MonashHealth

Clinicians, Consumers, Evidence
Centre for Clinical Effectiveness

Scoping Review

Head Injury and Patients on Anticoagulant/Antiplatelet Therapies

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Executive Summary

Background

The Centre for Clinical Effectiveness was requested to review the evidence for managing patients who present with mild trauma to the head and are known to be on oral anticoagulant, antiplatelet therapy.

Objective

The objectives of this scoping review were to determine:

A. How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?

B. What is the optimal timing and frequency of Computed Tomography (CT) brain scans in the period following the minor head trauma (e.g. fall) to determine if intracranial bleeding has occurred?

Methods

A search of medical databases and websites known to the author were searched. Documents providing information for the management of oral anticoagulants and/or dual anti-platelet agents for adults who have sustained a minor head injury and optimal timing and frequency of CT scans were included.

Results

The search of the evidence identified eight clinical practice guidelines[1-8], one systematic review with meta-analysis[9] and one observational cohort study[10]. The quality of the documents included were informally appraised. The majority were of good quality. It is important to note that the guidelines and systematic review included in this report contained studies considered to be low level evidence.

Summary of findings

Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?

Identified evidence[1, 2, 4-6, 8] suggests that patients with minor head trauma, on an anticoagulant with a confirmed intracerebral haemorrhage should have their anticoagulant therapy reversed. A summary of recommendations for reversal of antithrombotic agents in patients with intracranial haemorrhage were identified and reported.[1]

Objective B: What is the optimal timing and frequency of CT brain scans in the period following the minor head trauma (eg fall) to ensure that intracranial bleeding has not occurred?

Identified evidence suggests that an initial head CT scan should be performed on all head injury patients when they present.[2, 3, 5-9] The NICE (2014) guideline[3] and pathway[11] (2016) suggest that for patients with a head injury, specifically on warfarin, a CT scan should be performed within 8 hours. However, the Trauma Victoria[5] (2014) and Alfred Health[2] (2016) guidelines suggest that head injury patients who are on any type of anticoagulant should have an immediate CT scan. The evidence suggests that the frequency of additional head CT scans is dependent on the initial scan. Follow-up CT scans should be undertaken between 12 and 24 hours, or earlier if there are signs of clinical deterioration.

Conclusion

The evidence suggests that patients with minor head trauma, on an anticoagulant with a confirmed intracerebral haemorrhage should have their anticoagulation therapy revered and there are specific reversal agents recommended. The evidence found that there is variation between immediately and within 8 hours for patients presenting with head injury and on anticoagulants or antiplatelets for initial CT scans. The frequency of subsequent CT scans is dependent on the outcomes of the first scan and for patients identified as having an intracranial bleed, observation and secondary scans are recommended between 12 and 24 hours of the first scan unless there is evidence of clinical deterioration. The majority of documents identified are of good quality however, most are based on low level evidence.

Background

The Centre for Clinical Effectiveness was requested to review the evidence for managing patients who present with mild trauma to the head and are known to be on oral anticoagulant, antiplatelet therapy with or without mechanical heart valve or stent.

The review will inform the production of a guideline on how to manage oral anticoagulant and antiplatelet agents and frequency and timing of repeat brain imaging to detect intracranial bleeding in this specific patient group.

Objectives

The objectives of this scoping review were to determine:

A. How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?

B. What is the optimal timing and frequency of Computed Tomography (CT) brain scans in the period following the minor head trauma (e.g. fall) to determine if intracranial bleeding has occurred?

Search strategy

Medline and all evidence based medicine (EBM) databases were searched. In addition, websites known by the author to contain clinical guidelines and systematic reviews were also searched. Search terms and dates are provided in Appendix 1.

Document Selection

Titles and abstracts identified were exported to EndNote X7 (Thompson, Reuters, Carlsbad, California, USA). Documents identified were screened using inclusion criteria established *a priori.* Searches of health databases and websites were screened by one independent reviewer in consultation with colleagues. Documents were included based on the criteria outlined in Table 1. Based on search results a decision was made a posteriori to include documents published after 2010.

Data collection process

Data was extracted by one reviewer (MG). Recommendations and outcomes relevant to decisions A and B were extracted and are provided in Appendix 2 - Tables 3 and 4.

Inclusion Criteria

Table 1. Study eligibility criteria

Patient	**Inclusion:** Adults taking oral anticoagulants and/or dual anti-platelet agents (including for patients with mechanical valves or with cardiac stent in situ) who have sustained a minor head trauma (eg fall) **Exclusion:** All other patients		
Intervention/ indicator	**Inclusion:** Objective A: adjust, reverse, discontinue, or continue oral anticoagulant and/or anti-platelet agents Objective B: CT brain scan timing and frequency **Exclusion:** All other interventions/indicators		
Outcomes	**Inclusion:** Objective A: regimes for anticoagulant and/or antiplatelet agents for minor head trauma patients, adverse bleeding events Objective B: identification of further intracranial bleeding		
Study type	Guidelines, Pathways, HTAs, Systematic reviews and Randomised Controlled Trials (RCTs) addressing the specified outcomes are sought.	***Publication Date***	2008 onwards
		Language	English

Results

A total of 10 studies were included in this report. Searching identified eight clinical practice guidelines[1-8], one systematic review and meta-analysis[9] and one observational cohort study. [10]

The database searches identified 1142 citations. Seven additional records were identified through searches of guideline websites and documents known to the authors.

When a screening decision could not be made based on title and abstract alone, full text was retrieved. Forty-one full text documents were retrieved and 10 were included in the review (Figure 1).

