

Coumadin Rapid Reversal Protocol and PCC

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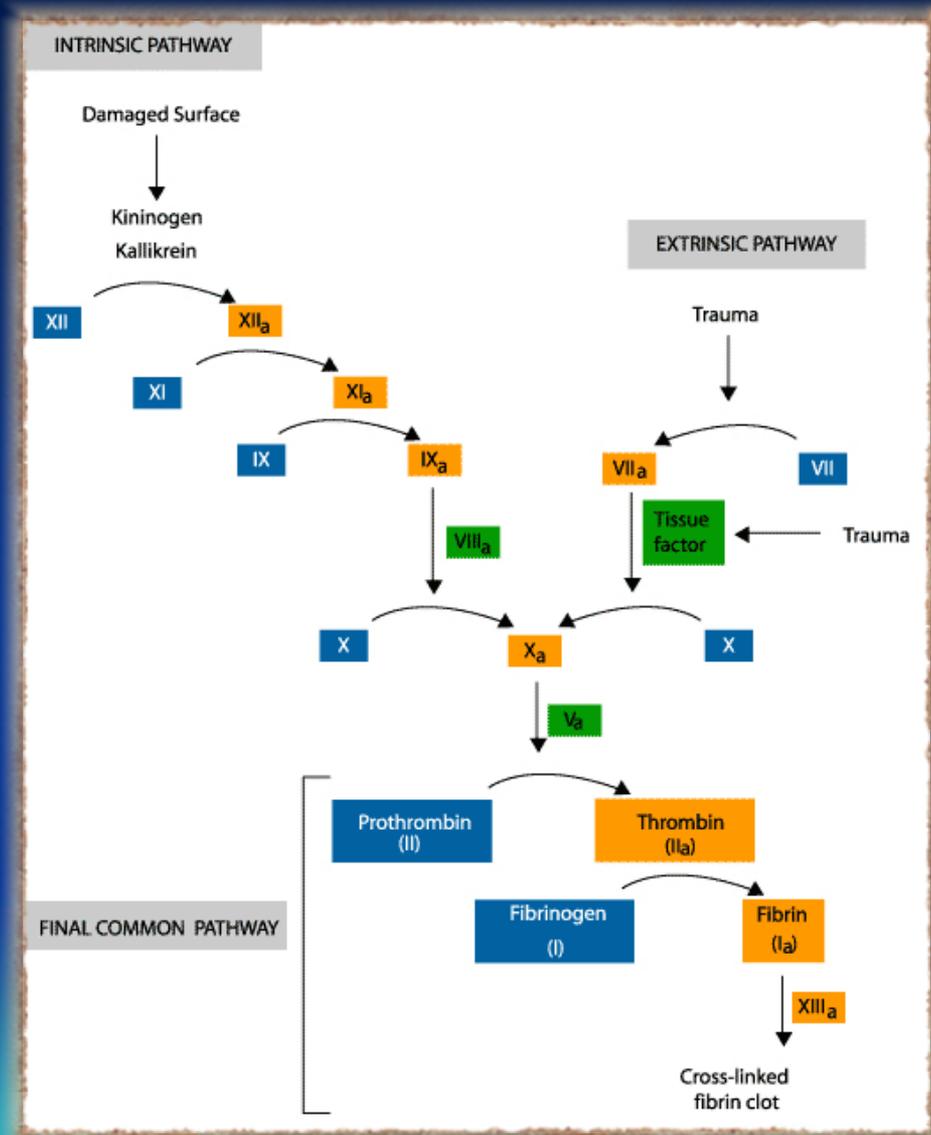


Problem Identification

- 2009 -Trauma Case Conference (M&M)
 - Deaths-head trauma-Coumadin-hmmmm
- 2010 – Trauma Committee
 - Neurosurgery
 - Literature search and review-ughhhh
 - Process/case review
 - Sub-committee-NS, EM, TS, Pharmacy



Clotting Cascade



Process

- Review current care
- Identification of potential roadblocks
 - Physician compliance
 - Costs
- Identification of opportunities
 - Early and accurate identification
 - Education
 - Physician
 - Nursing
 - prehospital



Retrospective Review

- All deaths (2003-2009), coumadin use, ICH
 - 64% of deaths > 60 yrs old (58/105)
 - 66% Head Injury (38/58)
 - 33% on Coumadin (13/38)
 - Mortality rate of 60%



Protocol Development

- 2/2010-Sub-committee assembled
 - multidisciplinary subcommittee of Trauma Committee
 - Multiple attempts over several months
- Inclusion-initially for trauma patients on coumadin who sustain intracerebral hemorrhages (Intracerebral hematoma, SDH, EDH, SAH)
 - Could be used for any patient on coumadin who sustains a life threatening hemorrhage

