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Management of Traumatic Intracranial Hemorrhage on Anticoagulant Regiment: A Literature Review

Tedy Apriawan[1,2], Ade Anugrah Kartosen[1,2], Ahmad ZS Ishlahy[1,2], Endang Pati Broto[1,2], Hana Ranu Herjuna[1,2], Khrisna Rangga Permana[1,2], Rizki Meizikri[1,2], Shaleh Drehem[1,2], Abdul Hafid Bajamal[1,2]

[1]Neurosurgery Department, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia
[2]Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia
Corresponding author: Rizki Meizikri (rizkimz@gmail.com)

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ABSTRACT

Oral anticoagulant and antiplatelet are often prescribed in clinical practice. These drugs are mainly consumed by geriatric patients to prevent or treat cerebrovascular, systemic embolism, or heart condition. Managing anticoagulated TBI patients is a challenging task for surgeons. This study aims to review available literatures regarding anticoagulated TBI patients and to suggest a treatment algorithm for such cases. Based on several retrospective and prospective studies, it might be wasteful to do a routine follow-up CT scan on anticoagulated TBI patients. The risk of new lesion development or presenting lesion progression seems to be especially low among patients with negative initial CT scan. We suggest to reserve repeat CT scan for patients with evident neurological deterioration. Tighter observation for anticoagulated patients with positive initial CT scan might be useful. Anticoagulation reversal is recommended by the American College of Cardiology, but some studies reported that reversal should be directed by INR. Acute antiplatelet cessation is still controversial for aspirin, but it is advised for clopidogrel. Preoperative management of both anticoagulant and antiplatelet should take into account the bleeding risk of the surgical procedure. Blind cessation and reversal of anticoagulant and/or antiplatelet might delay the timing of surgery and thus would better be avoided.

Introduction

Traumatic brain injury (TBI) accounts for around 9% of global mortality (Hutchinson, *2019*) and disability (Silver, J. & Ziejewski, M. North, 2018). The burden of TBI also affects elderly population due to global increase in life expectancy.[3] The elderly in general is more prone to traumatic brain injury (TBI) and traumatic intracranial hemorrhage due to age-related anatomical changes (Scotti, *2019*). The prevalent consumption of anticoagulant and/or antiplatelet consumption among this population might further complicate things (Andreotti, F. *2015*). Anticoagulant and antiplatelet are intended to prevent or treat cerebrovascular, systemic embolism, or heart condition (Prexl, 2018). Patients on anticoagulant or antiplatelet are at risk for hemorrhagic events following trauma and higher risk of mortality in traumatic brain injury (TBI) cases (Mina, 2002).

Managing anticoagulated TBI patients demands judicious weighing of the risk of catastrophic bleeding during and after surgery against the risk of thromboembolic events (Patel, R. B. 2019). Continuing the agents might make the surgeon wary of excessive bleeding during the procedure, while stopping the agents put the patients at risk of unwanted thromboembolic complication. This study aims to review available literatures regarding anticoagulated TBI patients and to suggest a treatment algorithm for such cases.

Type of Anticoagulants

Vitamin K antagonist

Vitamin K antagonist (VKA) such as warfarin is among the most widely used anticoagulants (Palaiodimos, 2019 and Barnes, G. D. 2015). VKA lessen the availability of vitamin K, thus affecting the production of vitamin K-dependent coagulation factors, namely factor II, VII, IX, and X (**Figure 1**) (Baglin, T, 2013). Warfarin dosing is challenging due to its narrow therapeutic index and inter-individual variability (Kearon, C. 2016). Warfarin could be prescribed with antiplatelet agents such as aspilet, clopidogrel, or both for patients with heart condition (Sorensen, R., 2019). Warfarin has been associated with incident of spontaneous intracerebral hemorrhage (Hart, R., Boop, B. & Anderson, 1995).

