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Original Article

Mechanical thromboprophylaxis for hip fractures in elderly patients: a prospective randomized controlled study

Dhirendra Kumar[1], Abhay Elhence[1], Rajesh K Rajnish[1], Nitesh Gahlot[1], Sandeep K Yadav[1], Saurabh Gupta[1], Kishor Kunal[1], Phuspindra Khera[2]

[1]Department of Orthopaedics, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India; [2]Department of Diagnostic and Interventional Radiology, AIIMS, Jodhpur, India

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Abstract: Background: Hip fractures, most common in the geriatric age group, can develop proximal deep vein thrombosis (DVT). There is no consensus regarding the ideal method or duration of prophylaxis, particularly in a trauma patient. This study bridges this lacuna in data by making a random comparison between mechanical prophylaxis alone vis-a-vis combined with mechanical and Enoxaparin-based chemoprophylaxis. Materials and methods: 75 Elderly hip trauma patients from January 2019 to October 2020 at a single tertiary care center were randomly allocated into two groups using the sequentially numbered opaque sealed envelope method (SNOSE): one (n=44) receiving Enoxaparin and Mechanical prophylaxis and another (n=31) receiving Mechanical prophylaxis alone. All patients underwent CT (computed tomography) venography to screen for proximal DVT between days 5 to 10 of injury. The primary outcomes were the incidence of proximal DVT and pulmonary embolism (PE), and safety outcomes (wound complications and adverse systemic events) were recorded during the treatment. Results: No symptomatic or asymptomatic proximal DVT and death incidence was reported in either group. One case of pulmonary embolism was seen in the combined prophylaxis group. There was no significant difference between the groups regarding the above-mentioned parameters mentioned. Conclusions: There is no significant difference in the incidence of proximal DVT between mechanical alone and combined chemical-mechanical prophylaxis in elderly patients sustaining hip trauma. The incidence of proximal DVT can be reduced by mechanical prophylaxis alone. It was efficacious and safer than combined mechanical and enoxaparin prophylaxis in preventing venous thromboembolism in elderly hip trauma patients.

Keywords: Hip trauma, elderly fracture, deep vein thrombosis, thromboprophylaxis, mechanical prophylaxis, enoxaparin

Introduction

Hip fractures are most common in the geriatric age group [1]. The combination of aging, lower extremity trauma, hospitalization, immobilization, and orthopedic surgery puts hip fracture patients at risk of developing DVT [2]. Hip fractures are more liable to develop a thrombus in the pelvic veins, which may be due to direct injury to the pelvic vein or from a surgical procedure, thermal damage during cement polymerization, compression from the hematoma, and long-term immobilization [3]. The pathogenesis of DVT in trauma patients begins at the time of injury, and thrombin production starts within 24 hours of trauma and reaches to peak level in about two weeks [4].

Along with the increase in-thrombin level, there is a decrease in the level of antithrombin III due to the release of tissue factors from the injured tissue [4, 5]. This imbalance in coagulation factors in trauma patients makes the entire milieu hypercoagulable. This hypercoagulable state leads to thrombus formation at distant sites from the injury [4-6]. Venous thromboembolism (VTE) is the third most common cause of death among patients who survive the first 24 hours and the most common cause of death after a week of traumatic injury [7, 8].

Moreover, proximal DVT is associated with a greater risk of pulmonary emboli than distal DVT, which does not often result in embolization and may resolve spontaneously [9, 10]. The

Figure 1. An intermittent pneumatic compression device used in our study to provide mechanical prophylaxis against DVT. DVT, deep vein thrombosis.

embolic risk of proximal venous thrombi varies from 35% to 50%, whereas distal venous thrombi are 0% to 13% [11, 12]. Incidence of VTE and proximal DVT following hip fracture is reported to be between 42 to 50% and 2.6% to 30%, depending on the injury, mode of screening, the timing of screening, prophylactic use, and population studied [3, 13-21].