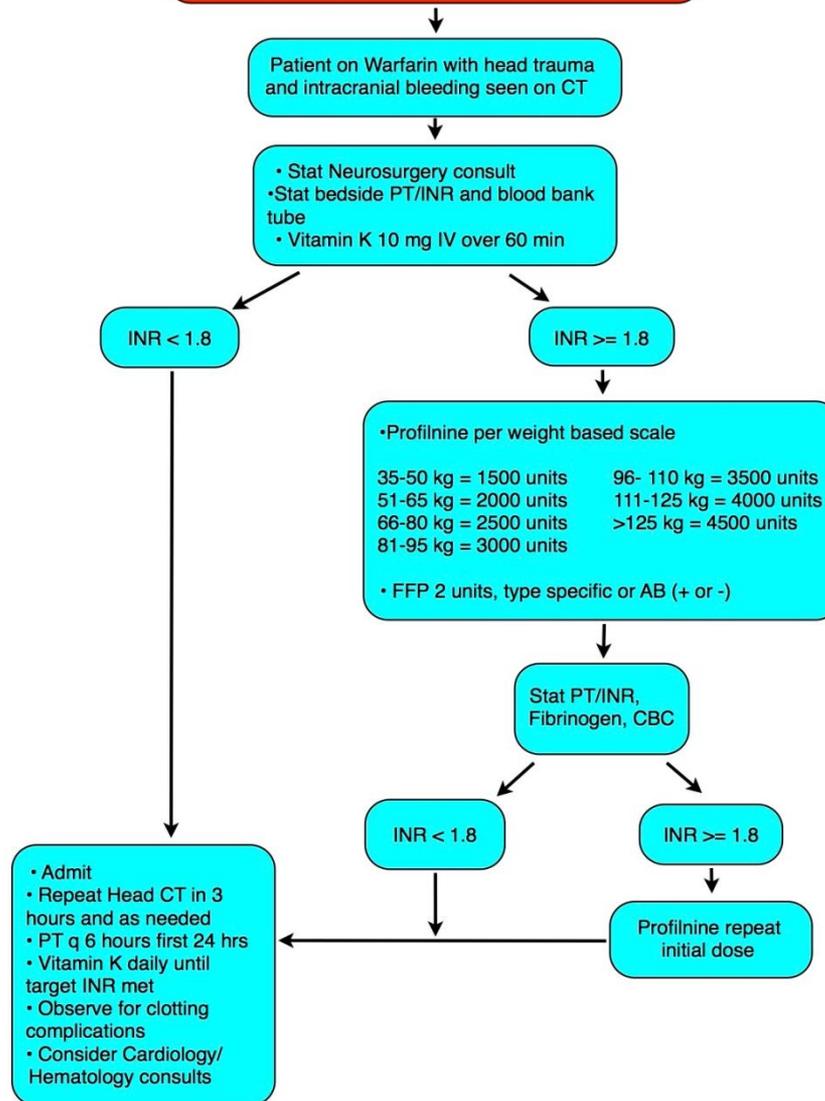


Protocol Development

- Working guideline developed
- P & T committee
- Policy written
- Education
 - Grand Rounds-both physician and nursing
 - Powerplan development



Warfarin Rapid Reversal Pathway



1 year later

- Over/under triage
- Time to CT (25 minutes)
- Time to reverse (67 minutes)
 - 12 patients received PCC
 - 3 deaths (mortality rate of 25%)



Our Data

- Bill Carr, UM Pharm D student
- 2011 Review



Patients

- 12 patients
- Pre-treatment INR = 2.9
- Post-tx INR = 1.4
- 24 hour post-tx INR = 1.1
- Time to first post-tx INR < 1.8 = 131 minutes (20-420)

Patient Data

- 10/12 patients had INR < 1.8 on first recheck
- Other two = 1.8 (from 3.6) and 1.9 (from 5.0)
- No patient had INR rechecked 15 minutes after PCC
- No patient had INR checked q 6 hrs



Mortality

- $3/12 = 25\%$
- Historical mortality
 - On Warfarin = 40-60%
 - No Warfarin = 10-20%



1 Year Review

- Gaps
 - Time to get FFP and PCC (blood bank and Pharmacy)
 - Time to infuse PCC (NSG)
 - Lab monitoring
 - When to re-anticoagulate



Final Thoughts

- It is not what you give that is important (PCC vs FFP), it is how quickly you reverse the coagulopathy that is the main determinant of reducing mortality
- Strongly consider cardiology and hematology consultations – regarding when and how to restart anti-coagulation

