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Article 1: Burn, Trauma, Critical Care; General Surgery
Timing of pharmacologic venous thromboembolism prophylaxis in severe traumatic brain injury: a propensity-matched cohort study. Byrne JP, Mason SA, Gomez D, et al. J Am Coll Surg 2016;223:621–631

Article 2: General Surgery
Interval appendectomy: finding the breaking point for cost-effectiveness. Senekjian L, Nirula R, Bellows B, Nelson R. J Am Coll Surg 2016;223:632–643

Objectives: After reading the featured articles published in this issue of the *Journal of the American College of Surgeons* (JACS) participants in this journal-based CME activity should be able to demonstrate increased understanding of the material specific to the article featured and be able to apply relevant information to clinical practice.

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ARTICLE 1

(Please consider how the content of this article may be applied to your practice.)

Timing of pharmacologic venous thromboembolism prophylaxis in severe traumatic brain injury: a propensity-matched cohort study

Byrne JP, Mason SA, Gomez D, et al.
J Am Coll Surg 2016;223:621–631

Learning Objectives: After study of this article, surgeons should understand the current evidence surrounding venous thromboembolism (VTE) prophylaxis practices in patients with severe traumatic brain injury (TBI), and be better positioned to inform up-to-date thromboprophylaxis guidelines specific to these patients at their institution.

Question 1

Which statement summarizes the current recommendations of evidence-based thromboprophylaxis guidelines with respect to the optimal timing for initiation of prophylaxis in patients with severe traumatic brain injury?

a) Prophylaxis with low molecular weight heparin (LMWH) or unfractionated heparin (UH) should be initiated within 48 hours of arrival at the hospital, except in patients who demonstrate change in size of intracranial hemorrhage on repeated head CT scan.
b) LMWH or UH should be initiated within the first 72 hours. Where pharmacologic prophylaxis is

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contraindicated, insertion of an inferior vena cava filter should be considered.
c) No recommendations are made for the optimal timing of thromboprophylaxis initiation.
d) LMWH or UH should be initiated within 24 hours of arrival. Mechanical prophylaxis should be used in all patients. Where pharmacologic prophylaxis is contraindicated, insertion of an inferior vena cava filter should be considered.
e) Prophylaxis with LMWH or UH should be initiated early, once repeated head CT demonstrates stability of intracranial hemorrhage.

Critique: There is limited high quality evidence to inform the safe and effective initiation of VTE prophylaxis in patients with TBI, and the timing of prophylaxis initiation in this patient population is not addressed in current guidelines. The most recent CHEST guidelines state the following for patients with major trauma, including TBI: "For major trauma patients, we suggest use of low-dose unfractionated heparin (Grade 2C), low molecular weight heparin (Grade 2C), or mechanical prophylaxis, preferably with intermittent pneumatic compression (Grade 2C), over no prophylaxis." A recent systematic review by Chelladurai et al (2013) concluded that there was insufficient evidence to comment on the effectiveness or optimal timing for initiation of thromboprophylaxis in patients with severe TBI. Our study aimed to address this gap in the literature.

Question 2

The most common agents used for thromboprophylaxis are LMWH and UH. Which of the following statements summarizes the current evidence for selecting LMWH or UH for thromboprophylaxis in patients with severe TBI?

a) Current evidence suggests that UH is safer for use in patients with severe TBI because shorter half-life and opportunity for reversal with protamine sulfate are associated with lower risk of hemorrhagic complication.
b) At present, there is no evidence suggesting that one agent is more effective at preventing thromboembolism or safer in patients with severe TBI.
c) Current evidence suggests that LMWH may be more effective than UH at preventing thromboembolism in patients with severe TBI.
d) Although LMWH is more effective at preventing thromboembolism in patients with severe TBI, it is more associated with complications related to intracranial hemorrhage compared with UH.
e) UH should be the agent of choice for thromboprophylaxis in patients with severe TBI because UH is more effective at preventing thromboembolism, and is safer, than LMWH.

Critique: Both UH and LMWH act via interaction with antithrombin III. Unfractionated heparin is a mixture of molecules varying in molecular size (3−30 kDA) and chemical activity. Low molecular weight heparin contains molecules of smaller size (<8 kDA), which more specifically accelerate inactivation of factor Xa. Longer elimination half-life allows for once-daily dosing of LMWH. Although practitioners may have traditionally favored the use of UH for thromboprophylaxis in patients with severe TBI due to the perception that shorter half-life might be associated with a lower risk of intracranial hemorrhage, there is a lack of evidence to support this practice. At present, there is no evidence to support the notion that one agent is safer than the other. Although there is no level I evidence comparing the use of LMWH vs UH in patients with severe TBI, there is evidence that LMWH is more effective than UH at preventing thromboembolism in patients with major trauma. Geerts et al (1996) demonstrated, in a randomized controlled trial (RCT), that LMWH was associated with lower rates of deep vein thrombosis compared with UH in patients with severe injury. Results from the PROTECT trial, an international multicenter RCT comparing LMWH with UH in critically ill patients, found that LMWH was significantly associated with lower rates of pulmonary embolism. The study examined in this article presented an analysis of patients with severe TBI, showing that LMWH was associated with lower risk of thromboembolism compared with UH (odds ratio 0.60; 95% CI 0.44 to 0.82).

Question 3

Which score or set of criteria may be used as an objective assessment of the risk of intracranial hemorrhage (ICH) progression, to guide the timing of initiation of thromboprophylaxis?

a) Glasgow Coma Scale motor component
b) Total Glasgow Coma Scale score
c) Modified Berne-Norwood criteria
d) Venous thromboembolism risk assessment profile (RAP)
e) Intracerebral hemorrhage score

Critique: Radiologic and clinical features that have been evaluated to assess the risk of ICH progression