Non-Vitamin K Antagonist Oral Anticoagulant

Non-vitamin K antagonist oral anticoagulant (NOAC) works by directly inhibiting thrombin or factor X (**Figure 1**) (Wang, Y. & Bajorek, B, 2014). The first NOAC to be approved by the United States' Food and Drug Administration (FDA) was Dabigatran in 2010 (Ashrafi, F., 2017). Dabigatran at 110 mg provided similar efficacy with that of warfarin in preventing stroke and systemic embolism, but with lower rates of major hemorrhagic complication (Connolly, S. J., 2009). Others NOACs such as rivaroxaban (Patel, M. R, 2019), apixaban (Granger, C. B, 2019), and edoxaban (Giugliano, R. P., 2013) then were also proven to be as effective as warfarin yet with less risk of adverse bleeding.

Unfractionated Heparin and Low molecular weight heparin

Low-molecular weight heparin (LMWH) such as enoxaparin is a class of anticoagulant which inactivates thrombin and factor X through an antithrombin-

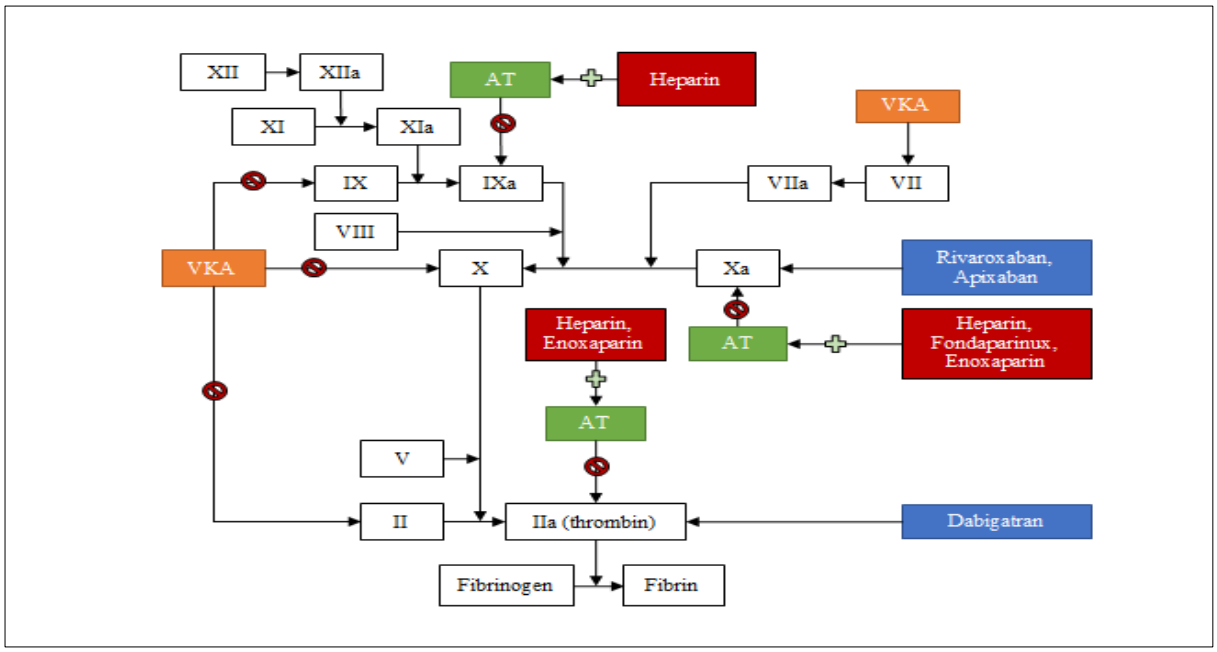

Figure 1. Anticoagulant action on coagulation cascade. [32,17]
(VKA: Vitamin K Antagonist; AT: Antithrombin)

dependent mechanism (**Figure 1**). Although its mechanism of action is similar to unfractionated heparin (UFH), LMWH is associated with less adverse effects (Alikhan, R, 2014, Barrera, L. M., 2013, Kahn, S. R., 2012).

Both UFH and LMWH are used to treat systemic thromboembolism (Hirsh, J. 2001) and acute coronary syndrome (Roffi, M, 2015). However, LMWH is available for outpatient setting in the form of subcutaneous injection and oral regiment while UFH is given intravenously. UFH is dosed on a case-by-case manner due to inter-individual difference of anticoagulant response to this drug. Monitoring of activated thromboplastin time (APTT) is advised for UFH administration.

