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# Utilization of anticoagulant and antiplatelet medications among geriatric patients with neurosurgical diseases

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## ABSTRACT

**Aim:** To study the utilization patterns of anticoagulant and antiplatelet medications among geriatric patients with neurosurgical conditions in the neurosurgical department at Khoula Hospital, Muscat, Sultanate of Oman.

**Introduction:** Anticoagulant and antiplatelet presumption is a worry in neurosurgical patients, that suggests a subtle balance between the risk of thromboembolism against the risk of peri- and postoperative haemorrhage. Patients taking those medications were found to have an increased risk of bleeding from traumatic and traumatic events.

**Materials and Methods:** A retrospective study of geriatric cases admitted to the Neurosurgery Department in Khoula Hospital (KH) as an example of a neurosurgical center in Sultanate of Oman, from January 2016 to 31st December 2019. Patients demographics, diagnosis, length of hospital stay (LOS), Glasgow Coma Scale (GCS), length of ICU admission, and treatment proposed were recorded.

**Results:** The most common diagnostic category was trauma (35.4%). 16.0 % of the patients were taking anticoagulant medications. Patients with traumatic brain injury (TBI) were found to have a higher rate of using anticoagulant medications (36.6%). There was a significant difference between the LOS, type of intervention, ICU admission, and the usage of anticoagulant and antiplatelet drugs ( $p < 0.05$ ). Enoxaparin was the most commonly used anticoagulant agent. 19.6 % of the patients were taking antiplatelet medications. This study was showed that aspirin is the most commonly used antiplatelet agent among different neurosurgical pathologies.

**Conclusion:** Patients with TBI were found to have a higher rate of using anticoagulant medications. Decisions regarding prescription and resumption of anticoagulants and antiplatelet medications should be taken on a case-by-case basis involves multidisciplinary and holistic approaches.

## INTRODUCTION

Anticoagulant presumption is a worry in neurosurgical patient that

## Keywords

anticoagulants,  
geriatric,  
elderly,  
bleeding,  
trauma,  
neurosurgery,  
antiplatelet



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suggests a subtle balance among the risk of thromboembolism against the risk of perioperative and postoperative hemorrhage (1). The ageing populace has resulted in an alteration in the demographics of trauma (2). Numerous of these patients are undergoing anticoagulation therapy and are also at high risk of falls and sustaining injury with possibly serious hemorrhagic complications (2). The main risk of systemic anticoagulation is bleeding, including intracranial hemorrhage, which must be well-adjusted against the recommended chronic anticoagulation for at least the duration of active cancer (3). Clinicians often face a patient with a brain tumor who requires anticoagulation for a deep venous thromboembolism (DVT) or pulmonary embolism (PE) or for cardiac reasons, such as atrial fibrillation or peripheral vascular disease. (3). Head injury embodies one of the most important and recurrent traumatic pathology in the emergency department (4). Among the diverse risk factors, preinjury use of warfarin has received considerable attention in trauma literature. Several studies were undertaken to elucidate the effect of warfarin anticoagulation on the mortality rate and risk of development of intracranial hemorrhage (ICH) in adult patients with minor head injuries (4). The risk of mortality in a patient anti-coagulated on warfarin with an ICH after head injury ranges in the literature from 16-80% (5). The Food and Drug Administration -USA- projected that 2 millions of people each year start using vitamin K antagonist. The use of anticoagulants is predicted to continue growing in the near future (1). Warfarin is a vitamin K antagonist, and works by inhibiting the enzyme vitamin K epoxide reductase. This is essential for calcium binding, allowing the linking to phospholipids surfaces to promote clotting (5).

Platelets are small, irregularly shaped subcellular fragments that are derived from megakaryocytes and play a major role in the maintenance of haemostasis (6). Antiplatelet agents are frequently being used in the management or prevention of cardiovascular disease (7) such as; deep venous thrombosis, atrial fibrillation, pulmonary embolism and coronary artery disease. They are also given postoperatively for prosthetic heart valves or stent placement (8). Patients taking these medications found to have an increased risk of bleeding from traumatic and traumatic events (7). Therapeutic mechanisms of antiplatelet agents include inhibition