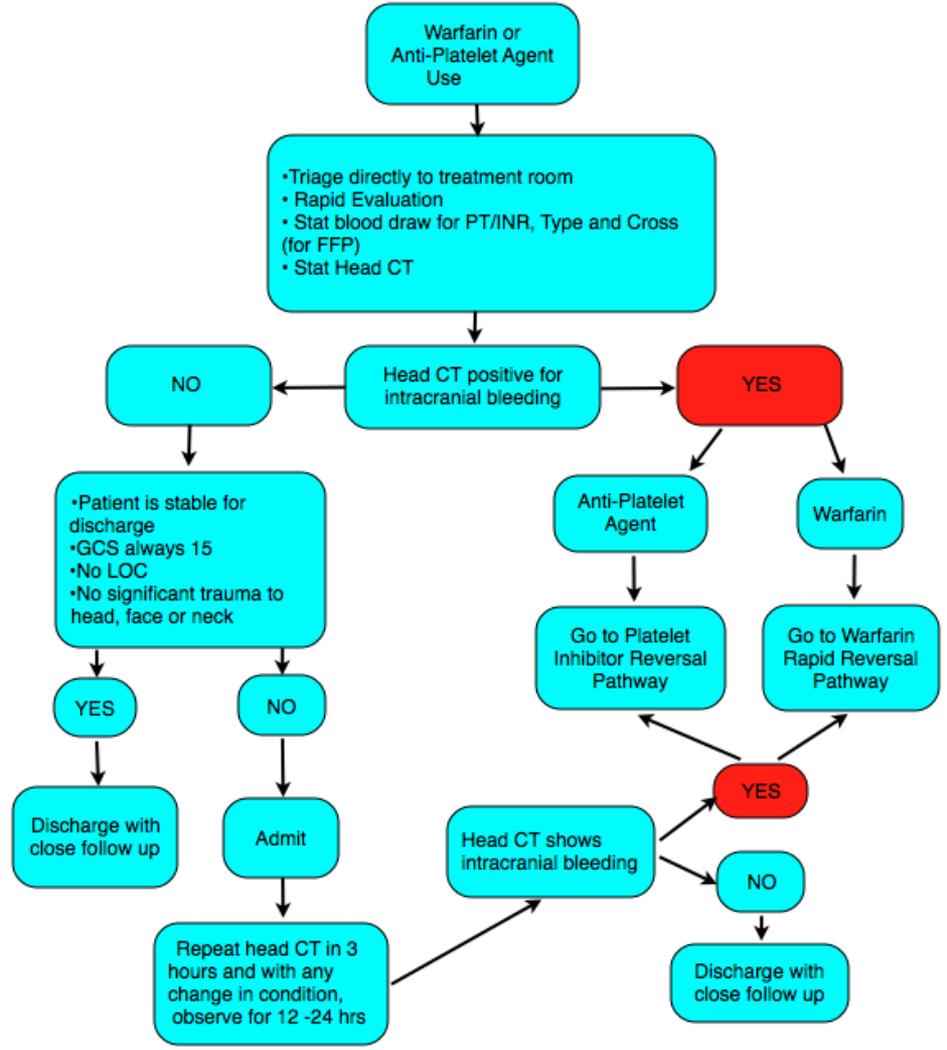


Now What?

- Concurrent review
- Changes to policy
- New anti-coagulants
- Platelet inhibitors



OAC/Platelet Inhibitor with Head Injury Pathway



STUDY SYNOPSIS



Kalina M., et al

- Kalina M, Tinkoff G, Gbadebo A, Veneri P, Fulda G. A protocol for the rapid normalization of INR in trauma patients with intracranial hemorrhage on prescribed warfarin therapy. *The American Surgeon* 2008; 74:858-61.
- Newark Delaware
- Prospective study



Kalina M., et al

- Patients on coumadin, with INR > 1.5 , with intracranial hemorrhage seen on CT
- Patients given weight based Proplex T (PCC) and 5 mg Vitamin K IV
- Repeat INR in 4 hours
- If INR still > 1.5 given FFP and/or more PCC

Kalina M., et al

- Control group was patients treated prior to implementation of PCC protocol
- 111 patients – 46 study, 65 control
- Protocol resulted in increased use of PCC (54.3% vs 35.4%)
- Decreased time to INR normalization (<1.5) 331.3 vs 737.8 minutes

Kalina M., et al

- Increased number of patients with therapeutic reversal – 73.2% vs 50.9%
- Decreased time to the OR – 222.6 vs 351.3 minutes
- No significant difference in ICU LOS, hospital LOS, or mortality.