Indirect Xa Inhibitor

This class of anticoagulant inhibits factor Xa through the help of antithrombin (AT) as co-factor (**Figure 1**) (Rupprecht, H. J. 2010). Indirect Xa inhibitor like Fondaparinux has been proven effective for patients with acute coronary syndrome or for deep vein thrombosis (DVT) prevention after major orthopedic surgery (Yusuf, S., 2011).

Anticoagulants and Risk of Traumatic Intracranial Hemorrhage

Various studies on anticoagulant/ antiplatelet effect on traumatic intracranial hemorrhage have been published (**Table 1**). Patients on anticoagulant and/or antiplatelet should have had higher risk of developing intracranial hemorrhage, yet published studies showed conflicting results.

Clopidogrel has been associated with at least similar risks of bleeding with warfarin in several published studies. Nishijima et al. reported that patients on clopidogrel (12%; CI 95% (8.4-16.4%)) is at higher risk of intracranial hemorrhage compared with those on warfarin (5.1%; CI 95% (3.6-7.0%)). Patients on clopidogrel is 2.3 times (95%; CI 1.48-3.63) more likely to suffer from intracranial bleeding (Nishijima, D. K., 2012). Moustafa et al. studied 293 TBI cases who were on antiplatelet agents and found that most patients with intracranial hemorrhage consumed aspirin (65.4%). This finding, however, is not statistically significant when compared with those consuming the same drug yet without any intracranial lesion ($p = 0.31$). Aspilet + clopidogrel in this study was found to be significant factor to the incident of traumatic intracranial hemorrhage ($p = 0.04$) (Moustafa, F., 2018).

In a study on 206 anticoagulated TBI cases, Cipriano et al. found 23 cases with intracranial hemorrhage, 19 of whom were on warfarin. The other four were on NOAC. In contrast, Jentzch et al. didn't find a significant difference between patients on VKA and those on NOAC (Jentzsch, T. 2015). Dunham et al. found that intracranial hemorrhage incident between patients on anticoagulant and/or antiplatelet was not statistically different from those not on any medications ($p=0.32$). Warfarin, known for its hemorrhagic complication, was also not significantly different from non-medicated subjects ($p=0.83$) (Dunham, C. M., 2014). According to Riccardi et al., warfarin yield higher rate (10.16%) of traumatic intracranial hemorrhage compared with NOACs (10.6% vs 2.8%; $p < 0.05$) (Riccardi, A., 2017).

Nishijima published yet another study in 2017 regarding out-of-hospital triage on adults with head injury. Of 2110 patients, 566 were on anticoagulant or antiplatelet. Fifty two of them were diagnosed with traumatic intracranial hemorrhage. In total, there were 137 subjects who were on warfarin, 303 on aspirin, 12 on NOACs, 71 on other classes of antiplatelet, and 72 on more than one type of medications. However it was not clear which medication dominated those 52 who were diagnosed with traumatic intracranial hemorrhage (Nishijima, D. K., 2017).

Inamasu et al. reported that among 82 patients with traumatic intracranial

hemorrhage, 37 (45.1%) was on anticoagulant or antiplatelet. The authors unfortunately did not specifically mention which agents were consumed by the subjects. This study found that poor Glasgow Outcome Scale (GOS) was more common in the oldest subgroup (≥ 85 yo), despite not statistically significant (p = 0.37) (Inamasu, J. 2010). Nishijima et al. in 2013 published a cohort study on 77 TBI patients, 27 of whom were on warfarin or clopidogrel. On 6-month-follow-up, unfavorable outcome was more prevalent among the warfarin/clopidogrel cohort. Similarly, Powers et al. and Won et al. also found that antiplatelet/anticoagulant consumption was positively correlated with death (OR 2.71, p < 0.001) and unfavorable outcome at discharge (Won, S. Y., 2017), respectively.

