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1 | Characteristics of Cerebral Venous Thrombosis Associated with Head Trauma

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Background and Aim: The treatment and course of cerebral venous thrombosis (CVT) associated with traumatic brain injury (TBI) is not well-characterized and is often managed conservatively. We reviewed the experience at a large tertiary Canadian hospital.

Methods: Cases of CVT between 2008–2018 were identified through free text search through hospital radiology reports and ICD-10 discharge codes. Total number of TBIs was verified through the provincial trauma database. We examined demographics and clinical characteristics; a single expert re-reviewed imaging.

Results: Of 3285 TBI, 54 had an identified concurrent CVT. Mean age was 48 (SD 17.8); 22% were female. Vascular imaging (CTA/V) was done the day of admission in 84%; delay to CTA/V was a median of 1d (range1–13). Almost all CVT (93%) were associated with skull fracture; all but 4 were ipsilateral to the side of the fracture. Most (67%) had at least one repeat CTV, occurring at a median of 3d (range1–74) after the initial scan. Two had evidence of secondary venous infarction on follow-up imaging. One was anticoagulated with unfractionated heparin with CVT as the indication; 69% received no anticoagulation and the remainder received chemoprophylaxis dosing at some point during their admission.

Conclusion: Trauma-associated CVT may have been under-ascertained in the absence of routine vascular neuroimaging for all TBI. Clinical course was also poorly characterized due to a lack of consistent clinical and neuroimaging follow-up. Routine vascular neuroimaging in the event of skull fracture with a consistent follow-up pathway will help to better determine optimal management.

2 | Prolonged TEG-Defined Hypercoagulability in Pelvic and Acetabular Fractures

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Introduction: Major orthopaedic fractures are independent risk factors for venous thromboembolism (VTE), and despite thromboprophylaxis patients who sustain a pelvic or acetabular fracture (PA) continue to have high VTE rates (12% incidence). Thrombelastography (TEG) is a whole-blood, point-of-care test that can provide an overview of the clotting process. Maximal amplitude (MA) from TEG is the measure of clot strength and values ≥65 mm can be used to quantify hypercoagulability and increased VTE risk. The primary aim of this study was to use serial TEG analysis to quantify the duration of hypercoagulability, following PA fractures. We hypothesized that MA values will define hypercoagulability duration and distinguish patients with VTE events, with some PA patients having persistently elevated MA values beyond 4-weeks post-operatively, at the end of thromboprophylaxis.

Methods: This is a prospective cohort study of adult patients (≥18 years) with surgically treated PA fractures. Consecutive patients

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were enrolled from a single Level I trauma centre. Following informed consent, blood draws were taken at specific timepoints (upon admission, pre-operatively on day of surgery, post-operatively on days 1, 3, 5, 7 (or until discharge, whichever comes sooner), in follow-up at 2-, 4-, 6-weeks and 3-months post-operatively), for serial TEG analysis to provide a complete picture of the change in clotting tendency and duration. All patients received standardized thromboprophylaxis with low molecular weight heparin for 28 days post-operatively. Statistical analysis was done with one-sided t-tests and descriptive statistics, as appropriate, with a significance level of 0.05.

Results: From a total of 17 patients (three females) with a median age of 54 (IQR [47, 61]), eight patients sustained acetabular fractures (47%) and nine sustained pelvic fractures (53%), all of which had serial TEG analysis completed until 3-months post-operatively. Of the 17 patients enrolled, three (18%) were hypercoagulable upon admission. On post-operative day 1 (POD1), 41% were hypercoagulable and by POD3, the number of patients who were hypercoagulable nearly doubled to 81%. At POD5 all the patients were hypercoagulable, and all remained hypercoagulable until at least two weeks following surgery. The highest average MA values were 74.0 ± 2.0mm which occurred on POD7. Almost two-thirds (62.5%) remained hypercoagulable at the 4-week timepoint, when thromboprophylaxis is discontinued. One-third (33%) continued to be hypercoagulable at 6-weeks and 23% remained hypercoagulable at 3-months following surgery.