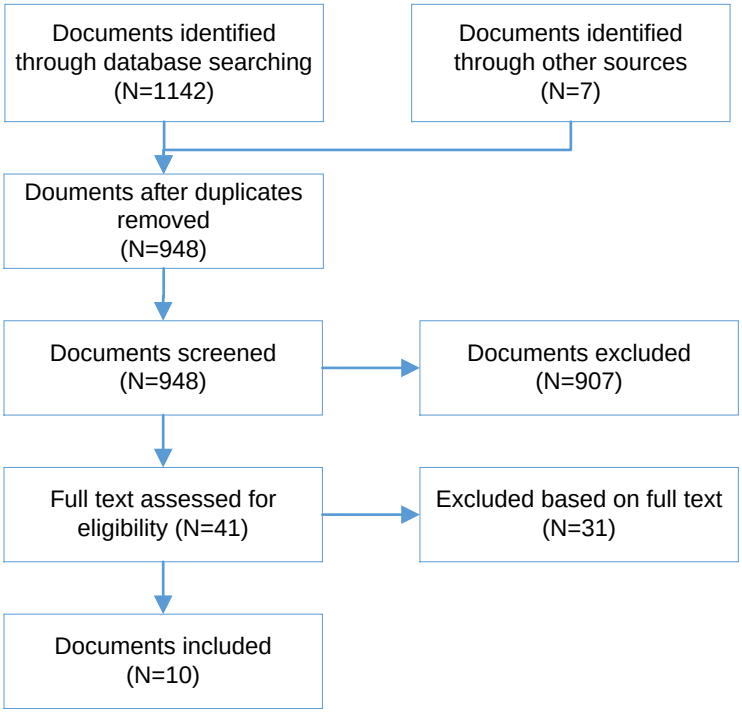

Figure 1. Search results and screening process used in the review

Quality of identified documents

The quality of the documents included were informally appraised (Appendix 2 – Table 5). Although the included guidelines and systematic review are of good quality, it is important to note that they are based on low level evidence, mostly observational, retrospective and prospective study designs. We were unable to confirm the methodology behind the development of two guidelines[2,4] however, these guidelines have been included as they may provide useful examples for Monash Health .

Summary of findings by decision

Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?

Identified evidence[1, 2, 4-6, 8] suggests that patients with minor head trauma, on an anticoagulant with a confirmed intracerebral haemorrhage should have their anticoagulant therapy reversed. A guideline developed by the NSW Health Ministry (2011) suggests that the evidence for reversing antiplatelet agents is less clear. However, there is a clear trend to suggest that mild head injury patients on anti-platelets have an increased risk of bleeding following intracranial haemorrhage but limited evidence to prove that anti-platelets independently increase the risk of intracranial haemorrhage for mild head injury patients.

A recent observational cohort study[10] found that resuming oral anticoagulant therapy in patients with traumatic intracerebral haemorrhage was associated with a lower rate of ischemic events, and a lower relative risk for recurrent intracerebral haemorrhage despite resumption of warfarin treatment. Warfarin resumption was associated with a lower risk for death within the first year after the event.

A guideline developed by the Neurocritical Care Society and the Society for Critical Care Medicine[1] provides specific recommendations for reversal of the following antithrombotic agents in patients with intracranial haemorrhage: Vitamin K Antagonists, Direct Thrombin Inhibitor, Unfractionated Heparin, Low Molecular Weight Heparin, Pentasccharide, Thrombolytic agents, Antiplatelet agents.

Decision B: What is the optimal timing and frequency of CT brain scans in the period following the minor head trauma (e.g. fall) to ensure that intracranial bleeding has not occurred?

Identified evidence suggests that an initial head CT scan should be performed on all head injury patients when they present.[2, 3, 5-9]

Timing of the first CT scan

The NICE (2014) guideline[3] and pathway[11] (2016) suggests that for head injury patients on warfarin treatment, a CT scan should be performed within 8 hours. The Trauma Victoria[5] (2014) and Alfred Health[2] (2016) guideline suggest that, for head injury patients, anticoagulants are an indication for immediate CT scan. The NSW Ministry for Health guideline[8] (2011) however, suggested that there is no direct evidence to confirm the best time for CT scans in relation to the time of injury.

Frequency of subsequent CT scans

The evidence suggests that the frequency of additional CT scans of the head is dependent on the results of the initial scan. The recommendations noted in the evidence are summarised in Table 2. If required, a follow-up CT scan should be undertaken between 12 and 24 hours, or earlier, if there are signs of clinical deterioration. However, the NSW Ministry of Health Guideline[8] (2011) states that "there has been some debate in the literature about whether mild head injury patients who have initially abnormal CT scans and require admission for hospital observation should have a routine repeat CT scan. The evidence from most of these small studies suggests that most mild head injury patients with minor abnormalities on CT scan do not require routine repeat CT scanning if they are clinically improving with a normal GCS and no neurological deficit unless they are anti-coagulated. The other question that is often asked is should elderly anti-coagulated patients with normal initial CT scans have routine repeat CT scans and if so when should they be performed and should the patient be admitted for observation. There is little evidence to guide management in these situations. The consensus appears to be that the older the patient, and the more the patient is anticoagulated (higher INR), the greater the risk of delayed bleeding. However, how to manage that risk remains unclear."