of platelet aggregation, so normal haemostasis is impaired, which may lead to an increased incidence of ICH and enlargement of hematomas in TBI, potentially increasing mortality and morbidity (9). For instance, patients taking an antiplatelet agent, with ICH occurring in approximately 3.6%–67.3% of patients on antiplatelet therapy and 1.6%–50.5% of patients not on this therapy (7). Also, posttraumatic ICH is associated with a mortality rate of 21% in patients on antiplatelet therapy. (6). Antiplatelet agents are necessary for patients undergoing neuroendovascular procedures, due to its preventative effect against thromboembolic consequences (9). Aspirin is the most common used drug while undergoing neuroendovascular procedures. Aspirin is typically initiated at least 3–5 days prior to some vascular procedures such as carotid or intracranial stenting (9). Clopidogrel is the other most common antiplatelet drug used while undergoing neuroendovascular procedures. Variation in individual response to clopidogrel has sparked a great deal of research and controversy in the cardiovascular and neuroendovascular areas. The incidence of clopidogrel hyporesponsiveness has varied from 21% to 53.1% in patients undergoing neuroendovascular procedures (9).

This study is conducted to investigate the prevalence of therapeutic antiplatelet and anticoagulant medications among geriatric patients admitted in neurosurgical department at Khoula Hospital, Muscat, Sultanate of Oman, which is the first of its kind in the region, to the best of our knowledge. The health care services in Oman are considered as having one of the best health care systems in the world according to World Health Organization reports (10,11). The Department of Neurosurgery in our hospital is the main neurosurgical center in the country with an average annual admission of 1600 patients (12,13) In this study, we chose a cut of 65 years and older according to the local definition, taking into account the increase in life span throughout the last decades as well as the improvement in the quality of life.

## METHODS

### Study group

This is a retrospective study conducted at Khoula Hospital located in Muscat, Sultanate of Oman. The study was approved by the Research Ethical

Committee at Khoula Hospital/ Ministry of health (PRO122020072). Medical records of 696 patients who are above the age of 65 and admitted to the neurosurgical ward January 2016 to 31<sup>st</sup> December 2019 were included. The study includes both Omani and non-Omani patients. Patients with the following features are excluded: non elderly patient (below 65 years), non-neurosurgical conditions, outside the study period (from 1st January 2016 to 31th December 2019), Patients with missing or incomplete data.

### Data collection

Data was obtained from the health information system included: patient demographics, diagnosis, length of hospital stay (LOS), Glasgow Coma Scale (GCS), length of ICU admission and treatment proposed. Then the information classified into continues and categorized variables and analysed accordingly.

### Data analysis

Research database was analysed and processed using the statistical package for the social sciences (SPSS) software (version23). The categorized variables were cross-tabulated using frequency tables. Chi-square test was used to obtain the significance of the association between categorized variables, using a P value of  $\leq 0.05$  as the cut-off for significance.

## RESULTS

The demographic characteristics of the included cases in the present study is represented in table 1. We have total of 669 patients with mean age of 73.3 admitted in the neurosurgical department at KH in Muscat the capital city of Sultanate of Oman in four years 'period (from 2016 to 2019). 2019 accounted for the highest number of admitted patients (30%).61.9% of the study cohort were more than 75-year-old. Male to female ratio was (1.63:1). Most of the patient were having GCS score of 14-15 (72.3%). The most common diagnostic category was trauma, accounted for 35.4% of the study cohort followed by oncology and vascular equally (16.3%).16.0 % of the patients received anticoagulant medications.19.6% of the patients received antiplatelet medications. Most of the patients underwent surgical intervention (73.1%). Majority of the patients stayed in the hospital less than 15 days (77%).

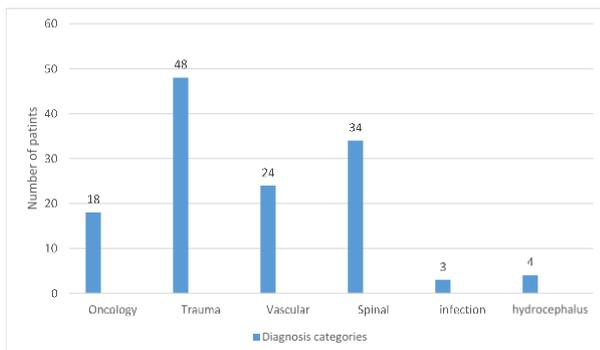
**Table 1.** Demographic characteristics of the patients