There were three objectively diagnosed VTE events (17.6%) (mean MA value 68.1mm ± 3.9mm). All VTE events occurred with acetabular fracture patients and all were males. There was a significant difference in age between patients diagnosed with VTE (73.3 ± 12.0 years) and those without (46.5 ± 17.0 years). Patients with VTE appear to have prolonged elevated MA values, as seen at 6-week follow-up, where they had an average MA of 68.6mm ± 3.5mm.

Discussion & Significance: Prolonged hypercoagulability occurred following pelvic and acetabular fractures with more than 30% of patients hypercoagulable at 6-weeks, and nearly 25% at 3-months. The prolonged hypercoagulability defined by serial TEG analysis may help predict VTE risk for patients with PA fractures. A larger future study could be performed, leading to clinical recommendations regarding thromboprophylaxis duration in this high-risk population.

3 | Physician and Patient Beliefs and Preferences in Pulmonary Embolism and Deep Vein Thrombosis Testing in People with Cancer

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Introduction: It is unclear whether evidence-based diagnostic protocols are followed when cancer patients are tested for venous thromboembolism (VTE). Evidence-based protocols reduce unnecessary diagnostic imaging, offer a patient-centered approach, and have the potential to standardize practice across medical specialties and settings. However, anecdote suggests that specialists who test people with cancer for VTE may prefer diagnostic imaging over clinical probability scoring and D-dimer testing. The aim of this study was to identify physician and patient knowledge, beliefs, values and preferences for VTE testing in cancer. This study was part of a program of research to set International Society of Thrombosis and Haemostasis standards for VTE testing in people with cancer.

Methods: This was an international qualitative interview study following COREQ guidelines. Semi-structured interviews with physicians and cancer patients were conducted via Zoom. We used purposive sampling to ensure inclusion of physicians from all specialties who test people with cancer for VTE, practicing across all continents. We invited people treated for cancer who had and did not have experience of VTE testing. We used grounded theory to create a conceptual framework which explains physician and patient values and preferences for VTE testing. Transcripts were coded by three researchers independently, who met to discuss their findings and agree on common codes. Researchers were a Thrombosis physician and two undergraduate students who ensured reflexivity was incorporated into their analysis.

Results: A total of 32 physicians and 6 cancer patients were invited to interview. Of those invited, 23 physicians and 6 patients across 6 continents completed an interview. Interviews lasted between 21 and 86 minutes. Physicians reported a low threshold to test for VTE in people with cancer compared to those without cancer, because VTE was considered a fatal disease and highly prevalent in this patient population. Imaging was generally the only test used for VTE testing in cancer patients. Many participants relied on their Gestalt estimation of VTE probability when deciding whether to order imaging for pulmonary embolism or deep vein thrombosis. Most thought that low Wells score in combination with a negative D-dimer was not sufficiently sensitive to exclude VTE and anticipated the Wells score and D-dimer to be elevated. The Wells scores had poor face validity because they do not include cancer-specific variables and participants hoped to see a more nuanced formal score for VTE testing in cancer patients. Participants believed that their colleagues would support their diagnostic approach.

Patients reported they were used to having tests and CT scans. Patients felt it was important for their physicians to prioritize testing for VTE. Patients had full trust and confidence in their physicians’ testing decisions, particularly in decisions made by their oncologists.

Conclusion: Physicians have a low threshold to test people with cancer for VTE and tend not to use clinical probability assessment and D-dimer. Patients are comfortable having diagnostic imaging, feel VTE testing is important and have full trust in their physicians.
Objective: Cerebral venous thrombosis (CVT) is a rare cause of stroke that predominantly affects younger women with anticoagulation as the mainstay of treatment. However, the role of recanalization in guiding management remains uncertain. We aimed to explore: (1) whether recanalization degree is associated with functional outcomes and other outcomes, including development of chronic headache, epilepsy, dural arteriovenous fistula, neuropsychiatric sequelae and recurrence, and (2) clinical and temporal factors that may predict recanalization status.