Table 2: Recommendations for frequency of CT scans by results

1st CT scan results – when to perform a follow up scan			
No signs intracranial haemorrhage – Therapy reversed	**No signs intracranial haemorrhage – Therapy continued**	**Evidence of intracranial haemorrhage**	**No haemorrhage but other symptoms** (post traumatic amnaesia, headache, vomiting or other features of head injury – or cannot be discharged with a competent carer)
If the clotting profile is normal, CT brain scan shows no acute signs of haemorrhage, the patient is not in post-traumatic amnesia, and there are no other clinical features of head injury, the patient may be considered for discharge from the Emergency Department, Emergency Short Stay Unit, or acute care area after 4 hours observation. The patient will need to be discharged with a carer and Head Injury Instructions.[2]	The patient will remain on 1 hourly Glasgow Coma Scale (GCS) neurological observations for the first 24 hours unless this is outside the sites current inpatient guideline or as directed by medical team. A follow-up CT brain will be undertaken within the first 24 hours or upon any reduction in the GCS. [2]	The patient should be closely observed, including repeat CT at 12-24 hours, or earlier if any deterioration.[2]	Follow up CT brain should be performed at 24 hours, or earlier if clinical deterioration. [2]
Repeat CT scans 24 hours after an initial normal imaging are not necessary in most situations.[9]		Observe ≥24 hrs consider consult neurotrauma center and repeat CT (or MRI)[7]	
Follow up CT scan results			
	If the follow-up CT brain reveals no intracranial bleeding, frequency of GCS observations can be reduced. [2] If CT brain shows intracranial bleeding, refer to Neurosurgery urgently.[2]		If follow-up CT brain also shows no haemorrhage, no further CT brain is required unless clinically indicated. [2]

Conclusions

The evidence suggests that patients with minor head trauma, on an anticoagulant with a confirmed intracerebral haemorrhage should have their anticoagulation therapy revered and there are specific reversal agents recommended. The evidence found that there is variation between immediately and within 8 hours for patients presenting with head injury and on anticoagulants or antiplatelets for initial CT scans. The frequency of subsequent CT scans is dependent on the outcomes of the first scan and for patients identified as having an intracranial bleed, observation and secondary scans are recommended between 12 and 24 hours of the first scan unless there is evidence of clinical deterioration. The majority of documents identified are of good quality however, most are based on low level evidence.

References

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Appendix 1

Search Strategy

Guideline Resources

The following websites were searched for clinical guidelines.

Search terms included: Falls, Head trauma, Head Injury, Anticoagulation, and Antiplatelet

BMJ Best Practice	Cochrane Library	Clinical Practice Guidelines Portal (NHMRC)
TRIP Database	National Guideline Clearinghouse (NGC)	The National Institute for Health and Care Excellence (NICE)

Medical Databases

Information sources	***Date of search***
All EBM (Ovid) *	23/02/2017
Medline (Ovid) Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1950 to Present	23/02/2017

*(includes The Cochrane Database of Systematic Reviews, DARE, CENTRAL and ACP Journal Club)

Search terms

Search Terms in Medline*	
#	**Terms**
1	exp Anticoagulants/
2	exp Platelet Aggregation Inhibitors/
3	Anticoagula*.mp.
4	Antiplatelet*.mp.
5	1 or 2 or 3 or 4
6	exp Craniocerebral Trauma/
7	head trauma.mp.
8	6 or 7
9	exp Intracranial Hemorrhages/
10	exp Cerebral Hemorrhage/
11	exp Subarachnoid Hemorrhage/
12	exp Hematoma, Subdural/
13	Intracranial Hemorrhage, Traumatic/
14	Intracranial Hematoma.mp.
15	exp Basal Ganglia Hemorrhage/
16	((Intracranial or cerebral) and bleed*).mp.
17	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18	8 or 17
19	5 AND 18
20	Limit 20 to (english language and humans and yr="2008 -Current")
21	Filters for Guidelines, Systematic Review HTA, RCTs used from https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#guide

*(Similar terms (appropriately translated) were used in other databases.)

Appendix 2 – Evidence for Objectives

Table 3. Recommendations for Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?

Ref	Document type and Quality	Evidence for Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?
1	Guideline	Recommendations for reversal of: **VKA (p16), Direct Thrombin Inhibitor (p23), Unfractionated Heparin (p24), LMWH (p26), Pentasccharide (p27), Thrombolytic (p29), Antiplatelet Agent (p33)**

