Thromboprophylaxis after intracerebral hemorrhage

Oral anticoagulant (OAC) resumption does not increase the risk of recurrent ICH and can also reduce the risk of all-cause mortality. OAC cessation exposes patients to a significantly higher risk of thromboembolism, which could be reduced by resumption. The optimal timing of anticoagulation resumption after ICH is still unknown. Both early (< 2 weeks) and late (> 4 weeks) resumption should be reached only after very careful assessment of risks for ICH recurrence and thromboembolism. The introduction of new oral anticoagulants and other interventions, such as left atrial appendage closure, has provided some patients with more alternatives. Given the lack of high-quality evidence to guide clinical decision-making, clinicians must carefully balance the risks of thromboembolism and recurrent ICH in individual patients.

Li and Lip proposed a management approach which would facilitate the decision-making process on whether anticoagulation is appropriate, as well as when and how to restart anticoagulation after ICH.

Given the high risk of hematoma expansion in the early phase of acute ICH, most experts recommend reversing anticoagulation immediately.

Many clinicians start subcutaneous heparinoids in low doses 24 to 72 hours after ICH to prevent deep vein thrombosis, and after the first few days or a week, consider either increasing the dose to a full anticoagulation dose or making a transition to oral anticoagulants.

Many patients with lobar hemorrhage or cerebral amyloid angiopathy may remain at higher risk of anticoagulant-related ICH recurrence than thromboembolic events and would therefore be best managed without anticoagulants.

Those with deep hemispheric ICH, hypertension that can be well controlled, and a high risk of disabling thromboembolism may receive net benefit from restarting anticoagulation.

Urgent reversal of anticoagulation is standard in the acute phase of ICH.

The proposed ‘spot-sign score’ may predict both expansion and poor outcome. see Computed Tomography Angiography spot sign

Antihypertensive therapy likely reduces the risk of recurrence in patients with hypertensive hemorrhage.

Most patients with anticoagulation-related ICH have a presenting INR within the therapeutic range.

The risks of restarting warfarin are high on the first day, but much lower after several days.

A mainstay of medical management in ICH is prevention of venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE). Patients with ICH are at high risk for
DVT and PE, with 4-fold higher rates than in patients with acute ischemic stroke

Venous thromboembolism (VTE) is common after intracerebral hemorrhage (ICH). Guidelines recommend early VTE prophylaxis 3) 4).

American Heart Association/ American Stroke Association guidelines have recommended low-dose unfractionated heparin or low-molecular weight heparin use early after ICH since 2007 5), and currently recommend initiation between 1 and 4 days after ICH onset and after cessation of active bleeding (class IIb, level of evidence B) 6).

Multiple studies have observed that hematoma expansion is infrequently encountered after the first 24 to 48 hours in spontaneous patients with ICH 7) 8).

In contrast, clinically evident VTE occurs in up to 13% of patients with ICH, peaks between days 2 and 7 of hospitalization, and carries a high risk of fatality because of PE 9) 10) 11) 12). However, large randomized clinical trials of pharmacological DVT prophylaxis in patients with ICH have not been conducted. Several observational and nonrandomized studies have indicated that low-dose anticoagulation does not result in hematoma expansion after ICH 13) 14) 15) 16) 17) 18).

In an analysis of the Premier database, Prabhakaran et al. identified adult patients with ICH (International Classification of Diseases Ninth edition code 431) from 2006 to 2010 who survived to day 2 of hospitalization. They excluded those with trauma or who underwent craniotomy or angiography. They abstracted type of anticoagulant used and date of first administration. They used univariate statistics and multivariable logistic regression to assess factors associated with prophylactic anticoagulation after ICH.

Among 32 690 (mean age, 69.7 years; 50.1% men) patients with spontaneous ICH, 5395 (16.5%) patients received any prophylactic anticoagulation during the hospital stay. Among these patients, 2416 (44.8%) received prophylactic anticoagulation by day 2. The most commonly used agents were heparin (71.1%), enoxaparin (27.5%), and dalteparin (1.4%). The proportion of patients receiving prophylactic anticoagulation increased slightly during the study period from 14.3% to 18.0% (P<0.01 for trend). Use of prophylactic anticoagulation varied by geographic region (P<0.001) in the United States: Northeast (23.2%), South (19.0%), Midwest (10.8%), and West (9.8%). In multivariable analysis, geographic region remained an independent predictor of prophylactic anticoagulation after ICH.