Methods: Two independent authors (D.K., A.H.) performed a systematic review in MEDLINE, Embase and Cochrane Library from inception for studies reporting recanalization in CVT patients treated with anticoagulation. We did not include endovascular thrombectomy data in our inclusion criteria. Recanalization was divided as none, partial or complete, when definitions were provided by studies. Using the modified Rankin Scale (mRS), functional status was classified as favourable (mRS 0–1) or worse (mRS 2–6). We calculated a meta-analysis of unadjusted odds ratios (OR) using the Mantel-Haenszel method assuming random effects. We applied a risk-of-bias assessment to measure study quality and for sensitivity analysis.

Results: We screened a total of 727 articles, and identified 25 studies that met inclusion criteria for a total of 1379 patients. Lack of recanalization was significantly associated with unfavourable outcomes in comparison to those with any recanalization (OR 3.10, 95% CI, 1.59–6.07, p < 0.001). Development of chronic headache was found to be dose-dependent given degree of recanalization. The likelihood of chronic headache was not significantly different between none compared to partial recanalization status (OR 1.74, 95% CI, 0.62–4.86, p = 0.29). However, partial recanalization showed a significant correlation with chronic headache development when compared to complete recanalization (OR 4.19, 1.50–11.73, p = 0.01). Age greater than 50 years and cryptogenic etiology were significantly associated with lack of recanalization in follow-up: OR for none vs any recanalization was 4.14 (95% CI, 1.88–9.13, p < 0.001) and 3.63 (95% CI, 1.71–7.70, p < 0.001), respectively.

Conclusions: While a previous meta-analysis has examined the relationship between recanalization and functional outcome with the mRS, no work to date has explored the relationship between degree of recanalization in CVT and non-mRS outcomes, which may be more sensitive to characterize disability in this young patient population. We anticipate that our results will generate hypotheses that can be better assessed through ongoing large prospective studies in order to better inform management.

Disclosures: Dr. Field is the principal investigator of the SECRET trial and receives in-kind study medication from Bayer Canada.
**Future Directions:** We are continuously screening and enrolling patients into the COVID-BEACONS study. Once other biomarkers have been quantified, these data will be subjected to unbiased learning analyses to stratify groups of biomarkers that are likely to predict clinical outcomes. We will also use the COVID-BEACONS cohort as the validation cohort to verify previously identified biomarkers associated with mortality (i.e. sTM, PAI-1, plasminogen, and clot lysis times), which may then offer prognostic value for effective and efficient patient care. Better understanding of these biomarkers may offer novel therapeutic strategies to reduce this profound derangement in clotting.

6 | Risk of Thrombotic Complications Post-Hospital Discharge in Patients with COVID-19: A Retrospective Cohort Study

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**Introduction:** Coronavirus disease 2019 (COVID-19) is caused by SARS-COV-2, a novel virus that appeared in December 2019 and has since become pandemic. Infection with COVID-19 has been correlated with increased levels of inflammatory markers (Zeng 2020) which may be involved in the onset of venous thromboembolism (VTE) (Matos 2011). Studies observing the incidence of VTE among critically ill patients with confirmed COVID-19 infection report rates as high as 69% (OR, 1.74; 95%CI) (Wichmann 2020, Klok 2020, Cui 2020) suggesting an increased risk of VTE in this population. Additionally, previously published data report an increased risk of VTE within 3 months after hospital discharge in non-COVID patients (Littjos 2020). Descriptions of the burden of VTE post-discharge in patients with COVID-19 remain limited. One study of 140 patients followed up after discharge from a hospital admission for COVID-19 infection showed an incidence of VTE of 0.71% (Bourguignon 2020). Furthermore, in the context of sparse data, recent expert panel guidelines have proposed differing recommendations with regards to management of VTE risk in COVID-19 patients, including the post-discharge period (Lodigiani 2020, Middeldorp 2020). These differing opinions reflect the ongoing need for better understanding of the risk of VTE among COVID-19 patients post-hospital discharge.

**Objective:** The primary aim is to describe the risk of Venous Thromboembolism (VTE) in patients with COVID-19 infection within 30 days of discharge from hospital for COVID-19 infection whether from a designated COVID medical unit or directly from the Emergency Department (ED).