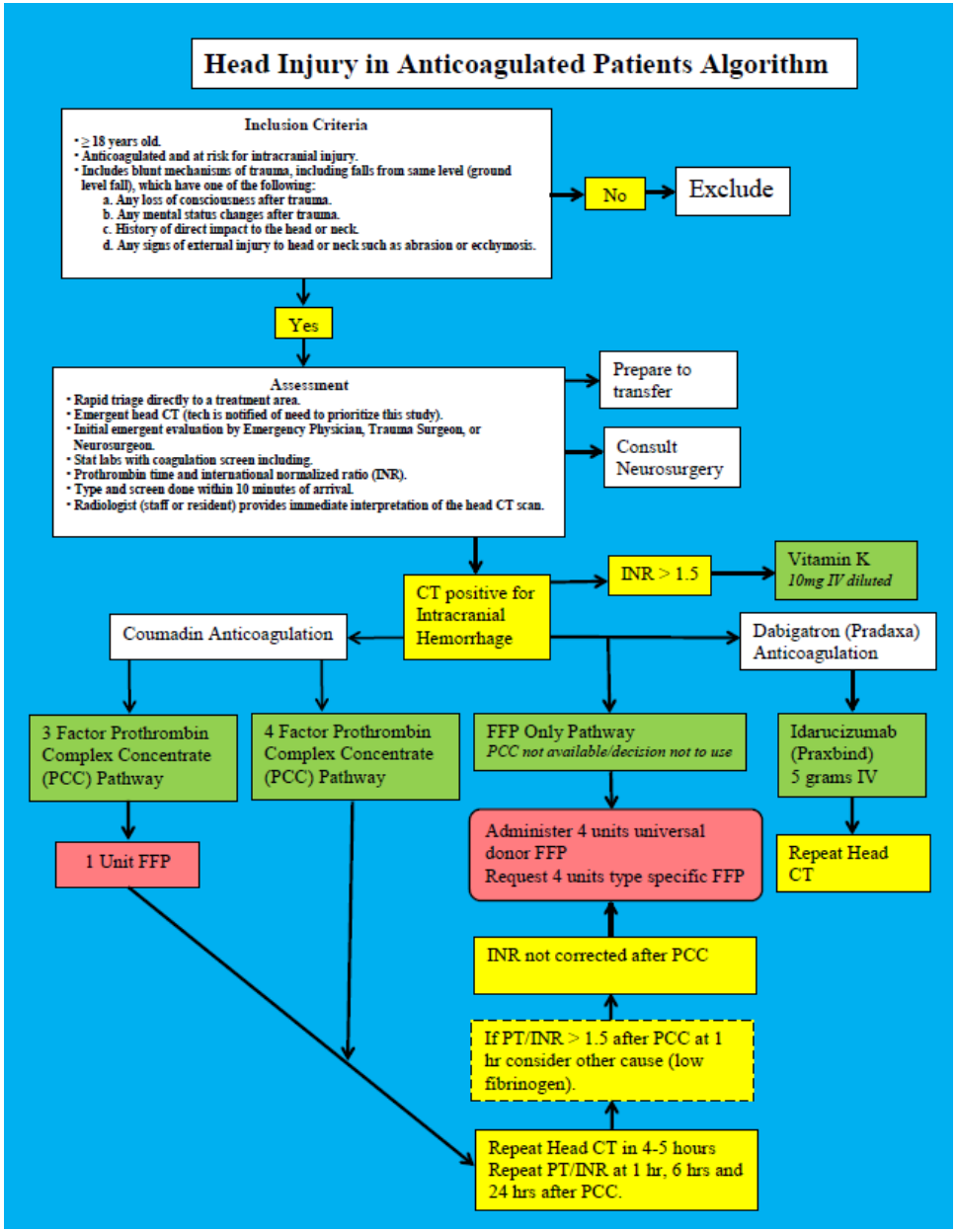
Table 5 Summary of recommendations for reversal of antithrombotic agents in patients with intracranial hemorrhage

Antithrombotic	Reversal agent
Vitamin K antagonists	If INR ≥ 1.4: Vitamin K 10 mg IV, plus 3 or 4 factor PCC IV (dosing based on weight, INR and PCC type) OR FFP 10–15 ml/kg IV if PCC not available
Direct factor Xa inhibitors	Activated charcoal (50 g) within 2 h of ingestion, Activated PCC (FEIBA) 50 units/kg IV OR 4 factor PCC 50 units/kg IV
Direct thrombin inhibitors	For dabigatran reversal: Activated charcoal (50 g) within 2 h of ingestion, AND Idarucizumab 5 g IV (in two 2.5 g/50 mL vials) Consider hemodialysis or idarucizumab redosing for refractory bleeding after initial administration For other DTIs: Activated PCC (FEIBA) 50 units/kg IV OR 4 factor PCC 50 units/kg IV
Unfractionated heparin	Protamine 1 mg IV for every 100 units of heparin administered in the previous 2–3 h (up to 50 mg in a single dose)
Low-molecular weight heparins	Enoxaparin: Dosed within 8 h: Protamine 1 mg IV per 1 mg enoxaparin (up to 50 mg in a single dose) Dosed within 8–12 h: Protamine 0.5 mg IV per 1 mg enoxaparin (up to 50 mg in a single dose) Minimal utility in reversal > 12 h from dosing Dalteparin, Nadroparin and Tinzaparin: Dosed within 3–5 half-lives of LMWH: Protamine 1 mg IV per 100 anti-Xa units of LMWH (up to 50 mg in a single dose) OR rFVIIa 90 mcg/kg IV if protamine is contraindicated
Danaparoid	rFVIIa 90 mcg/kg IV
Pentasaccharides	Activated PCC (FEIBA) 20 units/kg IV or rFVIIa 90 mcg/kg IV
Thrombolytic agents (plasminogen activators)	Cryoprecipitate 10 units IV OR Antifibrinolytics (tranexamic acid 10–15 mg/kg IV over 20 min or ε-aminocaproic acid 4–5 g IV) if cryoprecipitate is contraindicated
Antiplatelet agents	DDAVP 0.4 mcg/kg IV × 1 If neurosurgical intervention: Platelet transfusion (one apheresis unit)

PCC prothrombin complex concentrates, *LWMH* low-molecular weight heparin, *rFVIIa* recombinant factor VIIa, *DDAVP* desmopressin

