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Delayed Presentation of Patients with Acute Long Bone Fractures, Pelvic and Spinal Fractures in a Tertiary Hospital-Incidence of Deep Venous Thrombosis

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Abstract

Introduction: Venous Thromboembolism (VTE) can result in significant morbidity and mortality. Data indicate no significant change to the overall incidence and mortality from VTE. Incidence of Deep Venous Thrombosis (DVT) varies, it is as high as 80% in patients sustaining lower extremity trauma where prophylaxis is not used. All patients with delayed (>24 hours) presentation of an acute hip or femur fracture undergo preoperative Doppler ultrasound to rule out DVT. Preoperative DVT is shown to occur in as high as 9% to 62% of patients receiving prophylaxis. Despite all the attention given to preventing VTE in hospitalized trauma patients, still there are no strong evidence-based recommendations to guide the treating surgeon. The purpose of the present study was to establish the incidence of DVT in patients with delayed presentation after sustains long bone, pelvic and spine fractures.

Methods: A prospective observational study was performed over an 18-month period between November 2019 to May 2021. Data collected from patient's hospital records. A chi square test with 4 degrees of freedom with a medium effect 0.30, an error probability α=0.10, and a power of 1-β=0.80, a sample size of 108 was required.

Results: A total of 90 patients were identified. Included in the study were 39 patients on whom Doppler studies were done, of these 22 were females (54%) and 17 were males (46%). Mean age of 76 years (30-90 yrs.). Low energy falls accounted for 30/39 (76.9%) with neck of femur fractures being the most common type at 25/39 (64.1%) followed by intertrochanteric fracture 8 (20.5%), One of the intertrochanteric fractures was a high energy fracture 1/39 (2.6%) and the other high energy fractures included the tibia fractures 4/39 (10.2%). None of these patients had a previous history of DVT. There were 4 patients (9.7%) diagnosed positive with a thrombus of which 2/4 (50%) were pre-operative DVT. Of the 4 positives with thrombus, 3/4 (75%) was in female patients, 1/4 (25%) was in a male patient. Mortality in this study was 2/39 (5.1%).

Conclusion: The incidence of deep venous thrombosis was identified as 10.6% in our population study group. Routine ultrasound screening in patients with delayed presentation to exclude deep venous thrombosis in asymptomatic patients may be deemed necessary.

Keywords: Orthopedics • Venous thromboembolism • Deep venous thrombosis • Trauma

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Introduction

Venous Thromboembolism (VTE) can result in significant morbidity and mortality. Despite identification by healthcare initiatives as a preventable clinical event, data indicate that neither increased awareness nor more recent prophylactic regimens have resulted in a significant change to the overall incidence and mortality from VTE [1]. The reported incidence of DVT varies with method of detection, mode of prophylaxis, location of thrombus, and sample size, thus resulting in a wide range of numbers in the literature.

All patients with delayed (>24 hours) presentation of an acute hip or femur fracture should undergo pre-operative Doppler ultrasound to rule out DVT. The incidence of DVT is reported to be as high as 80%in patients sustaining lower extremity trauma where prophylaxis is not used. On the other hand, use of thromboembolic prophylaxis does not prevent formation of DVT completely, and pre-operative DVT is shown to occur in as high as 9% to 62% of patients receiving prophylaxis [2].

Despite all the attention given to preventing VTE in hospitalized trauma patients, there is little in the way of strong evidence-based recommendations to guide the treating orthopaedic surgeon.

What we were observing is that patients with long bone fractures, pelvic injuries and spine injuries that were being referred to our facility, presented after 48 hours of the injury and we also saw patients that referred themselves from other provinces with these types of injuries, most unfortunately there was never adequate documentation to say if chemical prophylaxis was ever initiated [3-7]. On arrival all patients are evaluated by the treating surgeon for signs of deep venous thrombosis and dehydration.

The lower extremities are evaluated for signs of deep venous thrombosis and pain with sudden ankle dorsiflexion. All patients are started immediately on low molecular weight heparin, as per the ACCP clinical practice guideline (8th Edition).

At least 2 cases of deaths were reported in the past year of patients who demised intra-operatively as a complication of pulmonary embolism who were initially seen at referring centers and transferred to our center [8].

There were also reports of elderly patients complicating in the wards with delirium of unknown origin or secondary to pulmonary embolism after presenting to our center more than 48 hours after the injury. This prompted the undertaking of the study.

In this study we conducted duplex Doppler's on patients referred to our center, Steve Biko Academic Hospital more than 48 hours post injury to detect the presence of deep venous thrombosis [9-12].