**Methods:** A retrospective cohort study was conducted using patients’ electronic medical records to identify eligible patients and to collect data. We included all consecutive patients admitted to the Jewish General Hospital with a diagnosis of COVID-19 between March 1st and June 1st 2020 who (i) returned within 30 days of discharge and (ii) received a diagnosis of acute VTE. The incidence risk of VTE as well as descriptive statistics on patient-related characteristics are reported.

**Results:** Based on data from the Jewish General Hospital (JGH) between March 1st – June 30, 2020, 697 patients were admitted for COVID-19. Among these, 413 were discharged; 6 patients returning to ED were diagnosed with VTEs resulting in an incidence risk of 1.45%. Patients were between the ages of 31–82 years, 50% were female, and the average time between discharge and presentation was 12.5 days (SD 8.5 days). Average length of stay for hospitalization for pulmonary embolism (PE) was 3.7 days (SD 2.5 days). Only one was critically ill and admitted to the Intensive Care Unit. All patients were diagnosed PE (4/6 patients with segmental PE and 2/6 with sub-segmental only). None of the patients were previously anticoagulated. Two out of the six patients had predisposing conditions (1 with pregnancy; 1 factor V leiden without previous thrombosis).

**Conclusion:** The risk of VTE post-discharge in a COVID-19 cohort is less common than initial data suspected. This study helps establish the burden of thrombotic complications in the COVID-19 post-discharge population and may guide the development of future recommendations on the role of extended thromboprophylaxis in this population.

7 | An Observational Pilot Study Investigating the Role of Coagulation in the Diagnosis of SEPSIS in the Emergency Department (SEPSIS-ED)

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**Introduction:** Inflammation and coagulation are linked to the innate immune response. Early recognition and diagnosis are essential to alter patient prognosis. We have shown that coagulation markers are important for prognosis in the intensive care unit. However, the role of coagulation markers to aid in sepsis diagnosis in the emergency department (ED) has had limited investigation.

**Methods:** SEPSIS-ED is an observational cohort study with a planned recruitment of 250 adult patients presenting to two ED’s with sepsis suspicion. Samples are collected at two-time points: initial patient
presentation to the ED (time point one, T1) and four hours after the initial sample collection (time point two, T2). Plasma cell-free DNA (cfDNA) levels are determined by the silica-membrane-based DNA purification method and UV spectrophotometry. Procalcitonin, protein C (PC), DNase I (deoxyribonuclease I), ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13), and von Willebrand factor (VWF) levels are measured using enzyme-linked immunosorbent assays. Each case with suspected sepsis is adjudicated using Sepsis-3 definition.1 Data is reported as median (Interquartile range) depending on whether normally distributed.

Results: We report data on 200 patients with 52.7% males and a mean age of 69.8 ± 17.7 years, including 83 septic and 117 non-septic patients. Septic patients had a 9.6% mortality at 28 days and a SOFA score of 4 (4) which was higher than the non-septic patient group (SOFA score 2 (2)). Septic patients had elevated leukocyte (12.7 (8.4) × 10^9/L) and neutrophil counts (10.9 (7.5) × 10^9/L) compared to the hospital standard. CfDNA levels were higher in septic patients (n = 21) and non-septic patients (n = 44) (T1, p = 0.39 and T2, p = 0.79). Procalcitonin levels were significantly higher in septic patients (n = 83) compared to non-septic patients (n = 117) at time point two (p = 0.03), while no difference was seen at time point one (p = 0.11) between the two patient groups. DNase I levels at both time points were not significantly different between septic (n = 21) and non-septic patients (n = 44) (T1, p = 0.09 and T2, p = 0.97). Procalcitonin levels were significantly higher in septic patients (n = 83) compared to non-septic patients (n = 117) at both time points (T1, p = 0.0009 and T2, p = 0.0003). PC levels declined four hours after admission to the ED in septic patients (n = 83) (p = 0.007), with no significant difference seen in mean values compared to non-septic patients (n = 117) (T1, p = 0.95 and T2, p = 0.13). In addition, ADAMTS13 levels in septic levels (n = 58) were lower than the non-septic patients (n = 54) (T1, p = 0.04 and T2, p = 0.03), with no difference in VWF levels among septic patients (n = 74) compared to non-septic patients (n = 100) (T1, p = 0.50 and T2, p = 0.16).