Despite the risk of DVT being considerably associated with hip fractures, thromboprophylaxis among trauma patients is still not universally practiced in India. This could be a lack of vigilance, underestimation of the problem, or complication of chemoprophylaxis [22, 23]. Given the morbidity and mortality of thromboembolism due to DVT in elderly patients with trauma, interest in DVT prophylaxis has grown over the years. The primary purpose of this study was to compare the incidence of VTE after hip trauma in elderly patients receiving mechanical only or combined mechanical and enoxaparin prophylaxis and the complications associated with prophylaxis.

Materials and methods

A prospective randomized controlled study was conducted at a tertiary care hospital. The Institutional Ethical Committee approved the study (*No. AIIMS/IEC/2018/156 dated 31/12/2018*) and informed written consent was obtained from all the patients before the start of the study.

Patients aged ≥ 55 years of either gender with hip fractures (pelvis and acetabular fractures, femoral head fractures, neck femur fractures, intertrochanteric fractures, and subtrochanteric fractures) admitted to orthopaedics emergency that presented within 72 hours of injury between 1st January 2019 and 30th October 2020 was included. All the patients were initially stabilized in accordance with ATLS protocol. Patients presented 72 hours post-injury, with active bleeding, renal insufficiency, active hepatobiliary diseases, allergic to the dye used, pregnant females, a history of a thromboembolic event, coagulation disorder, and having severe intra-cranial or spinal cord injury were excluded from the study.

All the patients were randomized into two groups (group M and group ME) using the SNOSE. Group M patients received only mechanical prophylaxis; group ME received mechanical and chemoprophylaxis with enoxaparin. Mechanical prophylaxis in group-M patients was given with an intermittent pneumatic compressive device (IPCD) over both legs using the Arjohuntleigh Flowtron Universal TM mechanical compression system. An inflation pressure of 40 mm of Hg over both calves with an inflation hold of 12.5 seconds and an inflation cycle of 60 seconds was used. IPCD was applied throughout the day and was removed during physiotherapy and nursing care (**Figure 1**).

Group ME patients were administered 40 mg of injection enoxaparin subcutaneously once a day and mechanical prophylaxis using IPCD on both legs. Injection enoxaparin was withheld the night before surgical intervention and resumed twelve hours postoperatively in patients who underwent surgery.

All the patients were clinically examined daily for DVT and pulmonary embolism's clinical signs and symptoms. Thromboprophylaxis continued throughout their hospital stay in both groups, and they were encouraged to mobilize uninjured limbs and joints while in bed. Computed tomography venography (CTV) of the bilateral lower limb was performed using Siemens SomatomTM definition flash dual source dual energy 2 × 128 slice CT scanner between the 5th to 10th-day post-injury because of the post trauma during this period and thrombus generation that occurs [3, 24]. CTV was acquired as contrast-enhanced CT at a 90-sec delay after intravenous injection of 90

Table 1. Demography of patients included in the study

	Group		Total
	M	ME	
Total	31	44	75
Mean Age	71.6±10.5	72.1±10.3	71.91±10.3
Male	21 (67.7%)	22 (50%)	43 (57.3%)
Female	10 (32.3%)	22 (50%)	32 (42.7%)
Injury			
Acetabulum fracture	3 (9.7%)	3 (6.8%)	6 (8%)
Neck of femur fracture	3 (9.7%)	16 (36.4%)	19 (25.3%)
Inter trochanteric fracture	22 (71%)	23 (52.3%)	45 (60%)
Sub trochanteric fracture	3 (9.7%)	2 (4.6%)	5 (6.7%)

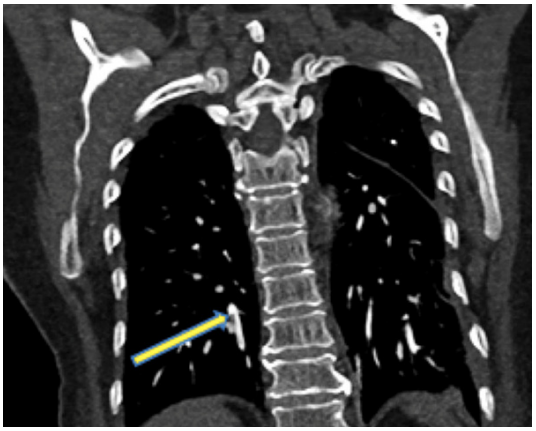

Figure 2. Coronal CTPA showing (arrow) a filling defect in the posterior segmental branch of the right pulmonary artery. CTPA, computed tomography pulmonary angiography.

