Repletion and Reversal for Anticoagulated Patients with ICH: The Neurocritical Care Perspective

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Resource Information

About This Resource

These slides are one component of a continuing education program available online at MedEd On The Go titled What's New in Treating the Anticoagulated Patient with ICH?

Program Learning Objectives:

- Describe the various therapies necessary to manage the care of anticoagulated patients with ICH in the neurocritical care setting, including reversal and repletion
- Illustrate the latest neurosurgical clinical trial data to optimize care for patients with ICH
- Categorize the specific recommendations from the recent ESO guidelines on the management of ICH in the anticoagulated patient and describe approaches to implement them
- Outline the 3 elements of ICH care bundling and how each optimizes the care of the anticoagulated patient

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Intracerebral Hemorrhage (ICH)

- 10-15% of all stroke
- Mortality 30-50%
- 74% functionally dependent at 12 months
- Incidence likely to double by 2050
  - Due to aging and increased use of anticoagulation

ICH, intracerebral hemorrhage.

Benjamin, et al. *Circulation*. 2017;135(10); Woo, et al. *Stroke*. 2013;44.

Hemorrhage Expansion

Images courtesy of Opeolu Adeoye, MD, MS, Washington University

Anticoagulation

- Any patient with intracranial bleed
- Anticoagulant medication
  - **What** is dose? **When** was last dose?
- Laboratory tests
  - CBC with platelet count, INR, PTT
  - Consideration of viscoelastic assays or platelet function assays

CBC, complete blood count; PTT, partial thromboplastin time.
Hemphill JC, et al. *Neurocrit Care*. 2017. 27(suppl 1):89-101.

Indications for Repletion or Reversal

Almost all patients with acute intracranial hemorrhage

- Pitfalls
  - Ultra-early prognostication
  - Waiting for a decline in exam to reverse
  - Not reversing “small” hemorrhages

- Considerations:
  - Time since last dose of DOAC or INR
  - Age and comorbidities
  - Location and size of hemorrhage
  - Institutional guidelines

DOAC, direct oral anticoagulant.

Vitamin K Antagonists Reversal (Warfarin)

AHA Guidelines:

- "…INR is elevated because of VKA should have their VKA withheld, receive therapy to replace vitamin K–dependent factors and correct the INR, and receive intravenous vitamin K
  (Class I; Level of Evidence C)

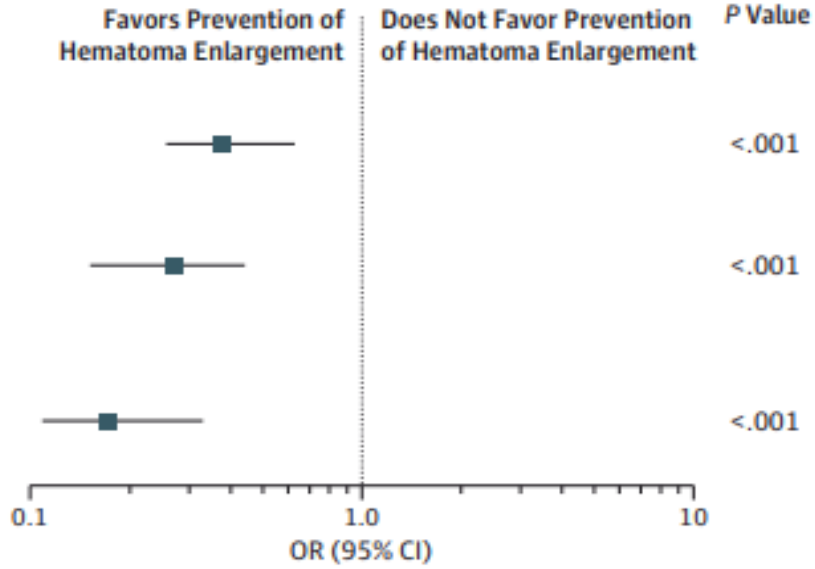
- PCCs may have fewer complications and correct the INR more rapidly than FFP and might be considered over FFP
  (Class IIb; Level of Evidence B)

Tomaselli GF, Mahaffey KW, Cuker A, et al. *J Am Coll Cardiol*. 2020;76(5):594-622.

ICH Timing of Anticoagulation Reversal

Figure 3. Adjusted Graphical Regression Analysis of Combined Associations of INR Reversal, Systolic Blood Pressure, and Timing With Hematoma Enlargement

	No. of Patients	Patients With Hematoma Enlargement, No. (%)	OR (95% CI)	*P* Value
INR <1.3				
Achieved	432	116 (26.9)	0.37 (0.26-0.59)	<.001
Did not achieve	421	191 (45.4)		
INR <1.3 within 4 hours				
Achieved	217	43 (19.8)	0.27 (0.15-0.43)	<.001
Did not achieve	636	264 (41.5)		
INR <1.3 within 4 hours and systolic BP <160 mm Hg within 4 hours				
Achieved	193	35 (18.1)	0.17 (0.11-0.33)	<.001
Did not achieve	498	220 (44.2)		



<u>Significantly</u> lower rate of hematoma enlargement in 1176 subjects when INR reversed to < 1.3 and SBP < 160 mmHg within four hours (18.1& versus 44.2%).

Kuramatsu JB, Gerner ST, Schellinger PD, et al. *JAMA*. 2015;313(8):824-36.

Repletion Strategies:

Recommend treatment for INR greater than 1.4 in VKA bleeding

Vitamin K: 10 mg IV

FFP

- Factors I (fibrinogen), II, V, VII, IX, X, XI, XIII, and antithrombin
- Large volumes often needed (10-15 ml/kg)
- Time to prepare and administer, risk fluid overload
- Risk transfusion reaction

PCC

- 4 Factor: 2, 7, 9, 10
- 3 Factor: 2, 9, 10
- Activated vs. inactivated
- Dose: Fixed or based on INR and weight
- Faster reversal, less volume
- Increased cost

Frontera, et al. *Neurocrit Care*. 2016;24;
Hemphill, et al. *Neurocrit Care*. 2017;27(Suppl 1):89-101.

Multiple Choice Question

Which of the following is the best reversal/repletion strategy for a patient presenting to the ED with a warfarin-associated intracranial hemorrhage?

A. PCCs only
B. Andexanet alfa
C. PCCs and Vitamin K
D. FFP and Vitamin K

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