Limitations: The study is limited by the moderate study size and presence of only two study sites. Even though we aim to evaluate patients early in the disease process using the ED, the precise onset of sepsis cannot be accurately determined due to the heterogeneity of the pathophysiological process.

Conclusion: Our preliminary data suggest suspected septic patients presenting to the ED have an associated coagulopathy (as demonstrated by a decrease in ADAMTS13) together with an initial inflammatory response. Our results provide a rationale to explore the impact of coagulation markers in facilitating earlier and accurate sepsis diagnosis.

Reference: 1. Singer M, Deutschman CS, Seymour C, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA - J Am Med Assoc. (2016), 315(8):801-10.

8 | Thrombin Activatable Fibrinolysis Inhibitor Alters Thrombus Stability and Pulmonary Embolism in a Sex-dependent Manner in Murine Venous Thromboembolism

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Introduction: Venous thromboembolism (VTE) is comprised of deep vein thrombosis (DVT) and subsequent pulmonary embolism (PE) whereby the thrombus embolizes and travels down-stream to occlude pulmonary arteries. Alternative to current anticoagulation therapies that increase bleeding risk is a potential to promote the breakdown of occlusive thrombi to restore blood flow (fibrinolysis). Thrombin-activatable fibrinolysis inhibitor (TAFI) is a major regulator of fibrinolysis and its levels have been positively correlated with the risk of thrombosis. In addition, the role of sex in VTE remains uncertain. Using a mouse model of VTE, the role of TAFI or sex on VTE will be investigated.

Methods: FeCl3-induced thrombi were formed within the femoral veins of male and female wild-type (WT) or TAFI-knockout (Cpb2-/-) mice. Thrombi were tagged with fluorescent CD41-specific antibody fragments then imaged at 10-minute intervals over 2-hours using fluorescent intraval videomicroscopy to quantify thrombus size and embolization events. Emboli were considered large when the fluorescence intensity was greater than 4 standard deviations above the average intensity within the area of interest. Excised lungs were subjected to histological analysis using Carstair’s stain and immunofluorescent staining to identify the quantity and composition of pulmonary emboli (PE) within pulmonary arteries/tissues. In vitro analyses using plasma were completed to elucidate differences in fibrinolytic potential and increased thrombin generation between mice. Nascent plasma isolated from male and female WT mice was used to complete clot lysis assays, whereas plasma isolated from WT and Cpb2-/- mice following the 2-hour VTE experiment was used to determine circulating thrombin-antithrombin complex levels with a murine-specific thrombin-antithrombin complex ELISA.

Results: Compared with WT mice, thrombi in Cpb2-/- mice exhibited 3.2-fold and 1.3-fold greater embolization events for males and females, respectively. When comparing by sex, thrombi in female mice exhibited 7.9-fold and 3.1-fold more than thrombi in male WT and Cpb2-/ mice, respectively. Male Cpb2-/ thrombi displayed a 10.3-fold greater thrombus size increase compared with male WT thrombi, while the opposite was true for female mice (5.8-fold greater in WT). Between WT, females showed a greater thrombus size increase (4.8-fold), while the opposite was true in Cpb2-/- males (12.4-fold). TAFI deficiency led to a 2.2-fold and 2.5-fold increase...
in PE burden in males and females, respectively, while sex had no influence. Quantitation demonstrated that lungs of female Cpb2-/­ mice contained pulmonary emboli with higher fibrin composition compared with WT. Emboli in Cpb2-/­ male mice exhibited a trend of increased fibrin content (1.4-fold) compared with WT, although not significant. Furthermore, clot lysis times remained similar between male and female WT mice using nascent plasma. Similarly, no differences were observed in circulating TAT concentrations between WT and Cpb2-/­ or male and female mice using plasma isolated after imaging.

Conclusion: Overall, Sex affects venous thrombus stability, with female mice showing more unstable thrombi through increased embolization. Furthermore, inhibition of TAFIa may lead to more unstable thrombi and increased risk of PE, particularly in females. These findings can be taken into consideration particularly for developing the most effective personalized VTE treatment strategies.