Table 1 Studies reporting on proportion of anticoagulated TBI patients who developed intracranial hemorrhage upon presentation

Authors	Study	(n) of Cases[$]	n(%) of Intracranial Hemorrhage	Causative Agent[*]	Initial GCS	(n) of Surgery
Jentzch et al.[35]	Retrospective	69	19 (27.5)	Rivaroxaban, Phenpocroumon	15	9
Cipriano et al.[6]	Prospective	206	23 (11.2)	Warfarin	13-15	0
Nishijima et al., 2012[33]	Prospective	1064	70 (6.5)	Clopidogrel	<8-15	24
Chenoweth et al.[43]	Retrospective	33	1 (3)	Dabigatran	14-15	0
Dunham et al.[36]	Retrospective	198	72 (36.4)	Aspirin, Clopidogrel	<12-15	n/a
Rendell and Batchelor[44]	Retrospective	82	12 (15)	Warfarin	<8-15	8
Mina et al.[45]	Prospective	94	25 (27)	Warfarin	14 ± 2.9	n/a
Brewer et al.[46]	Retrospective	141	41 (29)	Warfarin, Clopidogrel, Aspirin	15	5
Riccardi et al.[37]	Prospective	225	15 (6.7)	Warfarin	14-15	0
Siracuse et al.[47]	Prospective	5371	526 (9.7)	Warfarin, Clopidogrel	n/a	n/a
Fabbri et al.[48]	Retrospective	1366	180 (13.2)	Aspirin, Ticlopidine, Indobufen	14-15	n/a
Moustafa et al.[34]	Retrospective	293	26 (8.9)	Aspirin	13-15	6
Nishijima et al., 2017[38]	Retrospective	566	52 (9)	n/a	n/a	9

[$]Only anticoagulated TBI cases
[*]Agents which cause the most/the most statistically significant incident of traumatic intracranial hemorrhage within the respective study

Further studies to evaluate the risk of traumatic intracranial hemorrhage among anticoagulated patients are warranted. At the moment, warfarin and clopidogrel seems to be the most common causative drugs in such cases. These two agents also seems to be the most-studied ones. TBI patients who are on anticoagulant are prone to unfavorable outcome.

Anticoagulants and Risk of Traumatic Intracranial Hemorrhage Progression

There have been conflicting results on anticoagulant or antiplatelet effects on the

progression of intracranial hemorrhage (**Table 2**). Anticoagulated, non-traumatic patients were reported to have higher risk of expanding intracerebral hemorrhage (ICH) compared with those not on anticoagulant (Flibotte, J. J, 2004).

Ivascu et al. retrospectively studied 109 patients with pre-injury antiplatelet regiment. In this study, initial CT finding is divided into four grades, they are minimal (grade I), moderate (grade II), severe (grade III), and moribund hemorrhage (grade IV). This study found that the majority of patients had grade I (64.2%) and grade II (15.6%) hemorrhagic lesion on initial CT. Grade III and grade IV lesion on initial CT was found in only 9.2% and 11% of patients, respectively. Eighty one grade I and grade II patients were re-scanned and four (3.6%) patients showed progressing lesion (Ivascu, F. A. 2008).

Huang et al. 2019 published a retrospective study on 232 TBI patients who consumed warfarin with presenting GCS of 13-15. All patients had no intracranial lesion upon admission, but 4 patients (1.7%) were found to develop delayed intracranial hemorrhage within the first 24 hours. Two patients had subarachnoid hemorrhage on the follow-up CT scan, one patient had punctate hemorrhage, and one patient had interhemispheric subdural hematoma.

A prospective study by Menditto et al. found that 5 of 97 minor head injury patients with normal initial CT scan developed new hemorrhagic lesion on follow-up CT within the first 24 hours. However, only one of them required surgical intervention. Another two patients with two normal CTs were admitted few days later with symptomatic subdural hematoma (SDH) although none required surgery. Both patients had international normalized ratio (INR) of > 3 (Menditto, V. G. 2012).

A retrospective study on 234 patients on various anticoagulant or antiplatelet found that repeat CT found new hemorrhagic lesion in only two (0.85%) patients. Both patients were on dual antiplatelet therapy without anticoagulant (Scantling, D. 2017).

Joseph et al. revealed an interesting finding through two separated publications. The first study found that there were no statistical differences between TBI patients on aspirin than those not on any antiplatelet However, the second study reported that almost all TBI patients on clopidogrel suffered from intracranial hemorrhage progression upon repeat CT (Joseph, B. 2014).

In spite of the reported safety of NOACs Zeeshan et al. presented a contradicting result. In a comparison study between NOACs and warfarin, the authors found that progressing lesion is more common in NOACs than in warfarin group (26% vs 13%, $p = 0.03$). Worsening lesion in NOACs group also required more neurosurgical interventions (20% vs 9.2%, $p = 0.04$) (Zeeshan, M., 2013).