Ivascu FA et al

- Ivascu FA, Howells GA, Junn FS, Bair HA, Bendick PJ, Janczyk RJ. Rapid warfarin reversal in anticoagulated patients with traumatic intracranial hemorrhage reduces hemorrhage progression and mortality. *J of Trauma, Injury, Infection and Crit Care* 2005; 59:1131-39.
- William Beaumont Hospital, Royal Oak MI



Ivascu FA et al

- Non-PCC study
- Protocol to identify patients on coumadin at risk for traumatic intracranial injury
- Immediate head CT ordered, blood bank notified to thaw 2 units FFP, stat head CT reading



Ivascu FA et al

- Patients with CT evidence of ICH were rapidly given the 2 units of FFP and 10 mg of vitamin K.
- 2 additional units of cross-matched FFP were infused when available.
- Control group were historical patients before the coumadin protocol was established.



Ivascu FA et al

- Historical mortality – 48% for coumadin anticoagulated patients (10% for non-anticoagulated patients)
- 19/82 patients had ICH
- (63/82 patients without ICH admitted for 23 hours – none developed ICH)
- No significant differences between demographics of study patients and control patients



Ivascu FA et al

- Study vs control results
- 14 vs 31 minutes at triage
- 40 vs 132 minutes to obtain head CT
- Time from triage to initiation of anticoagulation reversal – 1.9 vs 4.2 hours
- Anticoagulation reversal (study) – 3.4 hrs
- Mean post-transfusion INR was 1.5 (1.3-1.9) 2 pts with INR > 1.6 treated with FFP

Ivascu FA et al

- Progression of ICH – 11% vs 40% (p<0.001)
- Mortality – 10% vs 48% (p<0.001)
- The 2 patients that died presented more than 10 hours after injury with severe ICH and neurologic changes.



Ivascu FA et al

- This study seems to point out that earlier reversal of coumadin coagulopathy will decrease progression of ICH and decrease mortality.



Foerch Study

- Foerch C, Arai KI, Van Cott EM, van Leyen K and Lo EH. Rapid reversal of anticoagulation reduces hemorrhage volume in a mouse model of Warfarin-associated intracerebral hemorrhage. *J of Cerebral Blood Flow and Metabolism* 2009; 29:1015-21
- Mass General, Harvard Univ



Foerch Study

- Warfarin-associated intracerebral hemorrhage has short term mortality >50%
- Goal of therapy is to achieve a rapid reversal of anticoagulation to prevent the ongoing hematoma expansion.
- Previous study showed anticoagulation in mice within human therapeutic range led to 2.5 fold increase in hemorrhage blood volume in the brain 24 hours after hemorrhage induction.



Foerch Study

- Anticoagulated mice (fed warfarin in drinking water) were randomly assigned to either saline or PCC treatment 45 minutes after hemorrhage induction.
- N = 12 per group



Foerch Study

- Hemorrhagic blood volumes
 - 6.5 vs 15.3 microliters $p=0.015$
- Survival rate at 24 hours
 - 92% (11/12) vs 55% (6/11) $p=0.043$
- All surviving animals showed a moderate to severe functional deficit at 24 hrs



Lankiewicz study

- Lankiewicz MW, Hays J, Friedman KD, Tinkoff G and Blatt PM. Urgent Reversal of warfarin with prothrombin complex concentrate. J Thromb Haemost 2006; 4:967-70.
- Milwaukee WI



Lankiewicz study

- Patients taking coumadin, INR > 2.0, active bleeding or need for immediate surgical intervention.
- Proplex –T
- All patients got Vit K
- 50% of patients got FFP



Lankiewicz study

- 58 patients
- 36 patients with CNS hemorrhage
 - 22 = ICH
 - 12 = subdural
 - 2 = SAH
- Eleven patients with GI bleeding (markedly higher INR's, median = 29)



Lankiewicz study

- 2 pts = cardiac tamponade, 2 pts = expl lap, 1 = severe epistaxis, 1 = aortic dissection, 1= hemothorax, 1= massive chest wall hematoma.



Lankiewicz study

- Mean pre-tx INR = 11.7
- Mean post-tx INR = 1.4 (only 2 above 2.0)
- The 29 pts who did not get FFP had similar pre-tx INR's, post treatment = 1.2
- Surgical procedures – 8 craniotomies, 3 laparotomies, 2 ventriculostomy drains, 2 pericardial drainage, 1 thoracotomy



Lankiewicz study

- No dictated or hand-written operative notes contained comments about excessive blood loss or inadequate hemostasis.



Lankiewicz study

- Complications
 - 1 = line associated upper extremity DVT (17 days after PCC)
 - 1 = recurrence of lower extremity DVT
 - 2 = non-Q wave MI's (both diabetic with known heart disease) (small elevations in Trop and/or CK and CK-MB)