9  |  Building Together: A Curriculum Proposal for Integrated Stroke Training in a Thrombosis Fellowship

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Background: Stroke and thrombosis specialties share a plethora of content knowledge and clinical application. There are unique challenges in managing secondary prevention and bleeding risk in this context. An integrated rotation fostered a collaborative relationship and reciprocal learning between both thrombosis and stroke specialties. We recently performed an ad hoc survey of several North American adult thrombosis fellowships to determine if integration of stroke teaching into thrombosis programs is standard in other programs. We found that direct integration of training programs is not prevalent. This was highlighted recently in a report of one academic centre’s experience integrating a stroke rotation into a thrombosis fellowship. The integration of stroke teaching into a thrombosis program was found to be positive and mutually enriching by facilitating a shared mechanistic understanding of arterial and venous thrombosis and unique cerebrovascular considerations for infarcted or hemorrhagic tissues. We aim to build on these experiences and propose a structured curriculum for a dedicated stroke rotation in a thrombosis fellowship for pharmacists and physicians.

Methods: A survey of the same adult thrombosis fellowship programs across North America will be conducted to gather an understanding of attitudes, beliefs, barriers, and expectations for the integration of a stroke rotation into a thrombosis fellowship. The programs will be asked to rate on a 5-point Likert scale the importance of several key factors for successful curriculum integration. Using a proposed framework, programs will then be asked to rank the importance of pre-specified curricula for the stroke rotation. Furthermore, fellowship directors and fellows surveyed will have the opportunity to contribute ideas, topics, and resources that they feel will improve the consensus-based proposed framework for an integrated curriculum. Objectives and a curriculum guideline will be developed to further detail an integrated program with a proposed framework for piloting a stroke rotation in thrombosis fellowships (thrombosis pharmacists and physician fellows), to be tested first at Sunnybrook Health Sciences Centre. Key curriculum highlights include acute stroke management, including code stroke team experience, imaging and neuroanatomy, secondary stroke prevention, and ambulatory stroke care.

Discussion: It is the hope that, with perspectives from North American thrombosis programs, and the published local experience, the first iteration of an integrated stroke and thrombosis curriculum can be developed for subsequent thrombosis fellows. Similarly, we hope this inspires neurology programs to explore incorporating thrombosis rotations into stroke fellowships.

Reference:
1. Carlin S, Geerts W, Khosravani H. The clot thickens—enhanced integration of stroke and thrombosis training. J Thromb Thrombolysis. 2021 Jul 7. 10.1007/s11239-021-02502-7. Online ahead of print.
Background: Soft tissue injury, immobilization, and hypercoagulability place orthopaedic surgery patients at high-risk for venous thromboembolism (VTE). If these patients have cancer that has spread to bone (metastatic bone disease, MBD), VTE-risk is increased 7-fold compared to non-cancer patients undergoing the same procedure, as malignancy and adjuvant therapies (i.e., chemotherapy and radiation) induce a hypercoagulable state (Blom et al., JAMA 2005). Extent and duration of post-operative hypercoagulability in MBD patients remains unknown and clinical guidelines for thromboprophylaxis to prevent VTE were developed for non-cancer patients, limiting applicability to MBD patients.

Results: Twenty-one participants (10 female, 47.6%) with a mean age of 70 years (SD ± 12) were enrolled. Participants remained hypercoagulable (MA > 65 mm) for 6-weeks post-operatively. VTE occurred in 5 patients (23.8%), and at diagnosis, mean MA was 68.1 mm (SD ± 4.6). Mean pre-operative MA values were significantly higher (p = 0.02) in patients who experienced VTE (68.9 mm, SD ± 3.5) versus those who did not (62.7 mm, SD ± 6.5). The first week post-operatively marked the highest-risk period for VTE complications, during which 4 VTE events (80%) occurred. Within this timeframe, paired t-tests (n = 21) of mean post-operative MA on day 3 (66.7 mm, SD ± 4.0) and 5 (67.7 mm, SD ± 5.9) were significantly increased (p = 0.003 and p = 0.007, respectively) compared to pre-operatively (63.8 mm, SD ± 6.4).