Ref	Document type and Quality	Evidence for Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?
2	Guideline	**If initial head CT shows evidence of intracranial haemorrhage** For patients with CT evidence of intracranial haemorrhage and who are on a direct oral anticoagulant (e.g., Rivaroxaban, Apixaban or Dabigatran), the drug should be discontinued immediately. In general, unlike Warfarin, reversal of the anticoagulant effect of these drugs should only be undertaken if neurosurgical intervention is required immediately or there is a high probability of requiring surgery within 4 hours. Otherwise, the case should be discussed with the haematologists and a clear plan for reversing the effects of the medication (should this become necessary) should be recorded in the notes. The patient should be closely observed, including repeat CT at 12-24 hours, or earlier if any deterioration. • Neurosurgery is to be notified immediately, and possibility of need for surgery considered. • Reversible drugs (i.e., Warfarin) must be reversed urgently according to relevant Alfred Health protocol. • Anti-platelet agents must be ceased. • DVT prophylaxis should be instituted with mechanical calf-compressors • Low molecular-weight heparin should not be prescribed initially. • Patient should be fasted, and monitored with hourly GCS. • Repeat CT brain if clinical deterioration, or within 12-24 hours if no deterioration. • Admit with daily review of the need for further imaging. • If repeat CT brain shows stable bleed, discuss with neurosurgery before re-commencing anticoagulation or antiplatelet agents, and before commencing low molecular-weight heparin for DVT prophylaxis. • Avoid sedating drugs that could impact upon GCS. **If initial head CT shows no intracranial haemorrhage but the patient has PTA, headache, vomiting or other features of head injury - or cannot be discharged with a competent carer:** • Cease the anticoagulation or antiplatelet if medically feasible. • DVT prophylaxis should be instituted with mechanical calf-compressors, and not low molecular-weight heparin. • Follow up CT brain should be performed at 24 hours, or earlier if clinical deterioration. • Patient should be monitored with 2 hourly GCS until repeat CT brain is done, and confirmation that there is no development of intracranial haemorrhage. • If follow-up CT brain also shows no haemorrhage, no further CT brain is required unless clinically indicated, the antiplatelet or anticoagulant drug may be reintroduced as clinically indicated, and the patient may have DVT prophylaxis with low molecular-weight heparin. Caution use if the patient is already on Warfarin / DAC, especially in the older person. • Avoid sedating drugs that could impact upon GCS. **In the event that anticoagulation or antiplatelet therapy is continued:** • Anticoagulation therapy should continue only if CT brain is completely normal, and the medical indications show that the benefits outweigh the risks of a possible intracranial haemorrhage. At the Alfred site the patient will be admitted only to 2 East, 2 West or a high dependency area. • The patient will remain on 1 hourly GCS neurological observations for the first 24 hours unless this is outside the sites current inpatient guideline or as directed by medical team. A follow-up CT brain will be undertaken within the first 24 hours or upon any reduction in the GCS. If the follow-up CT brain reveals no intracranial bleeding, frequency of GCS observations can be reduced. If CT brain shows intracranial bleeding, refer to Neurosurgery urgently, and as in 4 above.

Ref	Document type and Quality	Evidence for Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?
4	Guideline	**Diagnosis:** • Rapid triage directly to a treatment area. • Stat labs with coagulation screen including Prothrombin time (PT) and international normalized ratio (INR), and type and screen done within 10 minutes of arrival. • Emergent ordering of head CT scan. • An initial emergent evaluation by emergency physician, trauma surgeon, or neurosurgeon. • Immediate head CT interpretation by the radiologist and communication to treating physician **Treatment** • Patients without any signs of intracranial hemorrhage on the initial head CT scan are managed based on specific guidelines and/or treating physician discretion, which may include admission for observation or repeat head CT. • Patients with CT scan confirmation of intracranial hemorrhage and INR greater than 1.5 please give 10 mg of vitamin K given IV piggyback (Patients with history of allergic reaction to vitamin K will not receive it). **Prothrombin complex concentrate (PCC) pathway** A four-factor PCC and the preferred treatment/reversal agent in treatment of patients who are anticoagulated with warfarin and have intracranial hemorrhage. Relative contraindications to PCC use include: • History of thrombotic or thromboembolic event in past 6 weeks (DVT, PE, ischemic stroke, acute coronary syndrome, acute venous/arterial ischemia etc.). • Known prothrombotic condition (malignancy, DIC, hypercoagulable condition, hepatic disease, polytrauma, HIT, etc.). • If any of the above criteria is met or the patient has mechanical heart valve such as aortic or mitral valve replacement, please discuss with ER, trauma surgery, or neurosurgery attending the possibility of giving PCC. A four-factor PCC should be able to reverse warfarin anticoagulation without fresh frozen plasma (FFP) administration; therefore, side effects of FFP administration, such as risk for volume overload, may be avoided. However, trauma patients who require fluid resuscitation may benefit from the combined treatment of PCC with administration of two to four units of FFP as the initial treatment. Combined initial treatment (PCC with FFP) can be initiated at the discretion of the treating



Ref	Document type and Quality	Evidence for Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?	
		physician. • If INR 1.6-1.9, PCC may be considered as described above. Given the scarce evidence and the potential prothrombotic risk of PCC, FFP may be considered as an alternative (see FFP pathway below). • Check PT/INR (or EHP) at one hour, six hours and 24 hours after PCC administration. • If PT/INR is still greater than 1.5 after appropriate dosing of PCC in one hour, consider other possible causes such as a low fibrinogen. For patients whose INR does not correct after PCC, please switch to FFP pathway with the empiric administration of two to four units of thawed FFP. A three-factor PCC is also available and a viable option but the addition of one unit of fresh frozen plasma should be administered to aid in coagulation. **FFP alone pathway (If PCC not available or decision was made not to use it)** • Immediately transfuse 4 Units universal-donor FFP and request four units of type specific FFP to be sent as soon as possible. • Check INR after the first four units of FFP have been infused and follow your hospital guidelines or treating physician discretion for repeat FFP dosing as needed. **Dabigatron (Pradaxa) Pathway** Patients anticoagulated with dabigatron (Pradaxa) can safely be reversed with idarucizumab (Praxbind). The FDA recently approved Praxbind for reversal of anticoagulation. The recommended dose for Praxbind is five grams, provided in two separate 50 milliliter vials. Follow the manufacture administration recommendations. Following the administration of Praxbind a follow-up CT scan should be performed.	
5	Guideline	**Anticoagulation and head trauma** Any patient who is taking an anticoagulant such as warfarin or other oral anticoagulants (dabigatran, rivaroxaban, apixaban) is at high risk of developing a significant intracranial haemorrhage from minor head injury mechanisms. CT imaging of the brain should be performed on all patients with a history of head injury. Platelet inhibitor therapy (aspirin (e.g. Astrix, Cartia), dipyridamole (Asasantin, Persantin), clopidogrel (Iscover, Plavix), prasugrel (Effient), ticagrelor (Brilinta)) also increases the risk for haemorrhagic injuries but to a lesser degree. These patients often have significant comorbidities also, all of which will have a direct impact on surgical and intensive care decision making and treatment. The effects of anticoagulation and antiplatelet drugs may require their reversal, with consideration of the risks of exacerbation of the underlying condition.	