This was conducted over a period of 18 months, to evaluate the incidence of deep venous thrombosis in orthopaedic trauma population with delayed presentation to the treating tertiary center.

The purpose of the present study was to establish the preoperative prevalence of DVT in patients who had a fracture, and to determine what factors might have influenced this prevalence.

Specifically, we examined the correlation between the delays in admission from the time of injury to the development of DVT.

Materials and Methods

The study was conducted at the Department of Orthopedics in Steve Biko Academic Hospital, level 7, room 71314 and department of Vascular in Steve Biko Academic Hospital, level 8, room 821138. Patients enrolled in the study had their ultrasound Doppler done in level 8 by the vascular technician; patients were wheeled to the vascular department for the Doppler to be done. The machine used is a Toshiba Xario ultrasound system (Toshiba American Medical Systems Inc, 2441 Michelle Dr. P.O. Box 2068, Tustin CA 92780-7047). Blood smear were prepared and stained with Giemza stain to identify Batonella spp. within erythrocytes as well as to study the morphological changes which is occur in RBC. The entire blood smear examined for blood protozoa and appears negative for that.

Patient/research object selection

The population included all patients (long bone fracture, pelvic and spinal fracture) admitted at the Orthopedics trauma services at Steve Biko Academic Hospital from referring centers as they were being admitted, hospital records were used. For the purpose of this study, only patients who presented after 48 hours of sustaining their injuries were included. The instrument that was utilized to evaluate the presence of a DVT or absence thereof was a Toshiba Xario Ultrasound system in association with an angiogram, to this point we had no protocol on how to manage these patients as we had not seen any complications relating to this subset of patients. We included the patients for the period November 2019 to May 2021.

Inclusion criteria

- All skeletally mature patients
- Pelvic fractures
- Long bone fractures
- Spine injured patients
- Injury more than 48 hours
- Patients with Doppler's done within 7 days of admission at treating hospital

Exclusion criteria

- All skeletally immature
- Upper limb fractures isolated
- All pregnant patients
- Patient known with thrombo-embolic disease on treatment

The outcome of interest was incidence of deep venous thrombosis in this subset of patients group and to aid in protocol development for treatment of this patient group. The data collected included:

- Age and gender
- The date of the injury
- Date of admission at referring center and our hospital
- Time interval from injury to referral
- Findings of duplex Doppler
- Any interventions after Doppler
- Patient outcome

Statistical analysis

A power analysis using G* Power version 3.1.9.2 indicated that in order to perform a chi square test with 4 degrees of freedom with a medium effect size of 0.30, an error probability α=0.10, and a power of 1-β=0.80, a sample size of 108 is required.

In the case of categorical variables frequencies and cross tabulations will be computed, while inferential statistical techniques such as Pearson's chi square or Fisher's exact tests will be performed to test for associations between the location of the DVT and the type of injury, or between the location of the injury and whether vascular intervention will be necessary before surgery.

For continuous variables such as the time span in days between the date of the incident and the date of admission at the treating center, descriptive statistics such as means and standard deviations was computed.

Correlation coefficients will be computed between the time spans from the dates of the incident, admission at referring center, admission at the treating center and doing the Doppler ultrasound test. Data was captured in Excel and statistical analyses were performed in SAS 9.4 or IBM SPSS Statistics version 24 at the 5% confidence level.

Results

A total of 90 patients formed the basis of the study. 51 (56.6%) were excluded and these are patients on whom duplex Doppler was not done within the 7 days of admission, 39 (42.4%) were included in the study. None of these patients had a previous history of DVT.

The patients were 22 females (54%) and 17 males (46%) with a mean age of 76 years (30-90 years). Low energy falls accounted for 30/39 (76.9%) with neck of femur fractures being a common fracture type accounting for 25/39 (64.1%) followed by intertrochanteric fracture 8 (20.5%), One of the intertrochanteric fractures was a high energy fracture 1/39 (2.6%) and the other high energy fractures included the tibia fractures 4/39 (10.2%). There were four (10.2%) patients with a positive Doppler ultrasound for a thrombus. The thrombus developed in 3/4 (75%) in female patients, 1/4 (25%) in male patients. Of these, pre-operative DVT was detected in 2/4 patients (50%). And post-operative DVT occurred in 2/4 (50%).

Time of injury to presentation was a mean of 11 days with a range of 99 days and time of injury to Doppler ultrasound had a mean of 22 days with a range of 164 days. Reason for late presentation is varied, large proportion the reason was unknown reason 27/39 (69.2%), injured outside province 5/39 (12.8%), transfer from private hospitals due to depleted medical aid funds 4/39 (10.2%) and from other referring centers 3/39 (7.6%). We had a mortality of 2 patients in this study (5.1%) (Table 1).