Conclusion: Current thromboprophylaxis guidelines use a population-based approach to prescription, without considering individual risk factors associated with elevated VTE-risk (i.e., type and extent of malignancy; chemotherapy or radiation treatment). Subtherapeutic dosage and early termination of thromboprophylaxis while the patient remains hypercoagulable and at high VTE-risk are potential outcomes. Standard practice recommends thromboprophylaxis (i.e., low molecular weight heparin) for 4-weeks post-operatively, however, mean post-operative MA values indicate that patients remained hypercoagulable at 6-weeks post-operatively, after thromboprophylaxis discontinuation. This suggests that current thromboprophylaxis dosage and duration may be inadequate to address prolonged hypercoagulability in patients with MBD. Therefore, VTE may be prevented more effectively in this population by adjusting dosage concomitantly with increased VTE-risk during the first week post-operatively and extending duration beyond 4 weeks.
12 | A Quality Assurance Protocol to Prevent Thrombotic Disease in Hospitalized COVID-19 Patients

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Background: Patients admitted to hospital with COVID-19 are at increased risk of developing venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE). At the start of the pandemic, high VTE rates of 15–20% were reported in hospitalized COVID-19 patients in China and Europe. Importantly, these events occurred despite use of standard anticoagulation prophylaxis. Based on this increased rate of VTE, an intermediate weight-based dose anticoagulation prophylaxis protocol was implemented at The Ottawa Hospital (TOH) in April 2020 for hospitalized COVID-19 patients.

Purpose: The main objective of this study is to determine the efficacy and safety of this new protocol.

Methods: A retrospective chart review was conducted of all COVID-19 patients admitted to TOH between April 2020 and January 2021. Data collected included patient demographics, clinical data, thromboprophylaxis received, and outcomes. The primary outcome measure was the rate of VTE (DVT/PE) up to 90 days post-discharge and confirmed on imaging. The safety outcome was the rate of major bleeding up to 90 days post-discharge according to the ISTH major bleeding criteria which consists of fatal bleeding, or bleeding in a critical area, or bleeding causing a fall in hemoglobin level of 20 g L−1.

Results: We identified 329 patients hospitalized with COVID-19 at TOH during the study period. In this study population, the mean age was 67 years, 52.6% were male, the average length of stay was 22 days and 23.1% of patients were admitted to the Intensive Care Unit. Of hospitalized COVID-19 patients, 264 received thromboprophylaxis: 14.8% received therapeutic doses (N = 39), 37.5% received intermediate doses (N = 99), and 47.7% received standard dose (N = 126). In the patients that received intermediate dose anticoagulation, VTE events occurred in 7 patients and major bleeding events occurred in 6 patients.

Conclusion: The current study showed much lower rates of symptomatic VTE among hospitalized COVID-19 patients of approximately 7%. An intermediate weight-based thromboprophylaxis strategy in hospitalized COVID-19 patients was effective and safe.

13 | Platelet-mediated Hypercoagulability Following Hip Fracture Surgery

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Introduction: Thrombelastography (TEG) is a point-of-care tool that can measure clot formation and breakdown using a whole blood sample. We have previously used serial TEG analysis to define hypercoagulability and increased venous thromboembolism (VTE) risk following a major fracture requiring surgical treatment (Gary, Schneider et al. J Orthop Trauma 2016). Additionally, we have used serial TEG analysis to quantify the prolonged hypercoagulable state and increased VTE risk that ensues following a hip fracture (You, Skeith, Korley, Schneider. Can J Surg 2021). Recently developed cartridge-based platelet mapping (PLM) using TEG analysis can be used to activate platelets at either the adenosine diphosphate (ADP) receptor or at the Thromboxane A2 (AA) receptor, in order to evaluate clot strength when platelets are activated only through those specific receptors. This study aimed to validate platelet contribution to hypercoagulability, in order to identify potential therapeutic targets for VTE prevention. We hypothesized that there would be a platelet-predominant contribution to hypercoagulability following a hip fracture.