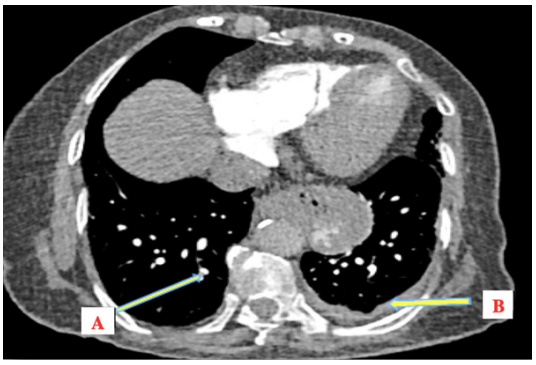

Figure 3. Axial CTPA showing a filling defect in the segmental branch of the right pulmonary. Artery (A) and pleural effusion on the left side (B). CTPA, computed tomography pulmonary angiography.

ml of non-ionic contrast Iohexol containing 350 mg of iodine per ml at a flow rate of 4.5 ml/sec through the antecubital vein.

Statistical analysis

Statistical analysis was done using SPSS v25 (IBM Corp., Armonk, NY, USA). Continuous variables were compared using a student t-test, and categorical variables, including the mean difference in the incidence of thromboembolism between two groups, were compared using the chi-square test. The *p*-value of < 0.05 was considered statistically significant.

Results

A total of 75 patients with hip fractures were included in our study, of which 31 patients were randomized to group M and 44 were randomized to group ME. The mean age of the patients in group M was 71.7±10.5 years, and in group-ME was 72.1±10.3 years. Out of 31 patients in group M, 22 (71.0%) had an intertrochanteric fracture (IT), 3 (9.7%) had neck femur fracture, 3 (9.7%) had acetabulum fracture, and 3 (9.7%) had subtrochanteric femur fracture. While in group ME, out of 44 patients, 23 (52.3%) had an intertrochanteric fracture (IT), 16 (36.4%) had neck femur fracture, 3 (6.8%) had acetabulum fracture, and 2 (4.6%) subtrochanteric femur fracture (**Table 1**).

We did not observe either symptomatic or asymptomatic DVT or death in either of the two study groups. Pulmonary embolism without DVT was reported in 1 patient (2.3%) of the group ME. Axial and coronal sections of the CT-pulmonary angiography of this patient are shown in **Figures 2** and **3**. There was no statistically significant difference between the two groups regarding these outcomes shown in **Table 2**.

There was no major fatal bleeding event from any critical site. A localized erythema was seen in 2 (4.5%) patients in group ME and none of the patients in group M. The adverse cardiac event in the form of atrial fibrillation was reported in 1 (2.3%) patient of the group ME. Postoperative delirium was noted in another patient of group-ME and 2 (6.5%) of group-M patients. An increased frequency of micturition was reported in 2 (4.5%) patients of the group-ME and 3 (9.7%) group M patients. One (2.3%) patient in group ME had respiratory distress and had a negative DVT and CTPA-scan.

Table 2. Distribution of primary outcome in both groups

Group	Asymptomatic Proximal DVT		Symptomatic proximal DVT		Death		PE		Postoperative total patients	
	Absent	Present	Absent	Present	Absent	Present	Absent	Present	None	Present
M	31	0	31	0	31	0	31	0	31	0
ME	44	0	44	0	44	0	43	1	43	1
Chi	0		0		0.000		0.71		0.71	
p-value	1		1		1.000		0.39		0.39	

PE, pulmonary embolism. DVT, deep vein thrombosis.