Category	Number of patients (%)
<b>Number of patients admitted each year</b>	
2019	202 (30.0%)
2018	172 (25.7%)
2017	154 (23%)
2016	141 (21.3%)
<b>Total</b>	<b>669</b>
<b>Age</b>	
$\geq 75$	414 (61.9%)
$< 75$	255 (38.1%)
<b>Gender</b>	
Female	255 (38.1%)
Male	414 (61.9%)
<b>GCS on arrival</b>	
15-14	484 (72.3%)
13-12	49 (7.3%)
11-9	36 (5.3%)
$< 8$	100 (15%)
<b>Diagnostic category</b>	
Oncology	109 (16.3%)
Trauma	237 (35.4%)
Vascular	109 (16.3%)
Spine and Peripheral nerve diseases	176 (26.3%)
Infection and functional	13 (2%)
Hydrocephalus	25 (3.7%)
<b>Anticoagulant drugs</b>	
Yes	107 (16.0)
No	562 (84.0)
<b>Type of interventions</b>	
Surgical	489 (73.1%)
Observational	180 (26.9%)
<b>Length of stay (LOS)</b>	
$\leq 15$ days	515 (77%)
$> 15$ days	154 (23%)

### Utilisation of anticoagulant medications

Figure 1 illustrates the utilization of anticoagulant medications among different diagnoses (131 patients out of 669 patients). Patients with TBI found to have higher rate of using anticoagulant medications (36.6%) followed by patients with spinal diseases and vascular pathologies, respectively (25.9%, 18.3%). There was no significant relationship between the utilization of anticoagulant medications among different neurological diseases investigated

( $p=0.920$ ). The association between usage of anticoagulant medications among patients and other variables (type of injury, LOC, type of intervention, age, and ICU admission) is shown in table 2. It demonstrates that there was no significant difference between the utilization of anticoagulant medications the type of injury, as both traumatic and non-traumatic patients were using anticoagulant medications in a similar way ( $p=0.674$ ). Also, it is showing that there was a significant difference in the LOS and the usage of anticoagulant drugs, in which patients who were not using anticoagulant medications found to stay shorter in the hospital ( $p<0.05$ ). Additionally, patients who were undergone surgical intervention were using anticoagulant medications much less than patients who were on conservative management ( $p=0.001$ ). Added to that the significant relationship that found to be between the ICU admission and the utilization of anticoagulant medications, in which majority of the patients who were not on anticoagulant therapy were not admitted to the ICU ( $p<0.05$ ). Also, there was no association between the usage of anticoagulant medications and the age of patients (above and below 75 years) ( $p=0.198$ ). Figure 2 illustrates the utilization of anticoagulant agents among different diagnoses. It is showing that enoxaparin was the most commonly used anticoagulant agent among different neurosurgical pathologies in the present study ( $n=93$ ), followed by warfarin ( $n=15$ ). Heparin was only used by 3 patients in this study.

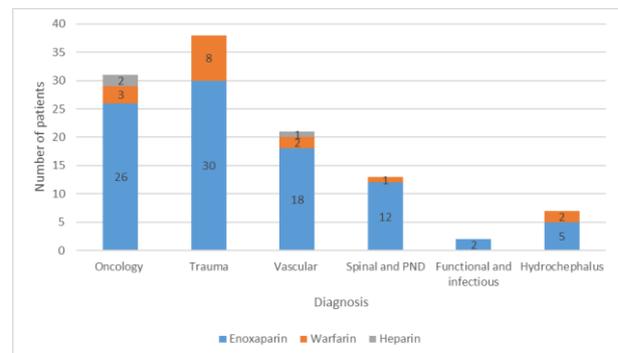


**Figure 1.** The utilization of anticoagulant medications among different diagnoses.

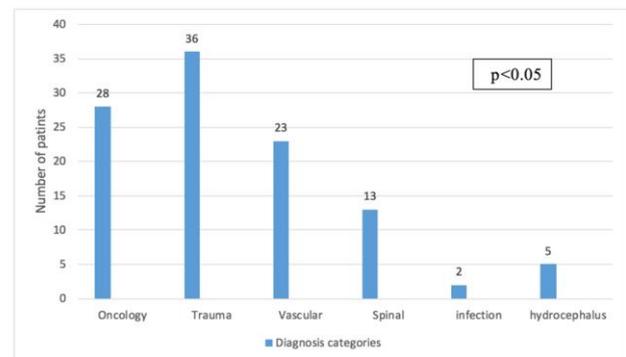
### Utilization of antiplatelet medications