In a study by Parra et al., dabigatran causes 4 of 5 patients to suffer from deteriorating intracranial bleeding. That said, all of those five also consumed warfarin, aspirin, or clopigogrel. Eleven of twenty five patients who consumed rivaroxaban and apixaban in this study also experienced progressing lesion (Parra, M. W, 2013). That said, Feeney et al. found that NOACs in general yield significantly lower mortality (4.9% vs. 20.8%; $p < 0.008$) and lower rate of surgery (8.2% vs. 26.7%; $p = 0.023$) than warfarin (Feeney, J. M., 2016).

Table 2 Studies on progression/development of intracranial hemorrhagic lesion among TBI patients with anticoagulant and/or antiplatelet

Authors	Study	Agents	(n) of Cases*	(n) of Surgery	Initial GCS	New/Progressing Lesion on Follow-up CT n(%)
Studies with Unremarkable Initial CT Scan						
Huang et al.	Retrospective	VKA	232	0	13-15	4 (1.7)
Menditto et al.	Prospective	VKA	97	1	14-15	7 (7.2)
Scantling et al.	Retrospective	VKA, NOAC, AP	234	0	15	2 (0.85)
Kaen et al.	Prospective	VKA, AP	137	0	14-15	2 (1.4)
Barmparas et al.	Retrospective	NOAC, AP	249	0	< 8-15	2 (0.8)
Peck et al.	Retrospective	VKA, AP, LMWH	424	0	14.8 ± 0.9	4 (0.9)
Studies with Remarkable Initial CT Scan						
Ivascu et al.	Retrospective	AP	109	n/a	13.6 ± 2.8	4 (3.6)
Beynon et al.	Retrospective	VKA, NOAC	128	83	9-15	23 (17.9)
Jentzch et al.	Retrospective	VKA, NOAC	69	9	15	5 (5.7)
Cipriano et al.	Prospective	VKA, NOAC	206	0	13-15	3 (1.5)
Nishijima et al., 2010	Retrospective	VKA	40	11	12-15	7 (17.5)
Nishijima et al., 2012	Prospective	VKA, AP	1064	24	<8-15	4 (0.37)
Joseph et al., 2014	Prospective	AP	72	4	<8-15	18 (25)
Joseph et al., 2014	Prospective	AP	71	7	<8-15	65 (91.5)
Deloughery et al.	Retrospective	VKA	54	n/a	±10	15 (27.7)
Zeeshan et al.	Prospective	VKA, NOAC	210	27	8-15	36 (17.1)
Oyama et al.	Retrospective	VKA	25	5	13 ± 2.4	4 (20)
Parra et al.	Retrospective	VKA, NOAC	45	n/a	±14	11 (24.4)
Pruitt et al.	Retrospective	VKA, AP	644	99	13-15	45 (7)

*The number shown represents patients who are on anticoagulant and/or antiplatelet

Based on several retrospective and prospective studies on table 1, it might be wasteful to do a routine follow-up CT scan on anticoagulated TBI patients. The risk of new lesion development or presenting lesion progression seems to be especially low among patients with negative initial CT scan. We suggest to reserve repeat CT scan for patients with evident neurological deterioration. Tighter observation for anticoagulated patients with positive initial CT scan might be useful.

Reversing Anticoagulants and Perioperative Management

Upon receiving TBI patients with known history of anticoagulant and/or antiplatelet, it is important to know if their hemostatic function is within physiologic limit. Guidelines on how and when to reverse anticoagulant are available,

although none is specifically related to trauma cases.

The American College of Cardiology's (ACC) consensus suggests that bleeding at critical site, including intracranial, should prompt cessation of any anticoagulant. Bleeding which causes hemodynamic instability, hemoglobin (Hb) drop of ≥ 2 g/dL, or the need of ≥ 2 unit of red blood cells (RBC) are also considered major (Tomaselli, G. F. 2017).

Thrombocytopenia or other pro-hemorrhagic condition should be tackled prior to administering reversal agents (**Table 3**). If the patients are on VKA, 5-10 mg of Vitamin K should immediately be injected. Interestingly, ACC put surgical procedure before reversing anticoagulated state if the patients are in dire need of the said procedure.