Discussion

The mean age of the hip fracture in our study was 71.65±10.35 years, and the contribution of the male and female genders was 57.3% (33/75) and 42.7% (32/75), respectively. Age has rarely been documented as an independent risk factor for VTE among trauma patients, despite being an established risk factor for VTE in elderly post-arthroplasty patients in multiple studies [25]. Zhang et al. (2015) concluded that age > 80 years was an independent risk factor for VTE after knee and hip arthroplasty, while patients with age between 60 and 70 years did not demonstrate any increase in the incidence of VTE [26]. There is an inconsistent correlation between the incidence of VTE and gender, as some studies in the literature have shown an increased incidence in males while others have shown an increased incidence in females [27, 28]. However, the current study shows no correlation between VTE with age and gender.

In the present study, the most common mode of injury was slip and fall at home (83.9% in group M-26/31; 77.3% in group ME-35/44), followed by hip fractures due to road traffic accidents (9.7% in group M-3/31; 15.9% in group ME-7/44). The findings of this study are consistent with the findings of Ahuja *et al.* (2017), who concluded in their study that in ages more than 50 years, slip and fall were the most common mode of injury [29].

Documented modalities of thromboprophylaxis in trauma include chemoprophylaxis, mechanical prophylaxis, and prophylactic inferior vena cava filters. Mechanical prophylaxis enhances venous blood return and stimulates endogenous fibrinolytic activity through actions on vascular endothelial cells, which can dissolve the thrombus and prevent thrombus formation. Mechanical devices usually have a good safety profile, while skin irritation and compliance remain the most common mechanical prophylaxis problems [30]. Compartment syndrome and peroneal nerve palsy are rare adverse events. Most studies have recommended chemoprophylactic agents as the standard drug for post-trauma patients in pre- and postoperative VTE prophylaxis [31, 32]. However, these agents are associated with several side effects, such as hemorrhage, wound-related issues, and osteoporosis. Moreover, despite thromboprophylaxis with LMWH, DVT was detected on venography in 23% to 31% of the patient [33].

Our study noted VTE without coexisting thrombus in the lower limb in 2.27% (1/44) of the ME group. On further evaluation, this patient was found to have diffuse atherosclerosis of the abdominal aorta, celiac artery, renal artery, superior mesenteric artery, and arteries of bilateral lower extremities. The result of this study is comparable to a study by Stannard *et al.*, who screened 222 elderly pelvic trauma patients via Magnetic resonance venography and duplex ultrasound and were given combined mechanical and enoxaparin thromboprophylaxis. The incidence of VTE without thrombus was noted in 0.9% (2/222), and VTE with thrombus was noted in 5.8% (13/222) [34]. In our study, proximal DVT and death were not reported in any case of the two groups. However, in the study by Stannard *et al.,* the incidence of proximal DVT among hip trauma patients was 5.86% (13/222), despite mechanical and chemical prophylactic measures [34]. Stannard et al.'s higher incidence of proximal DVT can be attributed to the larger sample size, longer study duration (1997 to 2002), and the difference in the timing and modality used for DVT screening [34].

Another possible explanation for our study's lower rate of proximal DVT could be hereditary

and acquired traits [35]. These genetic traits include low blood homocysteine, activated protein C resistance, and low prevalence of factor V Leiden in the Asian population. Patients with factor V Leiden are at ten times more risk of developing thrombus as compared to those with antithrombin III, protein C, or protein S deficiency [36]. Factor V Leiden was found in 0.45% of Asians compared to 5.27% of white people while screening 4,047 people in the United States [37]. Among the acquired traits, obesity and heart failure associated with VTE development are less prevalent in Asians [38].

We did not see any VTE in the M group, making an absolute risk reduction of 0.023 and NNT of 44 for this group. Also, the ARR with any prophylaxis, when compared with Khan *et al.* compared to prophylaxis in the Asian population, was 0.023, making NNT to be 44 [14].