The utilization of antiplatelet medications among different diagnoses ( $n=107$ ) is illustrated in Figure 3. Patients with TBI found to have higher rate of using

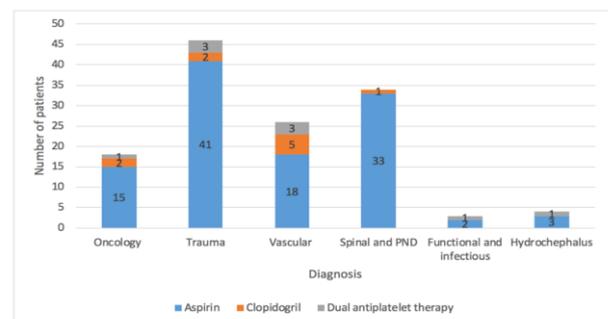
antiplatelet medications (33.6%) followed by patients with oncological and vascular pathologies, respectively (26.1%, 21.4%).



**Figure 2.** Utilization of anticoagulant agents among different diagnoses.



**Figure 3.** The utilization of antiplatelet medications among different diagnoses.



**Figure 4.** Utilization of antiplatelet agents among different diagnoses.

There was a significant difference in the utilization pattern of antiplatelet medications among different neurological diseases investigated ( $p<0.05$ ). Table 3 is representing the relationship between utilization of antiplatelet agents among patients and other variables. It demonstrates that there was no

significant relationship between the usage of antiplatelet medications and the type of injury (traumatic vs non-traumatic) ( $p=0.746$ ). Additionally, there was a significant difference in the LOS and the usage of antiplatelet medications ( $p=0.034$ ). Patients who were undergone surgical intervention were using antiplatelet medications in a much lesser rate compared with patients who were on non-surgical conservative management ( $p=0.032$ ). Added to that, there was a significant difference between the ICU

admission and the utilization of antiplatelet medications ( $p=0.02$ ). Also, there was no association between the usage of antiplatelet drugs and the age of patients (above and below 75 years) ( $p=0.906$ ). Figure 4 showed the utilization of antiplatelet agents among different pathologies. Aspirin was the most commonly used agent in the present study ( $n=112$ ), followed by clopidogrel ( $n=10$ ). Dual antiplatelet therapy (aspirin with clopidogrel) was only used by 9 patients in this research.

**Table 2.** The relationship between the usage of anticoagulant medications and type of injury (trauma vs. non trauma), length of stay, type of intervention (surgical vs. observation), age group, and ICU admission.

Category	Type of injury		Length of stay		Intervention		Age		ICU admission	
	Trauma	36	More than 15 days	51	Surgical	92	More than 75 years	56	Admitted to ICU	40
	Non trauma	71	Less than 15 days	56	Observation	15	Less than 75 years	51	Not admitted to ICU	67
P-value	P= 0.674		P<0.005		P=0.001		P= 0.198		P<0.005	

**Table 3.** The relationship between the usage of antiplatelet medications and type of injury (trauma vs non trauma), length of stay, type of intervention (surgical or observation), age group, and ICU admission.

Category (p-value)	Type of injury		Length of stay		Intervention		Age		ICU admission	
	Trauma	48	More than 15 days	21	Surgical	86	More than 75 years	84	Admitted to ICU	12
	Non trauma	83	Less than 15 days	110	Observation	45	Less than 75 years	47	Not admitted to ICU	119
P-value	P= 0.746		P= 0.034		P= 0.032		P=0.906		P=0.002	

## DISCUSSION

### Utilization of anticoagulant medications

Anticoagulants are important treatments for numerous medical conditions including DVT, pulmonary embolism, and non-valvular AF. Importantly; The triad of anticoagulation, age above 65 years, and minor head injury was considered lethal by Karni et al. on a retrospective review of 278 patients with minor head injuries and CT-documented ICH (14). Patients with TBI found to have higher rate of using anticoagulant medications followed by patients with spinal diseases and vascular pathologies, respectively. In comparison, Claudia et al reported that 75 patients out of 1410 included in the study was on anticoagulants at the time of TBI (4) An important issue to be raised in elderly patients with higher risk of thromboembolic events, is weighing up the balance between thrombotic risk and falls or bleeding risk which can