In general, prothrombin time (PT) and/or an activated partial thromboplastin time (aPTT) should be checked in all anticoagulated patients. PT and INR are recommended for patients taking VKA. INR is also used to guide reversal agent dosing. Patients taking dabigatran ideally require more sophisticated lab indicators, such as dilute thrombin time, ecarin clotting time, and ecarin chromogenic assay. However, these examinations are not readily available in many hospitals, thus thrombin time (TT) and aPTT should be requested. The ideal assessment for rivaroxaban, apixaban, and edoxaban is chromogenic anti-Xa assay. As this is also not widely available, PT can be requested instead.[67] Repeat INR testing within 15-60 minutes of PCC administration and serially every 6-8 hours for the next 24-48 hours are recommended (Frontera, J. A. 2016).

Table 3 Assessment of VKA and NOACs and their reversal agent (Tomaselli, G. F, 2017)

VKA	**NOAC**	
	Dabigatran	**Apixaban, Rivaroxaban, Edoxaban**
Monitor INR and aPTT	Monitor TT and aPTT	Monitor PT
4F-PCC • INR 2-4 → 25 u/kg • INR 4-6 → 35 u/kg • INR > 6 → 50 u/kg **OR** 4F-PCC • 1000 u for any major bleed • 1500 u for intracranial hemorrhage **OR** FFP 10-15 ml/kg	Idarucizumab 5 mg IV **OR** 4F-PCC 50 u/kg IV **OR** aPCC 50 u/kg IV If patient is known to have recently ingested the drug (2-4 hours), oral activated charcoal could be considered	4F-PCC 50 u/kg IV OR aPCC 50 u/kg IV If patient is known to have recently ingested the drug(s) (2-4 hours), oral activated charcoal could be considered

4F-PCC: Four-factor prothrombin complex concentration
aPCC: activated prothrombin complex concentration

Keeling et al. published a paper on how to stop anticoagulants perioperatively (**Table 4**). Should surgery be needed promptly, VKA can be stopped immediately. The cessation of NOACs is more complicated as creatinine clearance need to be calculated prior to halting the agents. If the surgery is a major procedure with high bleeding risk, the gap between stopping the medication to the surgery is also longer (Keeling, D. 2016).

Table 4 Recommendation on pre-operative anticoagulant management.[69]

	Pre-Emergency	Pre-Elective	
VKA	Stop immediately Vit. K 5 mg IV **OR** 4F-PCC according to INR	Stop 5 days prior to procedure	
	Cr. Clearance (ml/min)	**Low Bleeding Risk (h)**	**High Bleeding Risk (h)**
Dabigatran	≥ 80	24	48
	≥ 50 - < 80	24-48	48-72
	≥ 30 - < 50	48-72	96
Rivaroxaban	≥ 30	24	48
	< 30	48	72
Apixaban	≥ 30	24	48
	< 30	48	72
Edoxaban	≥ 30	24	48

Patients who are long-term consumer of VKA can be candidate for bridging therapy. Bridging therapy refers to administering alternative anticoagulants who are more short-acting around the time of scheduled surgery. The notion behind this strategy is to minimize the risk of operative bleeding while also mitigating the risk of systemic thromboembolism, although some studies on did not show fully favorable outcome bleeding-wise (Eijgenraam, P., 2013).

The preferred drug for bridging therapy is usually enoxaparin 1 mg/kg twice a day subcutaneously. Two days after VKA is stopped (3 days before surgery), enoxaparin is started until 24 hours before the surgery. Twenty four or 48 hours after surgery, enoxaparin is resumed along with VKA and be stopped after 4 to 6 days. Considerations for bridging therapy is listed on **Table 5**.