	Thrombosis	Non-thrombosis	Overall
Number	4	35	39
Age	01 76	11 68	
Gender			
Female	3	19	22
Male	1	16	17
Fractures			
Neck of femur	2	23	25
Trochanteric	1	8	9
Tibia	1	3	4
Vertebral	0	1	1
Investigation			
Doppler	4	35	39
Ct-PA	1	3	4
Pulmonary embolism			
Yes	1	2	3
No			

Table 1. Thrombosis and non-thrombosis of patients.

Discussion

There are many studies regarding the incidence and treatment of postoperative thromboembolism related to major orthopaedic surgeries. The current study focused on the pre-operative development of DVT due to its strict inclusion criteria of Doppler ultrasound within 7 days of admission [13]. We took an interest in pre-operative DVT that develops in delayed presentation of long bone fractures, pelvis and spine, since this is caused due to time delay before surgery. Little is known regarding DVT before fracture onset in the general population. We assumed that DVT develops after injury, not before a fall or fracture and the main contributory factor in our assumption is immobility.

Deep venous thrombosis complicated with pulmonary embolism is third commonest cause of death in an orthopedic trauma patient [14-17]. Early thrombo-prophylaxis has shown to reduce the incidence to up to 50% in patients at high risk. Patients with lower extremity fractures are known to be at high risk of developing Deep Venous Thrombosis (DVT).

There have been many reported risk factors for VTE and recurrent VTE. According to SIGN (2010):

- Risk factors for VTE include age, obesity, varicose veins, family history of VTE, thrombophilia's, combined oral contraceptives, hormone replacement therapy, anti-oestrogens, pregnancy, puerperium, immobility, immobility during travel, hospitalization, anaesthesia and central venous catheters.
- Risk factors for recurrent VTE include previous unprovoked VTE, male gender, obesity and thrombophilias. Practically every patient admitted to a hospital has at least one of the above risk factors.
- Strong risk factors for VTE include a fracture of the hip or leg, hip or knee replacement, major general surgery, major trauma and Spinal Cord Injury (SCI).
- Moderate risk factors include arthroscopic knee surgery, central venous catheters, chemotherapy, congestive heart or respiratory failure, hormone replacement therapy, malignancy, oral contraceptive therapy, paralytic stroke, pregnancy/postpartum, previous VTE and thrombophilia.

- Weak risk factors include bed rest >3 days, immobilization and bedridden, increasing age, laparoscopic surgery, obesity, pregnancy/antepartum and varicose veins. Risk factors for VTE are cumulative.

Factors that are independent predictors of VTE in trauma patients include following: spinal cord injury, lower extremity or pelvic fractures, need for a surgical procedure, insertion of a femoral venous line or repair of a major vein, increasing age, prolonged immobility and delayed in commencement of thrombo-prophylaxis.

Any delay in surgical treatment for a hip fracture can be caused by numerous factors, which range from the time required to stabilize a patient's medical condition to the availability of operating rooms [18]. Regardless of the cause, surgical delay increases the pre-operative immobilization, which is one of the most important factors in the development of DVT. It has been recommended that thromboprophylaxis with low-molecular-weight heparin or low-dose unfractionated heparin be initiated during the time between hospital admission and surgery.

Venous Thromboembolism (VTE) can result in significant morbidity and mortality. Despite identification by healthcare initiatives as a preventable clinical event, data indicate that neither increased awareness nor more recent prophylactic regimens have resulted in a significant change to the overall incidence and mortality from VTE.

Venous thromboembolic events comprise Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) and represent a significant cause of death, disability and discomfort after trauma-associated hospitalization. While DVT may present clinically silent, PE is the third most common cause of death in patients that survive the first 24 hours after trauma.

Proximal DVTs, occurring in the deep femoral and pelvic veins, pose the greatest risk for embolisation to the lungs, which is one of the most feared short-term risks [19-22]. After a DVT in the thigh, pelvis or inferior vena cava, each representing a proximal DVT, the rate of patients undergoing PE ranges between 27% and 60%. The risk of thromboembolism is assessed to be much lower in distal clots. In patients presenting with an acute symptomatic PE, the incidences of a distal (distal to the popliteal vein) or proximal (iliac, femoral, popliteal) clot are approximately 20 and 50%, respectively.