Methods: Patients aged 50 years or older with an operative hip fracture were enrolled in this prospective cohort study. Exclusion criteria were: prior history of VTE, active malignancy, or pre-injury therapeutic dose anticoagulation. Serial TEG and PLM analyses were performed at admission, post-operative day (POD) 1, 3, 5, 7 and at 2-, 4-, 6- and 12-weeks post-operatively. All patients received thromboprophylaxis with low molecular weight heparin (LMWH) for 28 days post-operatively. Hypercoagulability was defined as maximal amplitude (MA; a measure of clot strength) over 65mm based on TEG analysis. Independent samples t-tests were used to compare MA values with this previously established threshold (Gary, Schneider et al. J Orthop Trauma 2016: 30:294–8; You, Skeith, Korley, Schneider. Can J Surg 2021: 64(3):E324–29). Patients who received arthroplasty were compared with those who underwent fracture fixation.

Results: Twenty-one patients were included, with a mean age of 72.7 (SD = 13.2) years and 52.3% (n = 11) being female. Eleven patients (52.3%) were treated with arthroplasty, while the remainder underwent surgical fixation of their hip fractures. TEG analysis demonstrated hypercoagulability (mean MA over 65mm) at all follow-up timepoints until 12-weeks. PLM identified a platelet-mediated hypercoagulable state based on elevated ADP-MA and AA-MA, with more pronounced platelet contribution demonstrated by the AA pathway. Patients treated with arthroplasty had significantly increased AA-MA compared with ADP-MA at POD 3 and at the 12-week follow-up.

Discussion: Serial TEG analysis can be used to identify hypercoagulability and increased VTE risk following surgical treatment for a hip fracture. PLM analysis suggests a platelet-mediated hypercoagulable state that may benefit from an anti-platelet agent that targets the AA platelet activation pathway, such as Aspirin. This research also supports differences in hypercoagulability between patients treated with arthroplasty compared to those who undergo fracture fixation.

Significance/Clinical Relevance: This study supports further investigation into the safety and efficacy of anti-platelet use following hip fracture surgery. If oral thromboprophylaxis using an inexpensive and widely available anti-platelet agent, such as Aspirin is found, this could improve the ease and cost associated with post-hip fracture thromboprophylaxis.
ABSTRACT

14 | Safety and Pharmacokinetics of Direct Oral Anticoagulants after Bariatric Surgery: A Systematic Review

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Background: Direct oral anticoagulants (DOACs) are highly effective to prevent and treat thromboembolism. Bariatric surgery likely impairs the absorption of DOACs, thereby making the optimal use of DOACs after bariatric surgery unclear.

Objective: To evaluate the efficacy and safety of DOACs after bariatric surgery in adults.

Methods: We systematically searched MEDLINE, EMBASE, Cochrane Library, CINAHL and ClinicalTrials.gov from January 1, 2000 to June 15, 2021 for randomized and non-randomized studies evaluating the use of DOACs after bariatric surgery. Two reviewers independently screened titles, abstracts and full-text articles. Clinical and pharmacokinetic outcomes were pooled by random-effects meta-analysis with inverse variance weighting. We used the Newcastle-Ottawa scale to assess risk of bias in non-randomized studies excluding case reports. We assessed certainty of the evidence with GRADE. PROSPERO registration: CRD42020202636.

Results: From 2,519 records identified, we included 27 studies (n = 3,234 patients): no randomized trials, 7 cohort studies, 6 case series, and 14 case reports. Incidence rates for arterial thromboembolism, venous thromboembolism and major bleeding were: 0.87 (95% confidence interval [CI] 0.01–5.34), 2.48 (95% CI 0.40–7.96), and 4.47 (95% CI 1.33–10.9) events per 100 patient-years, respectively. The pooled proportion of peak DOAC drug levels within the expected range was 58% (95% CI 39–74%). The certainty of evidence was very low for all outcomes due to high risk of bias.

Conclusion: There appears to be substantial risk of DOAC malabsorption after bariatric surgery that could importantly affect clinical outcomes and net benefit. Additional cohort and registry studies are warranted given how frequently such patients require anticoagulant therapy.