Table 5 Consideration for bridging therapy[69,70]

Conditions	Consideration
VTE	VTE within the previous 3 months Patients who previously suffered from VTE despite being on therapeutic anticoagulation, who now have a target INR of 3.5
AF	Patients with previous stroke/TIA in the last 3 months $CHADS_2$ score of 5-6 (Patients with previous stroke/TIA + 3 or more of the followings:) • Congestive heart failure • Hypertension (> 140/90 mmHg on medication) • Age ≥ 75 yo • Diabetes mellitus
MHV	MHV other than those with a bileaflet aortic valve and no other risk factors

VTE: Venous thromboembolism
INR: International Normalized Ratio
AF: Atrial Fibrillation
TIA: Transient Ischemic Attack
CHADS score: Congestive heart failure, Hypertension, Age ≥ 75 yo, Diabetes, Stroke
MHV: Mechanical Heart Valve

There is no obligation to stop antiplatelet, more so if the patient is on aspirin monotherapy. However, it is advised to stop aspirin 3 days before to 7 days afer a surgery with high bleeding risk. Intravenous tranexamic acid could be administered prior to high bleeding risk surgery. Platelet transfusion should be reserved for when tranexamic acid is deemed inadequate to stop peri- or post-operative bleeding, and when there is no adequate time to properly stop the drugs. Platelet transfusion is best given two hours after last aspirin ingestion or > 12-24 hour after last clopidogrel ingestion.[69] General recommendation for peri-operative antiplatelet management in elective cases can be seen on **Table 6**.

Table 6 General recommendation for pre-operative antiplatelet cessation

Agents	Low Risk Bleeding	High Risk Bleeding
Aspirin	Continue	Elective • Stop -3 to +7 days if antiplatelets is for secondary prevention of cardiovascular disease • Continue if patients had recent ACS (surgery should be deferred if possible) • Continue if surgery can't be postponed, but clopidogrel should be stopped Emergent • Tranexamic acid ± Platelet transfusion
Clopidogrel	Continue	• Continue if patients had recent ACS (surgery should be deferred if possible) • Stop -5 days if surgery can't be postponed Emergent • Tranexamic acid ± Platelet transfusion

Aggressive warfarin reversal protocol has reduced mortality from 50% to 10% in a study.[50] Although it is recommended to stop and reverse anticoagulant before surgery, a study found that thromboembolic complication did not significantly differ between reversed and non-reversed cohorts despite the former achieved normal INR earlier. The reversal agent used in this study was recombinant activated factor VIIa (rFVIIa) (Nishijima, D. K., 2010). rFVIIa also did not yield better outcome, although it was reportedly effective to normalize INR. INR was significantly decreased using human factor IX complex, fresh frozen plasma, and/or vitamin K in another study (Oyama, H. 2013).

In a retrospective study, INR of 2-3 (therapeutic range) seemed to be safe among TBI cases. Interestingly, INR of < 2 (subtherapeutic range) has a relative risk of 1.89 (95% CI 0.65 to 5.55) for intracranial hemorrhage. Similarly, Brewer et al. reported that the mean INR of patients with intracranial hemorrhage was lower than those without intracranial hemorrhage (1.97 ± 0.92 vs 2.3 ± 1.2; (p 0.0987)).[46] Franko et al. retrospectively analyzed 1,493 TBI cases and revealed that ICH and mortality were more prevalent with higher INR especially at a value of > 4 (Franko, J., 2006).

Medium elevation of INR equals modest deficiency of clotting factors,[74] thus any efforts to further lower it might not be fruitful. Plasma transfusion to achieve normal INR might also delay surgery.[77] Nevertheless, in 2016 Frontera et al. published a guideline for antithrombotics reversal in intracranial hemorrhage, in which reversal for patients with INR ≥ 1.4 is advised. Reversal within first 10 hours results in less risk of intracranial hemorrhage progression according to a small study (Andrews, H. 2017).

Proposed Algorithm

Although our literature review mainly consist of low-quality evidence, important points can be noted to construct an algorithm for anticoagulated TBI patients with intracranial hemorrhage. **Figure 2** illustrate our proposed algorithm.

The presence of intracranial lesion after traumatic events is the first factor to consider before proceeding to further treatment. If intracranial lesion is found, the next step is to decide if it is bound for surgery. The absence of intracranial lesion or surgical indication warrants 24-hours observation. Should neurological deterioration occurs during observation, repeat CT scan is recommended.

The type of anticoagulant should first be identified before proceeding to surgery. VKA consumption should be stopped and IV vitamin K should be administered. There is no agreed value of INR on which anticoagulant reversal should be performed. At the moment, we suggest a cut-off point of 1.4 as a guide to reverse anticoagulant. The next step is to identify whether the patient is on antiplatelet. Available evidence suggest that clopidogrel has to be discontinued. Tranexamic acid is recommended for patients who are on antiplatelet, while platelet transfusion should be selectively transfused.