often be challenging and compounded by the presence of lower number of evidences to guide decisions regarding reinstitution of anticoagulants. (15,16). There was no significant relationship between the utilization of anticoagulant medications among different neurological diseases investigated in the current study ( $p=0.920$ ). In contrast to our study, Pieracci et al. conducted a study to evaluate the effect of anticoagulants on elderly patients and concluded that patients on warfarin had increased severity of head injury, had more chances of ICH (17). Another study investigated the effect of anticoagulants among patients with glioblastoma stated that anticoagulants was associated with inferior overall survival compared to no use on multivariate analysis ( $p=0.001$ ) (18). In comparison to this study; another study stated that patients with primary and metastatic brain tumours, can safely use anticoagulants under careful monitoring, except

for patients with untreated tumours with a high rate of intracranial haemorrhage (i.e., metastases from melanoma, choriocarcinoma, thyroid carcinoma, hepatocellular carcinoma, and renal cell carcinoma). In patients with cerebrovascular pathologies such as cerebral aneurysm, it has been showed that oral anticoagulants in safer than parental ones.

Our study demonstrates that there was no significant difference between the utilization of anticoagulant medications and the type of injury, as both traumatic and non-traumatic patients were using anticoagulant medications in a similar way. In contrast, another study found that there was an exponential correlation between the intensity of anticoagulation the risk of ICH from traumatic events (19). Additionally, patients who were undergone surgical intervention were using anticoagulant medications much less than patients on conservative management. Kawamata et al addressed post-craniotomy usage of anticoagulants in retrospective review of 27 patients. Seventeen of those patients (63%) underwent craniotomy for evacuation of intracerebral or subdural hematomas. Also, there was no association between the usage of anticoagulant drugs and the age of patients (above and below 75 years) ( $p=0.198$ ). Another study by Sharma et al reported that Warfarin consumption is independently associated with higher mortality among a cohort of 384 TBI elderly patients (20)

Enoxaparin was the most commonly used anticoagulant agent among different neurosurgical pathologies in the present study followed by warfarin. Another study by Calvin et al found that almost one fifth of elderly patients older than 65 years old admitted to an American level one trauma centre with head injury were on warfarin, reflecting the importance of impact of warfarin on management and outcome of head injuries (21). This can be explained by the co-existence of other comorbidities that requires anticoagulation therapy such as warfarin more than other anticoagulants (21). An observational study on a cohort of 114 patients with severe blunt trauma (severe TBI excluded) showed that use of oral anticoagulants was associated with significantly lower mortality group 8.3% vs. warfarin group 29.5%,  $p < 0.015$ ) (15). Yet; some physicians may be hesitated to prescribe anticoagulants, especially for the very old or frailest patients, as they are perceived to be at higher risk for the consequences of traumatic events (TBI) (20)

### Utilization of anticoagulant medications

Patients with TBI found to have higher rate of using antiplatelet medications in our study. In comparison to our study; another study showed that 40.7% who sustained blunt head trauma were taking antiplatelet medications and having consequent acute ICH following the head trauma (2). Posttraumatic ICH was associated with significantly increased mortality rate in patients on antiplatelet therapy when compared to controls in previous studies (9,10). These findings are supported by a study by Major et al who found evidence that posttraumatic ICH is associated with a mortality rate of 21% in patients on antiplatelet therapy (11). The risk for ICH appears to be dose dependent with aspirin, the most studied agent, but exists with other antiplatelet agents as well (12). The utilization of those medications was correlated with increased ICH volume growth at 12 hours, volume of intraventricular haemorrhage increased chance of death at 14 days, and poor outcome at 3 months (13,14,15). Yet, the decision to stop all antiplatelet medication needs to be carefully considered, weighing the size and morbidity of the ICH against the reason the agents were initiated. In another hand, platelet function testing appears advisable prior to neurovascular procedures, particularly in patients with risk factors for variable response to antiplatelet medications (16). Another important issue to be considered is that in all studies the assessment of pre-injury use of antiplatelet agents was based on the patient's history and not on assessment of platelet activity through laboratory examinations, thus, incompliance of patients regarding the intake of prescribed medications as well as ineffectiveness of antiplatelet agents in some will affect the overall effect of antiplatelet medications in the body system (4).

This study also showed that there was a significant relationship between the utilization of antiplatelet medications among different neurological diseases investigated. Correspondingly, a previous study conducted to evaluate the effect of antiplatelet medications on neurosurgical conditions showed that pre-injury antiplatelet agents were associated with three times higher mortality among elderly patients where it was due to a functional rather than quantitative factors (2).