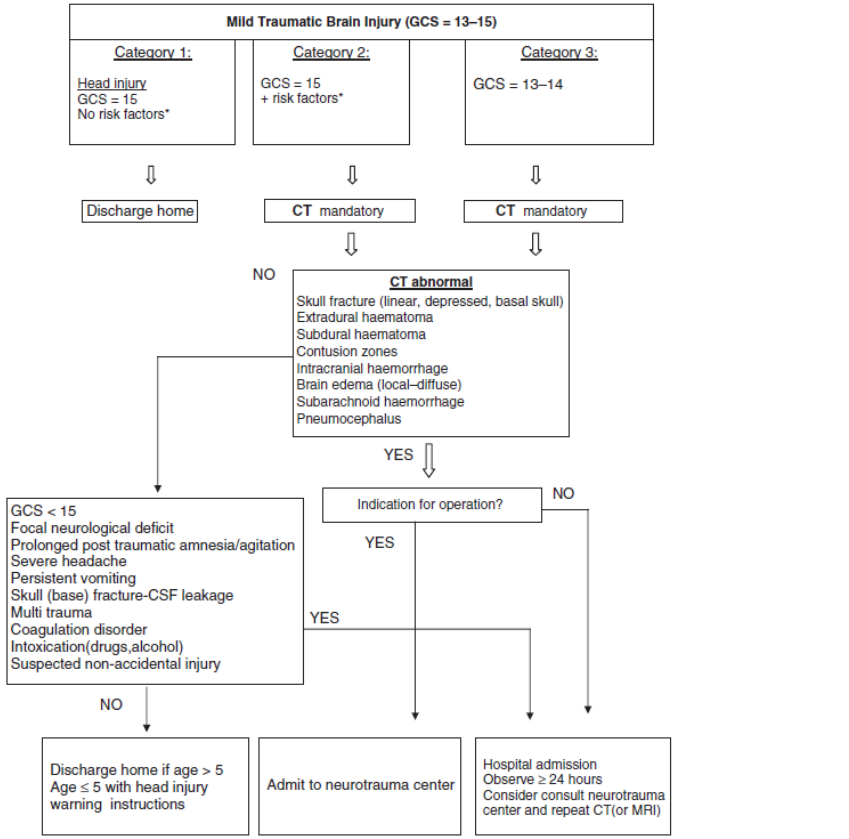
Ref	Document type and Quality	Evidence for Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?
		Where intracranial haemorrhage is present, patients on anticoagulation medication may deteriorate because of extension of their bleed leading to mass effect, brain compression and herniation. In these patients, reversal of medications should be commenced with appropriate reversal agents. Consultation with ARV should take place prior to administration. For immediate reversal of anticoagulation in patients with bleeding due to warfarin, prothrombin complex concentrates (Prothrombinex-VF in Australia) are preferred over fresh frozen plasma (FFP). The dose for prothrombin complex concentrates is 35–50 units/kg IV. This aims to achieve complete reversal of an excessive INR within 15 minutes. The dose for life-threatening bleeding should be the maximum 50 units/kg.xviii FFP is not routinely needed in combination with prothrombin complex concentrates unless there is life-threatening bleeding. If life-threatening bleeding is present the dose of FFP is 150–300 mL by IV infusion. Where Prothrombinex-VF is unavailable the dose for FFP is 15 mL/kg IV infusion. Time is required for determining the patient's blood type (or use group AB plasma), thawing of the product and subsequent infusion. Vitamin K is essential for sustaining the reversal achieved by PCC or FFP. IV administration produces a more rapid response than oral administration in the short term. The dose is 5–10 mg IV. Specialist haematological advice should be sought for guidance on reversal of anticoagulation due to new novel anticoagulants such as dabigatran, rivaroxaban and apixaban. For such patients, consult with MTS emergency, trauma and haematology staff via ARV.
6	Guideline	<u>Level 3 evidence</u> Patients taking warfarin who present in the acute setting with an MTBI should have their international normalized ratio (INR) level determined. Anticoagulated patients with supratherapeutic INR values and a normal initial brain CT scan result remain at significant risk for interval development of intracranial hemorrhage and should be admitted for a period of observation.
8	Guideline	Individual factors predicting risk of intracranial injury and therefore the need for CT scanning in patients with mild head injury: *Coagulopathy or bleeding disorder* • Known coagulopathy or bleeding disorder is both a strong indication for early CT scan and also an indication to check the INR and to consider reversal of anticoagulation. Anticoagulated patients with any evidence of haemorrhage on CT scan should have early rapid reversal of anticoagulation. Patients with a supra-therapeutic INR (>4) should be considered for either partial or full reversal and admitted to hospital for prolonged observation. Prolonged observation and follow up repeat CT scan should be considered for any anticoagulated patients or patients with bleeding disorders • Ivascu et al (2005) demonstrated that early rapid reversal of warfarin in patients with intracranial haemorrhage significantly improved mortality. (p33) • Mild head injury patients who are warfarinised are at significantly increased risk of traumatic intracranial haemorrhage particularly if they are elderly or overwarfarinised. Note that this increased risk applies to asymptomatic patients. They should all receive an urgent CT scan and have an early INR checked. Patients who have a traumatic injury on CT scan or who have a supratherapeutic INR (>4) should be admitted for observation and should be strongly considered for short term reversal of their anticoagulation as they are at high risk of acute deterioration and death. A routine repeat CT scan within 24 hours or an urgent repeat CT scan if there are any signs of deterioration is recommended for these patients. • The evidence is less clear about the risk of traumatic ICH associated with anti-platelet agents or bleeding disorders • There is a clear trend to suggest patients on anti-platelets have an increased risk of bleeding following intracranial haemorrhage but limited evidence to prove that anti-platelets independently increase the risk of intracranial haemorrhage for mild head injury patients.
10	Observational Cohort Study	<u>Prognosis for patients with Traumatic ICH</u> During the first year of follow-up, 27 patients experienced an ischemic stroke or SE, whereas 89 experienced a recurrent ICH almost solely driven by diagnoses of recurrent traumatic ICH (87 [97.8%]).Patients who resumed warfarin therapy had a lower rate of ischemic stroke or SE (2.1 per 100 person-years vs 4.1 per 100 person-year; AHR, 0.40; 95%CI, 0.15-1.11) (Figure 2), but the difference was not statistically significant. The adjusted relative risk for recurrent bleeding with resumption of warfarin treatment was 0.45 (95%CI, 0.26-0.76), and resumption of treatment was associated with a lower adjusted relative risk for all stroke (AHR,

