Timely Anticoagulant Thromboprophylaxis is Safe and Effective in the Care of Patients Suffering Traumatic Brain Injury.

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Abstract
Despite the high prevalence and associated morbidity of Venous Thromboembolism (VTE) development, thromboprophylaxis in the neurosurgical setting remains a source of contention due to concerns of iatrogenic haemorrhage progression associated with anticoagulant thromboprophylaxis. Opinions of ideal time to initiate chemical prophylaxis for VTE within the neurosurgical community vary between clinicians. It is nevertheless rarely disputed that timely and appropriate prophylaxis of VTE reduces morbidity. This review aims to determine the safety and efficacy of chemical VTE prophylaxis within the neurosurgical setting. The consequences of VTE can be devastating and patients with neurotrauma are amongst those at greatest risk. With this in mind, the neuroscience nurse must be meticulously conscientious for the prevention of VTE in the neurosurgical setting. The neurosurgical nurse has a close affiliation to the patient, is often the first to observe the clinical signs and symptoms associated with VTE, is responsible for implementing prevention strategies and assisting with treatment for those who unfortunately develop a Deep Vein Thrombosis or Pulmonary Embolism (PE).

Key Words: Venous thromboembolism, thromboprophylaxis, neurosurgical, head trauma, enoxaparin, intracranial bleeding.

Introduction
Venous Thromboembolism (VTE) encompasses both Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) (Welch, 2010). Accounting for the death of 5-10% of hospital inpatients, PE is the most common avertible cause of inpatient death (Cohen, Tapson, Bergmann, Goldhaber, Kakkar, Deslandes, Huang, Zayaruzny, Emery & Anderson, 2008). Virchow’s triad as explained in Delaune, Nanda & Barker (2008) defines the three contributing factors associated with VTE formation. These factors are venous stasis which is reduced or stagnant blood flow in deep veins, venous injury which causes the release of procoagulant factors within the bloodstream as part of the normal clotting mechanism and hypercoagulability which refers to a more intrinsically active clotting state, often as a result of traumatic injury (Maclean, 2014).

The quoted incidence of DVT in the neurosurgical setting varies from 9-50% (Delaune et al., 2008), with patients suffering from multi-system traumatic injuries in addition to their neurotrauma, being at the greatest risk (Reiff, Haricharan, Bullington, Griffin, McGwin & Rue, 2009). Despite the high prevalence and associated morbidity of VTE development, thromboprophylaxis in the neurosurgical setting remains a source of contention due to concerns of iatrogenic haemorrhage progression associated with anticoagulant thromboprophylaxis. There is further reticence to use early chemical VTE prophylaxis due to the absence of a national care standard and the nature of previous studies which are majority, limited to retrospective and observational studies (Phelan, 2012).

Method
A literature search was conducted utilising the electronic databases CINAHL, PubMed and MEDLINE in August 2014 using the keywords venous thromboembolism, thromboprophylaxis, neurosurgical, head trauma, enoxaparin and intracranial bleeding. Articles were limited to English papers, which were published from 2008 to present. The reference lists of articles were searched for additional publications. A total of 30 papers were reviewed and 15 included in the review combining both contemporary literature and seminal work pieces.
Review of the literature