Less than 20% of patients with ICH receive anticoagulation for deep venous thrombosis in the United States. When used, the time to initiation is <2 days in less than half of the patients. Further study should focus on understanding variations in practice and emphasize guideline-driven care 19).

Case series

Ianosi et al. from the Institute of Medical Informatics, UMIT - University for Health Sciences, Medical Informatics and Technology, Hall, Department of Neurology, Neurological Intensive Care Unit, Medical University of Innsbruck, Department of Clinical and Experimental Medicine, University of Sassari, Italy, Department of Neuroradiology, Medical University of Innsbruck, Department of Neurosurgery, Medical University of Innsbruck, Austria, analyzed 134 consecutive patients admitted to a tertiary
neurointensive care unit with diagnosed spontaneous intracerebral hemorrhage, obtained informed consent and without previous anticoagulation, a severe coagulopathy, hematoma evacuation, early withdrawal of therapy or eligibility for DVT prophylaxis according to their institutional protocol. Significant late hematoma expansion (HE) was defined as ≥6mL increase of hematoma volume between neuroimaging within 48h and day 3-6. Multivariate analysis was performed to identify risk factors for late HE, poor 3-month outcome (mRS≥4) and mortality.

Patients had a median Glasgow Coma Scale Score of 14 (IQR 10-15), ICH volume of 11mL (IQR 5-24) and were 71 years old (IQR 61-76). 56% (N=76) received early DVT prophylaxis, 37% (N=50) late DVT prophylaxis and 8 (6%) had unknown bleeding onset. Patients with early DVT prophylaxis had smaller ICH volume (9.5mL, IQR 4-18.5; versus 17.5mL, IQR 8-29; p=0.038) and more often were comatose (26% versus 10%, p=0.025). Significant late HE (N=5/134, 3.7%) was associated with larger initial ICH volume (p=0.02) and lower thrombocyte count (p=0.03) but not with early DVT prophylaxis (p=0.36). Early DVT prophylaxis was not associated with worse outcome.

Significant late HE is uncommon and DVT prophylaxis within 48h of symptom onset may be safe in selected ICH patients 20).

To determine characteristics associated with early chemoprophylaxis (CP) after ICH in the Get With The Guidelines-Stroke registry. METHODS:

In this observational cohort study, we identified patients with ICH between January 1, 2009 and September 30, 2013, who (1) were non-ambulatory and/or not comfort care measures by hospital day 2; (2) were not transferred to another acute care facility; and (3) had known VTE prophylaxis status at end of hospital day 2. Categories for VTE prophylaxis were as follows: (1) mechanical non-CP or (2) CP with or without mechanical prophylaxis. Early prophylaxis was defined as occurring by hospital day 2. Using multivariable logistic regression, we assessed patient, hospital, and geographic factors independently associated with early CP use. RESULTS:

Among 74 283 patients with ICH from 1358 hospitals, 5929 (7.9%) received early CP, 66 444 (89.4%) received early mechanical/non-CP, and 1910 (2.6%) had no prophylaxis, mechanical or CP, within the first 2 days. There was no increase in early CP use over the study period; 60% of hospitals provided early CP to <9% of patients. In multivariable analysis, female sex, atrial fibrillation, diabetes, coronary, carotid, and peripheral artery disease, prior ischemic stroke or transient ischemic attack, hospital size >500 beds, and geographic region were independently associated with early vs no early CP use. CONCLUSION:

Nationwide, the large majority of ICH patients receive early mechanical VTE prophylaxis only, without CP. Patient comorbidities and hospital characteristics such as geographic location are determinants of higher use of early CP 21).

Wu et al. identified patients from their stroke registry (6/03 to 12/07) who presented with ICH only or ICH + intraventricular hemorrhage (IVH) and received either LMWH SQ or UH within 7 days of admission and had a repeat CT scan performed within 4 days of starting DVT prophylaxis. We calculated the change in hematoma volume (Δvol) from the admission and post treatment CTs. HV was calculated using the (ABC/2) method and IVH volumes were calculated using a published method of hand drawn regions of interest (ROI)

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They identified 73 patients with a mean age of 63 yo and median NIHSS 11.5. The mean baseline total HV was 25.8ml ± 23.2ml. There was an absolute Δvol from pre and posttreatment CT of −4.3ml ± 11.0ml. Two patients developed hematoma growth. Repeat analysis of patients given pharmacological DVT prophylaxis within 2 or 4 days after ICH found no increase in hematoma size.

Pharmacological DVT prophylaxis given SQ in patients with ICH and/or IVH in the subacute period is generally not associated with hematoma growth 22).

References


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