Ref	Document type and Quality	Evidence for Objective A: How anticoagulants or antiplatelet agents should be managed for patients with minor head trauma?
		0.36; 95% CI, 0.16-0.84) and death (AHR, 0.35; 95%CI, 0.23-0.52). Conclusions Spontaneous hemorrhagic stroke and **trauma-induced ICH confer different prognoses in patients with AF, and recommendations on resumption of warfarin treatment should consider this difference.** Warfarin treatment resumption after a spontaneous hemorrhagic stroke event was associated with a lower rate for subsequent ischemic events, whereas the relative risk for recurrent ICH was increased; however, statistical uncertainty precludes firm conclusions of excess harm associated with treatment. **Resumption of OAC therapy in patients with traumatic ICH was associated with a lower rate of ischemic events and a lower relative risk for recurrent ICH despite resumption of warfarin treatment. In both groups, warfarin resumption was associated with a lower risk for death within the first year after the event.**

Table 4. Recommendations for Objective B: Frequency and timing of CT Scan

Ref	Document type and Quality	Objective B: What is the optimal timing and frequency of CT brain scans in the period following the minor head trauma (eg fall) to ensure that intracranial bleeding has not occurred?
2	Guideline	**Patients taking anticoagulant or antiplatelet agents** Any patient taking anticoagulant or antiplatelet agents who presents, with or without loss of consciousness: • Following reported head strike • External or radiological signs of craniofacial trauma • High speed MVA • Impaired conscious state (GCS<15) • Post traumatic amnesia (PTA) ***should have head CT and, if not an inpatient, be admitted for observation***. If the clotting profile is normal, CT brain shows no acute signs of haemorrhage, the patient is not in PTA, and there are no other clinical features of head injury (e.g. persistent headache, vomiting, focal neurological deficits), the patient may be considered for discharge from the Emergency Department, Emergency Short Stay Unit, or acute care area after 4 hours observation. The patient will need to be discharged with a carer and Head Injury Instructions. **If initial head CT shows evidence of intracranial haemorrhage** For patients with CT evidence of intracranial haemorrhage and who are on a direct oral anticoagulant (e.g., Rivaroxaban, Apixaban or Dabigatran), the drug should be discontinued immediately. In general, unlike Warfarin, reversal of the anticoagulant effect of these drugs should only be undertaken if neurosurgical intervention is required immediately or there is a high probability of requiring surgery within 4 hours. Otherwise, the case should be discussed with the haematologists and a clear plan for reversing the effects of the medication (should this become necessary) should be recorded in the notes. The patient should be closely observed, including repeat CT at 12-24 hours, or earlier if any deterioration. • Neurosurgery is to be notified immediately, and possibility of need for surgery considered. • Reversible drugs (i.e., Warfarin) must be reversed urgently according to relevant Alfred Health protocol. • Anti-platelet agents must be ceased. • DVT prophylaxis should be instituted with mechanical calf-compressors

Ref	Document type and Quality	Objective B: What is the optimal timing and frequency of CT brain scans in the period following the minor head trauma (eg fall) to ensure that intracranial bleeding has not occurred?
		• Low molecular-weight heparin should not be prescribed initially. • Patient should be fasted, and monitored with hourly GCS. • Repeat CT brain if clinical deterioration, or within 12-24 hours if no deterioration. • Admit with daily review of the need for further imaging. • If repeat CT brain shows stable bleed, discuss with neurosurgery before re-commencing anticoagulation or antiplatelet agents, and before commencing low molecular-weight heparin for DVT prophylaxis. • Avoid sedating drugs that could impact upon GCS. **If initial head CT shows no intracranial haemorrhage but the patient has PTA, headache, vomiting or other features of head injury - or cannot be discharged with a competent carer:** • Cease the anticoagulation or antiplatelet if medically feasible. • DVT prophylaxis should be instituted with mechanical calf-compressors, and not low molecular-weight heparin. • Follow up CT brain should be performed at 24 hours, or earlier if clinical deterioration. • Patient should be monitored with 2 hourly GCS until repeat CT brain is done, and confirmation that there is no development of intracranial haemorrhage. • If follow-up CT brain also shows no haemorrhage, no further CT brain is required unless clinically indicated, the antiplatelet or anticoagulant drug may be reintroduced as clinically indicated, and the patient may have DVT prophylaxis with low molecular-weight heparin. Caution use if the patient is already on Warfarin / DAC, especially in the older person. • Avoid sedating drugs that could impact upon GCS. **In the event that anticoagulation or antiplatelet therapy is continued:** • Anticoagulation therapy should continue only if CT brain is completely normal, and the medical indications show that the benefits outweigh the risks of a possible intracranial haemorrhage. At the Alfred site the patient will be admitted only to 2 East, 2 West or a high dependency area. • The patient will remain on 1 hourly GCS neurological observations for the first 24 hours unless this is outside the sites current inpatient guideline or as directed by medical team. A follow-up CT brain will be undertaken within the first 24 hours or upon any reduction in the GCS. If the follow-up CT brain reveals no intracranial bleeding, frequency of GCS observations can be reduced. If CT brain shows intracranial bleeding, refer to Neurosurgery urgently, and as in 4 above.
3, 11	Guideline Clinical Pathway	<u>Patients having warfarin treatment</u> • For patients (adults and children) who have sustained a head injury with no other indications for a CT head scan and who are having warfarin treatment, perform a CT head scan within 8 hours of the injury. A provisional written radiology report should be made available within 1 hour of the scan being performed. • See Pg 119 - 122 of full guideline
5	Guideline	<u>Early Management – CT Scan</u> CT scanning is the preferred method of imaging if available and should be performed early in the severe to moderate TBI group. Except for an uncomplicated minor head injury, ideally all patients with a significant head injury should have a CT scan. If it appears that the patient will require transfer to an MTS, the decision as to whether to conduct a CT prior to retrieval must be considered. In virtually all situations the CT scan will be repeated upon admission to the MTS, therefore whether the imaging will alter care in the early stages may be debatable. Any critical trauma patient must be very carefully monitored and attended while in the CT scanner. Definite indications for CT scanning are: the use of anticoagulants.