VTE is a common complication for hospitalised patients irrespective of their pathology, and no group of patients has a higher risk than those who have suffered traumatic injury (Urden, Stacy & Lough, 2015). Taniguchi, Fukuda, Daitoku, Minakawa, Odagiri, Suzuki, Fukui, Asano & Ohkuma (2009), conducted a prospective study of 37 patients stratified into risk categories which analysed the prevalence of venous thromboembolism in the neurosurgical setting. Their study group received thromboprophylaxis with graded compression stockings, with or without the use of intermittent pneumatic compression (IPC), but did not receive chemical prophylaxis. Their results suggested that mechanical prophylaxis alone was inadequate with the prevalence of DVT within their cohort at 13.5% which is within the expected baseline of risk in the untreated. Also of note, within their study group, of those found to have DVTs, there was a 60% prevalence of PEs requiring long term treatment. Similarly, Phelan (2012), conducted a critical literature review of 56 papers to determine the safety and efficacy of chemical VTE prophylaxis in the setting of neurosurgical patients. They reported rates of DVTs in patients who had suffered traumatic brain injury (TBI) in the intensive care unit (ICU) setting as being as high as 51%, with a subsequent post thrombotic-syndrome rate of 30%; a syndrome, it should be noted, associated with a poorer expected long term outcome than chronic fibrotic lung disease and diabetes. They advised that initiation of low molecular weight heparin (LMWH) prophylaxis was critical once haemorrhage progression was deemed stable, suggesting 48 hours postop to be the optimal time, due to the increasing requirement of invasive prophylaxis via use of devices such as inferior vena cava (IVC) filters beyond this period. Scudday, Brasel, Webb, Codner, Sombreg, Weigelt, Herrmann & Peppard (2011), also hypothesised that the use of anticoagulant prophylaxis would decrease the incidence of VTE without increasing intracranial haemorrhage in their retrospective case control study of 812 patients. Anticoagulant prophylaxis in the form of unfractionated heparin (UFH) or LMWH was initiated in 402 (49.5%) patients. 169 commenced anticoagulant prophylaxis within 48 hours of presentation, whilst 242 patients had treatment initiated within 72 hours. Findings of the study indicated that patients receiving anticoagulant prophylaxis in contrast to mechanical prophylaxis had a reduced VTE incidence of 1% and 3% respectively.

Opinions of ideal time to initiate chemical prophylaxis for VTE within the neurosurgical community vary between clinicians. It is nevertheless rarely disputed that timely and appropriate prophylaxis of VTE reduces morbidity. A study of Canadian practice conducted by Scales, Riva-Cambrin, Le, Pinto, Cook & Granston (2009), surveyed 160 neurosurgeons and intensivists, confirming that the majority of clinicians utilised anticoagulant prophylaxis in the neurosurgical setting despite the perceived risks of haemorrhagic progression. 88% of surveyed intensivists and 75% of surveyed neurosurgeons described the use of UFH, LMWH or other anticoagulant thromboprophylaxis for patients with diffuse axonal injury after severe traumatic brain injury. The majority (58%) who favoured anticoagulant thromboprophylaxis reported that they would initiate anticoagulant thromboprophylaxis within two days of injury. In the instance of patients suffering intracranial haemorrhage after severe traumatic brain injury, 60% of those surveyed reported that they would initiate anticoagulant thromboprophylaxis during the inpatient course. In this case however, the initiation time was more varied with 34% of those surveyed stating that they would commence anticoagulant prophylaxis within two days of surgery, 57% would commence within four days and 80% within one week. The use of anticoagulant thromboprophylaxis in patients who are considered high risk for the development of VTE undergoing intracranial neurosurgery is also supported by Barillari & Pasca (2009) who state that the use of IPC in addition to low dose UFH or LMWH postoperatively is more efficient than the use of IPC alone. This statement is based on their review of guidelines presented from the American College of Chest Physicians (2008), consensus conference on antithrombotic therapy. In spite of the observed efficacy of anticoagulant thromboprophylaxis, a clinical decision analysis study conducted by Scales, Riva-Cambrin, Wells, Athaide, Granston & Detsky (2010), revealed that the probability of no intracranial haemorrhage progression in the context of mechanical or anticoagulant thromboprophylaxis was associated with expected values of 0.90 (90%) and 0.89 (89%) respectively, meaning that the decision to anticoagulate patients was approximately equivocal in terms of its absolute risk. It went on however to conclude that given the implications of intracranial haemorrhage when measured against the implications of VTE, that the risks while equivalent numerically, were not necessarily contextually equal.
In favour of early anticoagulation, it has been shown that delayed time to treatment with appropriate anticoagulation therapy has been shown to have a significantly increased burden of disease. Reiff et al (2009) conducted a retrospective, multicentre study which included 15,269 eligible patients of which 2000 had sustained traumatic brain injury (TBI) investigating DVT risk dependent on admission time to commencement of prophylaxis. They found that patients suffering from TBI are associated with a high risk of DVT which became significantly greater when the presentation time to anticoagulant prophylaxis was longer. In their observed cohort when the time to commence prophylaxis was beyond 48 hours, DVT risk in TBI surged to 15.4%, compared with a significantly less risk of 3.6% in TBI patients who had prophylaxis initiated at 0-24 hours. In contradiction to their findings, the retrospective study by Salottolo, Offner, Levy, Mains, Slone & Bar-Or (2010), was not able to establish an association between the development of VTE and the timing of anticoagulant prophylaxis commencement.

