPCC dose is based on Factor IX component</td><td>– Elimination half-life: 48-120 hours
– Avoid IM and subcutaneous administration of vitamin K
– When vitamin K IVPB is <u>given alone</u>, expect reduction of INR within 6-12 hrs and repeat INR 8-12 hrs post-dose</td></tr>
<tr><td colspan="2">Monitoring:
- Repeat INR 30-60min after <u>initial</u> 4FPCC dose and Q 4-6 hour for next 24-48 hours</td></tr>
<tr><td colspan="2">REPEAT Dose:
- If signs/symptoms of bleeding, such as expanding hemorrhage, still present and INR continues to be elevated, may give an additional dose up to a cumulative dose of 50 units/kg or 5,000 units (whichever is lower)<table><tr><th>INR</th><th>REPEAT Dose</th><th>Max Dose</th><th>Max Cumulative Dose</th></tr><tr><td>2-4</td><td>25 units/kg</td><td>2,500 units</td><td rowspan="3">5,000 units</td></tr><tr><td>≥ 4-6</td><td>15 units/kg</td><td>1,500 units</td></tr><tr><td>>6</td><td colspan="2">Not recommended</td></tr></table>- 4FPCC cumulative dose > 5,000 units is not recommended.
- If repeat INR is still elevated (≥1.4) within 24-48 hours after max cumulative dose of 4FPCC, repeat dosing of 4FPCC is not recommended - use FFP instead.</td></tr>
</table>

References:
1. Frontera, JA, et al. Guideline for Reversal of Antithrombotics in Intracranial Hemorrhage, A Statement for Healthcare Professionals from the Neurocritical Care Society and Society of Critical Care Medicine. Neurocrit Care. 2016;24(1):6-46.
2. Cuker A, et. al. Reversal of direct oral anticoagulants: Guidance from the Anticoagulation Forum. Am J Hematol. 2019;94:697–709.
3. Panos NG, et al. Factor Xa inhibitor-related intracranial hemorrhage: results from a multicenter, observational cohort receiving prothrombin complex concentrates. Circulation. 2020;141(21):1681-9.
4. Tomaselli GF, et al. 2020 ACC expert consensus decision pathway on management of bleeding in patients on oral anticoagulants: a report of the American College of Cardiology Solution Set Oversight Committee. Journal of the American College of Cardiology. 2020;76(5):594-622.
5. Schulman S, Gross PL, Ritchie B, et al. Prothrombin complex concentrate for major bleeding on factor Xa inhibitors: a prospective cohort study. Thromb Haemost. 2018;118:842-851.
6. Prothrombin Complex Concentrate. Lexi-Drugs. Lexicomp Online [database online]. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com. Accessed 2021.