Ref	Document type and Quality	Objective B: What is the optimal timing and frequency of CT brain scans in the period following the minor head trauma (eg fall) to ensure that intracranial bleeding has not occurred?
6	Guideline	Level 2 evidence Clinicians should perform brain CT scan on patients that present with suspected brain injury in the acute setting if it is available.
7	Guideline	Recommendations for: **Clinical decision rules for CT**, **Initial Patient Management, Home discharge, Clinical Observation, Follow up (**Anticoagulation therapy = risk factor)  **Figure 1** Decision scheme for initial management in Mild traumatic Brain Injury (modified from the Dutch and Scandinavian guidelines) [16,29] GCS, Glasgow Coma Scale; LOC, loss of consciousness; PTA, post-traumatic amnesia; TBI, traumatic brain injury; CT, computed tomography; MRI, magnetic resonance imaging. *Risk factors are shown in Table 2, no risk factor in CHIP rule includes only one minor risk factor.
8	Guideline	Indications for CT scan for mild head injury (pg 7): • “Patients who are classified as high risk should have CT scans to exclude clinically important intracranial lesions” • “Known coagulopathy and particularly supratherapeutic anticoagulation are significant risk factors for intracranial injury and that these patients should have early CT scans and be considered for reversal of anticoagulation”

Ref	Document type and Quality	Objective B: What is the optimal timing and frequency of CT brain scans in the period following the minor head trauma (eg fall) to ensure that intracranial bleeding has not occurred?
		Timing of CT Scanning • "There is no direct evidence to confirm what the best time to perform CT scanning in relation to time of injury is. The primary role of early CT scanning in mild head injury is early recognition of extradural or subdural haematomas prior to clinical deterioration. Early neurosurgical intervention prior to clinical deterioration is associated with improved outcome. However, early CT scan may potentially miss other intracranial injuries such as delayed subdural haematomas or contusions which are slower to become evident. Fortunately, most studies have shown that an initial normal CT scan allows safe discharge and that the few patients who deteriorate usually have good outcome. Therefore, it is reasonable to suggest that CT scans should be performed shortly after a decision is made that one is necessary. Repeat CT scanning • There has been some debate in the literature about whether mild head injury patients who have initially abnormal CT scans and require admission for hospital observation should have a routine repeat CT scan. The evidence from most of these small studies suggests that most mild head injury patients with minor abnormalities on CT scan do not require routine repeat CT scanning if they are clinically improving with a normal GCS and no neurological deficit unless they are anti-coagulated. The other question that is often asked is should elderly anti-coagulated patients with normal initial CT scans have routine repeat CT scans and if so when should they be performed and should the patient be admitted for observation. There is little evidence to guide management in these situations. The consensus appears to be that the older the patient, and the more the patient is anticoagulated (higher INR), the greater the risk of delayed bleeding. However, how to manage that risk remains unclear.
9	Systematic Review and Meta-Analysis	<u>Risk of delayed intracranial hemorrhage in anticoagulated patients with mild traumatic brain injury</u> "We report a combined 0.6% (95% CI 0-1.2%) incidence of delayed ICH and conclude that repeated CT scans 24 hrs after an initial normal imaging are not necessary in most situations" The Systematic review presents several limitations: Small amount of available data, inclusion of retrospective and observational studies, unaccounted for risk factors. Further studies required to determine in type of injury had an effect on the incidence of ICH. Timing of first and second scans not well reported.

Table 5. Quality Appraisal Summary

Ref	Quality appraisal	Ref	Quality appraisal
1	Good quality guideline, based on moderate to very-low quality evidence.	6	Good quality guideline, recommendations based on low level evidence
2	Unable to confirm guideline methodology, evidence base unknown	7	Good quality guideline, recommendations based on varied levels of evidence and consensus based good practice points
3	Good quality guideline, based on observational studies.	8	Good quality guideline, based on low level evidence consisting of prospective and retrospective cohort studies as well as systematic reviews of cohort studies
4	Guideline methodology unknown, current evidence used quality unknown	9	Good quality systematic review and meta-analysis, consisting of prospective and retrospective studies.
5	Good quality guideline, levels of evidence for recommendations are not reported.	10	Good quality observational cohort study