Reticence to initiate anticoagulation is based on the perceived risk of haemorrhagic progression. However, some evidence suggests that intracranial haemorrhage rates within those treated with anticoagulant prophylaxis are significantly less than is intuitively assumed. In a retrospective study undertaken at an academic tertiary care facility including 4293 patients undergoing surgery for intracranial brain tumour, Chaichana, Pendleton, Jackson, Martinez-Gutierrez, Diaz-Stransky, Aguayo, Olivi, Weingart, Gallia, Lim, Brem & Quinones-Hinojosa (2013), reviewed 126 patients who acquired DVT and/or PE; 67% suffered solely DVT, 25% PE and 8% both. All were diagnosed within 30 days of surgery through a variety of means including ultrasound, CT pulmonary angiogram and ventilation perfusion scan. The majority of patients diagnosed with VTE (81 patients, 64%) were treated with UFH, and in follow up imaging only 5 (4%) had an intracranial haemorrhage. While the cohort studied was not focused purely on patients suffering TBI, given the degree of parenchymal injury associated with tumour and other surgery, a degree of extrapolation is not unreasonable. Similarly, Dudley, Aziz, Bonnici, Saluja, Lamoureux, Kalmovitch, Gurasaahany, Razez, Malek & Marcoux (2010), undertook a retrospective study that reviewed 694 cases of moderate to severe traumatic brain injury over a period of 5 years and analysed the use of LMWH for VTE prophylaxis. Eligible patients, 287 in total, were fitted with mechanical prophylaxis; both graded compression stockings and IPC, and were also commenced on LMWH at 48-72 hours post traumatic injury. It is important to note that in this instance, patients were commenced on LMWH only when two or more CT scans displayed intracranial haemorrhage. 186 patients underwent a CT scan within three weeks of commencing LMWH and only one (0.4%) developed progression of a known intracranial haemorrhage. The authors concluded that early LMWH commencement post traumatic brain injury showed a decreased incidence of VTE (7.3%) and should be considered safe given that only 0.4% suffered a progression of intracranial haemorrhage. Faroqui, Hiser, Barnes & Litofsky (2013), concluded that the use of anticoagulant prophylaxis in head injured patients appears to be effective in preventing DVT and PE without increase in haemorrhage rates in their retrospective study of 236 patients. They reviewed an anticoagulant VTE prophylaxis protocol after TBI mandating the use of anticoagulant prophylaxis (UFH or LMWH) at 24 hours post injury for all patients. The analysis compared two groups of patients; one cohort of 107 patients treated without this protocol and the other cohort of 129 patients were in the described manner. The incidence of PE in the former was 3.74%, and 0.78% in the latter. Curiously, without the protocol, the observed number of haemorrhagic progressions, (3 incidences) was higher than those treated with the protocol (1 incident). Similarly, Minshall, Eriksson, Leon, Doben, McKinzie & Fakhry (2011), retrospectively reviewed the charts of 386 patients admitted to an ICU with a hospital stay of greater than 48 hours with significant TBI over a 42 month period. Their aim was to compare the use of LMWH and UFH to better gauge haemorrhage progression risk in patients suffering severe traumatic brain injury and to explore the related rates of VTE. Of their study group; 158 patients were treated with LMWH, 171 were treated with UFH and 57 patients had sequential compression devices, the latter considered the control group. The observed incidence of VTE within the treated groups of patients was 0.9% and 1.9% respectively. Patients in the untreated group had a 47% mortality rate in stark contrast to the observed 5% in the LMWH group and 16% in the UFH group. In patients treated with UFH the incidence of DVT was 1% and 3.7% for PE, only marginally higher than those patients treated with LMWH. After the commencement of treatment, only 8 (5%) patients in the LMWH group and 20 patients (12%) in the UFH group had a progression of their in-
tracranial haemorrhage which, as with the study by Farooqui et al., (2013), is considera-
bly lower than their control group with a pro-
gression rate of 25%. Again, early initiation of
anticoagulant prophylaxis in patients with se-
vere TBI was shown to significantly reduce the
risk of VTE without significant risk of intracra-
nial haemorrhage progression. Depew, Hu,
Nguyen & Driessen (2008), suggested early
prophylaxis had merit following conducting a
retrospective study including 124 patients who
suffered blunt head trauma reviewed rates of
ICH progression with early prophylaxis. 62
patients were commenced on LMWH, 20 pa-
tients on UFH and 42 patients had pneumatic
compression devices alone. Of those with
chemical VTE prophylaxis, 10 developed VTE
and 3 developed ICH progression of which
only one was significant. In contrast, a deci-
sion analysis study conducted by Niemi &
Armstrong (2010) proposed that if bleeding
risk was high intraoperatively, the administra-
tion of anticoagulant prophylaxis should be
postponed until as late as possible, but conse-
dquences should be considered case depend-
ent. They concluded that patients considered
very high risk from thrombus development
should have anticoagulant prophylaxis imple-
mented provided risk of inadequate prevention
outweighed the risk of bleeding.