Wound complications with thromboprophylaxis were noted as dehiscence and local reaction/erythema. The latter was noted in two patients receiving chemoprophylaxis (4.5%). Another patient receiving enoxaparin prophylaxis developed transient hematuria, which was managed accordingly. A similar complication with Enoxaparin thromboprophylaxis in arthroplasty patients was noted in a study by Kunal *et al*. [39]. Respiratory distress without DVT was noted in 1 patient in the ME group. This patient did not have any significant findings on CTPA and responded well to oxygen therapy. This event can be due to undetected very small thrombi on CTPA, or dyspnea may be an uncommon adverse event related to the drug itself [40, 41]. However, there was no statistically significant difference ($P > 0.05$) between the two groups (ME vis-à-vis M) concerning the overall complication rate.

There is an increase in the prevalence of hip fractures 2-3 times in practically every continent, so it becomes a matter of concern for all healthcare providers [42]. Since symptoms and signs of DVT are non-specific and may be entirely lacking, its diagnosis requires special investigations and screening. CTV has high sensitivity and specificity at 100% and 96.6%, respectively, comparable to MRV for suspected DVT [43-45]. Ultrasonography requires changing the positions of patients, which is unsuitable in case of trauma, especially for those with hip fractures. Additionally, USG has a poor positive predictive value for screening of DVT, particularly proximally, and is operator-dependent [43, 46]. Alternative to USG, CTV is a better screening modality since it ensures a short examination time and has better speed and spatial resolution. CTV is also helpful in obese patients, can evaluate pelvic veins and inferior vena cava, is less operator dependent, and can be cumulated with computed tomography pulmonary angiography (CTPA) to detect pulmonary thromboembolism [47].

A reduced incidence of VTE and proximal DVT has been reported in the Indian population using both mechanical prophylaxis alone as well as combined mechanical and chemical prophylaxis (ME) compared to the global literature; 6-19% with combined mechanical and chemical prophylaxis and 2.6%-8% in mechanical prophylaxis alone [15-17, 48]. However, it is necessary to note that there is considerable variability and inconsistency in the investigation methods opted to detect proximal DVT and timing of screening for DVT by different studies in the literature and also that there is no consensus on the gold standard investigation to accurately document proximal DVT in elderly hip trauma patients [3, 15, 24, 31, 34, 45, 48]. It is also important to highlight that the literature is divided on the outcomes of the different investigation methods, venography, sonography, MR venography, and CT venography in detecting proximal DVT [34, 44, 45, 48, 49].

There are certain limitations of the current study. First, prior research indicates that VTE risk continues 90 days after surgery and after being released from the hospital [50]. In our study, all the patients were investigated for VTE with CTV between the 5^{th} to 10^{th} day of trauma. This one-time screening might lead to a significant number of undiagnosed patients and a possible explanation for low incidence. Second, the small number of patients (n=75) and the conduction of the study at a single center may not be sufficient to provide results that could be implemented in a vast country like India.

We believe that the future requires randomized trials encompassing a larger sample size which may help to delineate better the efficacy of mechanical agents alone vis-à-vis chemical VTE prophylactic agents, especially in the light of the variable timing of the above thromboprophylaxis intervention in different studies of the

world literature and the inconsistency and variable yields of the diagnostic modalities available to diagnose proximal DVT in elderly hip trauma patients.

Conclusion

In conclusion, we did not find a difference between the two groups regarding postoperative occurrence of DVT. Our study demonstrates that mechanical prophylaxis alone may reduce or eliminate the incidence of VTE in post-traumatic hip fractures in the elderly. Hence, mechanical prophylaxis can be considered equally efficacious and safer than combined mechanical and chemoprophylaxis with enoxaparin for preventing VTE in elderly patients with hip trauma. Timely institution of VTE prophylaxis is of paramount importance in the prevention of this complication. However, we need a multicentre RCT to get concrete evidence and formulate a guideline for thromboprophylaxis in elderly patients with hip fractures.

Disclosure of conflict of interest

None.

Address correspondence to: Abhay Elhence, Department of Orthopaedics, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India. Tel: +918003996926; E-mail: abhayelhence@gmail.com

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