Our study demonstrates that there was no significant difference between the utilization of antiplatelet medications the type of injury. In

comparison to our study, Mina et. al found a statistically significant mortality rate (47%) in those who had TBI and taking aspirin compared with controls (8%). This may be attributed to the severity of TBI or the dose of aspirin consumed by the patients as low aspirin doses showed to have a lower risk of bleeding compared with higher doses (12,17) Also the present study demonstrated that there is a significant difference in the LOS and the usage of antiplatelet drugs, in which patients who were not using antiplatelet medications found to stay shorter in the hospital. In comparable results, Scott et al reported that patients who were using antiplatelet medications were three times more likely to be discharged to long-term inpatient facilities and 14 times higher mortality rate as compared with those not on antiplatelet. Additionally, patients who were undergone surgical intervention were using antiplatelet medications much less than patients on conservative management. In contrast to our research; Bachelani et al found that neither history of aspirin intake nor platelet inhibition measured by a specific coagulation tests were associated with an increased risk of incidence or progression of ICH and consequent need to an operative intervention such as craniotomy (18). Added to that the significant relationship that found to be between the ICU admission and the utilization in which majority of the patients who were not on antiplatelet therapy were not admitted to the ICU. In comparison to a study conducted by Sharma et al which stated that antiplatelet therapy with aspirin and clopidogrel did not increase rate of mortality and did not affect length of hospital ICU stay (19). Also, there was no association between the usage of antiplatelet drugs and the age of patients (above and below 75 years). Prior research has shown that the geriatric population suffers from a higher rate of acute ICH. As the brain ages, there is volume loss in the brain parenchyma, making bridging cerebral vein more vulnerable to bleeding along with a significant decline in the elasticity of those veins. Moreover, the increase in aging population due to improvement of health care services in high income developing countries – like sultanate of Oman - has led to increased utilization of antiplatelet medications, likely contributing to the increased incidence of bleeds (2).

Aspirin is the most commonly used antiplatelet agent among different neurosurgical pathologies in

the present study followed by clopidogrel. In the same line to our study, a previous study showed that aspirin is the most common utilized antiplatelet drug. This can be attributed to the fact that it is widely available, well tolerated, and has extensive clinical evidence supporting its use in the cardiovascular protective properties. Yet, currently, the combination of aspirin and clopidogrel is recommended prior to some neuroendovascular surgeries such as stent deployment (4).

### Limitations

There were some limiting factors in the present study. It was a retrospective, single-centered study over a period of four-years which limit is our ability to investigate whether there is a prior use of anticoagulants and antiplatelet medications especially in patients with chronic diseases that carry a high thromboembolic risk. Analysis of coagulation profile was not routinely performed, so it is unclear if patients were compliant with their anticoagulant medications. Moreover, the study was conducted in tertiary health care facility so it doesn't include prescription patterns of medications from other health care facilities. Finally, the outcome of using anticoagulant and antiplatelet medications was not illustrated in the present study due to the lack of comprehensive data regarding mortality in the health information system used to collect the data.

### CONCLUSION

Patients with TBI found to have higher rate of using antiplatelet and anticoagulant medications. Aspirin and enoxaparin were the most commonly used antiplatelet and anticoagulant agents among different neurosurgical pathologies in the present study. Physiological changes and comorbidities are main contributors to the challenges faced in managing bleeding in geriatric age group which has to be considered essentially. There is a need for further work to explore the balance of thrombotic and antithrombotic factors in elderly patients with neurosurgical diseases and to investigate whether the laboratory measures of thrombotic potential can help identify those at highest risk of thrombosis. Decisions regarding prescription and resumption of anticoagulants and antiplatelet medications should be taken on a case-by-case basis involve a multidisciplinary and holistic approaches. The preventative benefit is of antiplatelet and

anticoagulant therapy from thromboembolic events of stroke or myocardial infarction have to be weighed against the risk of haemorrhage and death in those patients due to decreases ability of their body to withstand high energy traumatic accidents and their increased risk of frequent falls. It's worth mentioning that this study is the first of its kind in the region, to the best of our knowledge.

#### ABBREVIATIONS

DVT: deep venous thromboembolism,

GCS: Glasgow Coma Scale,

ICH: Intracerebral haemorrhage,

ICU: Intensive care unit,

LOS: length of hospital stays,

PE: pulmonary embolism.

#### DISCLOSURES

Nothing to disclose.

#### FUNDING

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#### CONFLICT(S) OF INTEREST

No conflict of interest.

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