Virchow's triad of venous stasis, endothelial injury, and hypercoagulability is traditionally considered the harbinger of thrombus formation. Major trauma is believed to lead to one, if not all three, risk factors [23-26]. Specific risk factors, including but not limited to spinal cord injury, pelvic fractures, lower extremity fractures, high injury severity, and longer ventilation times, place these patients at increased risk for symptomatic VTE.

Recent studies have explored the effects of circulating procoagulant and thrombogenic microparticles, as well as a decrease in antithrombin III levels, on thrombus formation in an effort to better understand the pathophysiology behind clot formation and embolization. Basic science investigators will continue to explore the potential modifiable factors involved in both *in vitro* and *in vivo* clot formation.

In an orthopaedic patient undergoing an operation, all of the above pathophysiologic processes included in Virchow's triad are present:

- Use of tourniquet, immobilization and bed rest cause venous blood stasis
- Surgical manipulations of the limb cause endothelial vascular injuries
- Trauma increases thromboplastin agents
- Use of Polymethylmethacrylate (PMMA) bone cements increase hypercoagulability. Therefore, in patients undergoing orthopedic surgery and those with orthopedic trauma, VTE prophylaxis and adherence to the respective guidelines is paramount.

A risk stratification of the risk for VTE in surgical patients without prophylaxis classifies orthopedic patients at the highest risk. The ACCP (2008) classified in-hospital patients without VTE prophylaxis in three categories (low, moderate and high risk).

- In the first category, patients who are fully mobile and those who are mobile and undergoing minor surgery are classified as having <10% risk.
- In the second category, most general surgery patients, open gynecologic or urologic surgery patients, and medical patients who are bedridden or sick are classified as having a 10% to 40% risk.
- In the third category, the average orthopedic patients who have undergone hip or knee arthroplasty or sustained a hip fracture, major trauma or SCI are included.

Randomized clinical trials have concluded that the rates of venographic documented DVT and proximal DVT 7 to 14 days after major orthopedic surgery in patients who did not receive any VTE prophylaxis are approximately 40% to 60% and 10% to 30%, respectively. After discharge from hospital, these orthopedic patients are still at risk for VTE. Hypercoagulability can persist for six weeks after a hip fracture, while venous function remains significantly impaired for up to 42 days following hip fracture surgery.

If a DVT is suspected, multiple imaging modalities are available for detection. While venography is the gold standard, color duplex ultrasonography is more widely used clinically, as it is easy to use, less invasive, is relatively inexpensive and has a high sensitivity and specificity.

Magnetic resonance phlebography and computed tomography phlebography are also available but used only infrequently. While d-dimer levels are useful in medical patients, the interpretation of elevated d-dimer levels in patients following surgery has unclear significance.

Current guidelines for venous thromboembolism prophylaxis in orthopedics source guidelines orthopedic trauma association

Major orthopedic surgery

- LMWH is considered the agent of choice and should be initiated within 24 hours provided there are no contraindications.
- Combined LMWH and calf pneumatic compressive devices over either regimen alone.
- Continuation of VTE prophylaxis for at least 1 month after discharge.
- Recommend against routine screening protocols for DVT in asymptomatic trauma patients.

Isolated lower extremity injury

- Do not recommend routine chemical prophylaxis in patients who do not have additional risk factors and are independently mobile.
- Recommend against routine screening protocols for DVT in asymptomatic trauma patients American College of Chest Physicians.

Major orthopedic surgery

- Extend outpatient prophylaxis for up to 35 d postop
- Dual prophylaxis with pharmacologic agent and IPCD while inpatient
- Recommend against screening Doppler ultrasonography before discharge Hip fracture surgery
- Prophylaxis for a minimum of 10-14 d
- Start LMWH either 12 h or more pre-operative or 12 h or more post-operative
- Recommend use of LMWH, fondaparinux, LDUH, adjusted-dose aspirin or Intermittent Pneumatic Compression Devices
- LMWH is preferred to other agents Isolated lower extremity injury
- No prophylaxis in patients who require leg immobilization American Academy of Orthopedic Surgeons.

Elective total joint arthroplasty

- Pharmacologic agents and/or mechanical compressive devices for VTE prevention for those who are not at elevated risk
- No specific agent recommended
- Patients and physicians discuss duration of treatment
- Recommend against routine duplex ultrasonography screening postoperatively Eastern Association for the Surgery of Trauma
- LDH has little proven efficacy in prevention of VTE as sole agent in high-risk trauma patients
- IPCD may have some benefit in isolated studies
- LMWH can be used in trauma patients with pelvic fractures, complex lower extremity fractures, and spinal cord injury when bleeding risk is acceptable
- Inferior vena cava filter should be considered in very high-risk trauma patients who cannot receive pharmacologic prophylaxis or have an injury pattern that would leave them immobilized for long periods of time
- Duplex ultrasonography may be used to diagnose symptomatic patients with suspected DVT without venography

Cochrane review

- No evidence that prophylaxis reduces mortality or secondary outcome of pulmonary embolus
- Pharmacologic prophylaxis is more effective than mechanical prophylaxis
- LMWH is more effective than UH
- Insufficient studies for comparison between pharmacologic agents are *vs.* Placebo or pharmacologic prophylaxis *vs.* mechanical prophylaxis.