Nursing Considerations
The essential role of the neuroscience nurse
is continually evolving. Neuroscience nurses
are conscientiously accountable for the coor-
dination of patient care throughout recovery
and are instrumental in the prevention of VTE
in the neurosurgical setting. Prevention of
VTE and risk reduction should be considered
fundamental nursing goals (Andrews & Ha-
bashi, 2010). Rapid patient assessment in
order to review effectiveness of care, quick
identification of issues and prompt manage-
ment of complications is essential in high risk
patients. Due to their close affiliation to the
patient, the nurse is often the first to observe
the clinical signs associated with VTE and is
responsible for implementing prevention strat-
gegies and treatment for those who develop
DVT or PE. DVT, as described in Scruth &
Haynes (2014), typically presents with pain in
the calf, often with redness, swelling and dis-
tended superficial veins. The affected calf is
often warmer to touch and Homan’s sign, pain
in the calf on dorsiflexion of the foot, may also
be present. Although a late sign of DVT, cya-
notic discoulouration due to deoxygenated ha-
emoglobin present within the stagnant veins,
may also be present (Söhne, Vink & Büller,
2009). As explained in Hix & Tamburri (2009),
the signs and symptoms of PE include dysp-
noea, tachypnoea, inspiritional chest pain,
chest wall tenderness, decreased spO2, cough,
cyanosis, tachycardia, fever and haemoptysis. PE may present with varied signs and this can often make the diagnosis challenging (Mathers, 2015). A possible PE
should be considered in any patient who dis-
plays or reports new onset of cardiorespiratory
signs and symptoms or any risk factors for
VTE (Hix & Tamburri, 2009).

The neuroscience nurse is also responsible
for providing sufficient patient education for
patients considered high risk or who have de-
veloped DVT or PE. In the context of ICU pa-
tients, Andrews & Habashi (2010), recommend
the use of minimal sedation where possible
continue anticoagulant prophylaxis for the prevention of VTE.

It is extremely important that the neuroscience
nurse be attuned to the potential for patients to precipitously deteriorate in the setting of
anticoagulant prophylaxis, particularly given
the inability to immediately reverse the effects
of anticoagulants such as, LMWH, given that
an exclusive antidote is not available (Niemi &
Armstrong, 2010).

Conclusion
VTE thromboprophylaxis in the neurosurgical
setting remains controversial and can be chal-
lenging and complex. As highlighted in the
review, the consequences of VTE can be dev-
astating and patients with neurotrauma are
amongst those at greatest risk. Complicating
that which would otherwise be a simple mat-
ter, the risk of haemorrhagic progression and
the consequences of postoperative bleeding lend credence to a more conservative ap-
proach, with delays to onset of chemical
prophylaxis being the most commonly de-
scribed intervention. As a nurse within the
neurosurgical field, the key challenges remain
early detection of VTE complications within
the untreated cohort of patients, and the early
detection of haemorrhage within the treated
population.

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References
American College of Chest Physicians (2008),