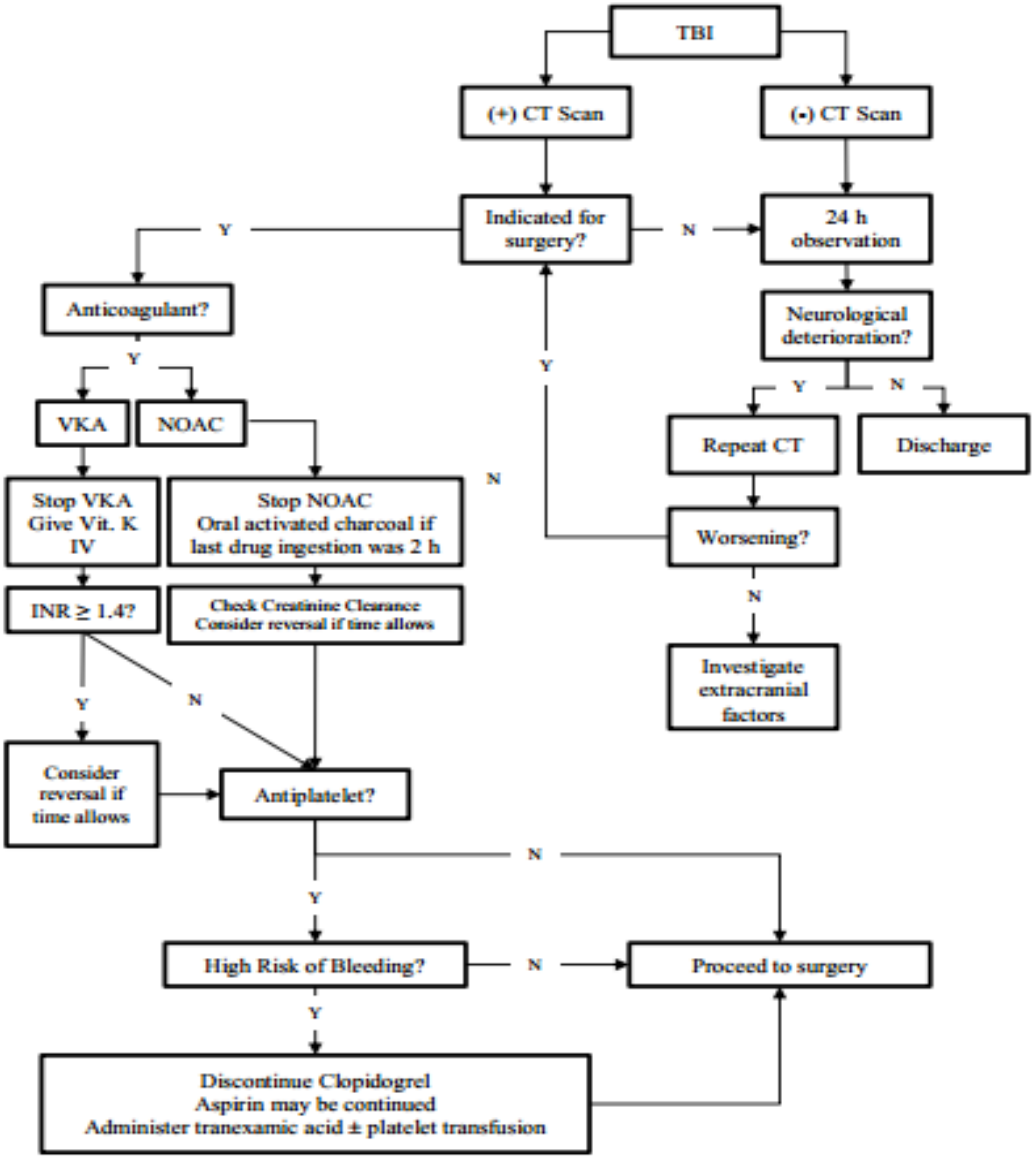

Figure 2. *Proposed algorithm of anticoagulated TBI patients*

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