In this study, ultrasonography was used to diagnose DVT. We chose ultrasonography based on its high accuracy and widespread acceptance. Ultrasonography is a simple, robust and non-invasive diagnostic tool and serves as a first choice in the diagnostic workup of DVT in lower extremities.

Although the sensitivity and specificity of venography and magnetic resonance imaging are within the range of ultrasonography, they may serve as an alternative or complementary imaging tool to ultrasonography.

The incidence rate is 10.2% in our population group, and pre-operative DVT is shown to occur in as high as 9% to 62% of patients receiving prophylaxis as stated in the literature. The incidence of DVT is reported to be as high as 80% in patients sustaining lower extremity trauma where prophylaxis is not used. Without any prophylaxis, Pulmonary Embolism (PE) is responsible for 5% to 10% of deaths in hospitalized patients. On the other hand, use of thromboembolic prophylaxis does not prevent formation of DVT completely, and preoperative DVT is shown to occur in as high as 9% to 62% of patients receiving prophylaxis.

The incidence of fatal PE in hospitalized patients is 0.1% to 0.8% after elective general surgery, 2% to 3% after elective hip replacement and 4% to 7% after hip fracture surgery. Our patient population averaged 69 years the 35 (89.7%) out of 39 patients had fragility fracture and time from injuries to presentations were independent factors for developing deep venous thrombosis as concluded by their study.

152 Korean geriatric patients who had suffered hip fractures hospitalized between January 2013 and December 2013. Their overall incidence of DVT was 2.6% (4/152). The mean time to arrival at emergency room after injury was 32.6 hours. The average time to hospitalization after injury was 237 hours for patients with DVT versus 27.5 hours for patients without DVT. DVT developed within 72 hours in two of the 137 patients (1.4%) and after 72 hours in two of the remaining 15 patients (13.3%) hospitalized. They confirmed that getting no treatment within 72 hours after injury increased the incidence of DVT [27]. Thus, we conclude from this study that a workup for DVT should be considered in cases where admission or surgery has been delayed for more than 72 hours after injury.

In a retrospective observational study found an incidence rates of preoperative and postoperative DVT were 32% and 56%, respectively. DVT on the uninjured side constituted 45% of all preoperative DVT and 43% of all postoperative DVT. Peripheral DVT constituted 90% and 84% of all preoperative and postoperative DVT, respectively. The incidence rates of preoperative and postoperative DVT in the patients with femoral neck fracture were high, and orthopedic surgeons should pay more attention to DVT as a complication.

The four-thrombosis identified in our study were: Popliteal vein, common femoral vein and two iliofemoral thrombosis. We had a mortality of 2 patients (5.1%) which was a bimodal, one elderly patient with a neck of femur fracture and a young patient who was a polytrauma patient. The incidence of fatal PE in hospitalized patients is 0.1% to 0.8% after elective general surgery, 2% to 3% after elective hip replacement and 4% to 7% after hip fracture surgery. The information on the frequency of VTEs among hospitalized patients after trauma varies widely, ranging from less than 1% up to 58% depending upon the demographics of the study population, the nature of the injuries and other factors.

The limitations of the study, firstly we had a short fall of patients due to the COVID 19 pandemic from end of March 2021 till May 2021 with the stringent COVID 19 protocols.

Secondly low percentage of Doppler's done which skews the accuracy our incidence. Another cause was patients with clinical symptomatic deep venous thrombosis were taken for further imaging without Doppler [28]. The diagnostic value of DUS for DVT is still controversial, but it is still the most widely used method in clinical practice. Venography was not used, which might also lead to under diagnosis. Another limitation was that the intrapelvic veins were not evaluated. Ultrasounds were done on the injured limb and the in uninjured limb was not investigated.

Conclusion

The incidence of deep venous thrombosis was identified as 10.2% in our population study group. Routine ultrasound screening in patients with delayed presentation to exclude deep venous thrombosis can aid in identification of deep venous thrombosis especially in asymptomatic patients. More studies with larger sample size are needed.

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