Deep vein thrombosis in medical and surgical Intensive Care Unit patients in a Tertiary Care Centre in North India: Incidence and risk factors

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Abstract

**Background and Aims:** Deep venous thrombosis (DVT) prophylaxis is underutilized, and there is a paucity of data reflecting the incidence of DVT in Indian Intensive Care Unit (ICU) population. We sought to evaluate the incidence and risk factors for DVT in medical and surgical ICU patients with DVT prophylaxis.

**Material and Methods:** The ICU patients more than 18 years old, expected to be in the ICU for more than 48 h were enrolled and DVT prophylaxis were given as per risk and were observed for clinical signs of DVT along with duplex ultrasound until in ICU. The patients receiving anticoagulant for some other reasons were excluded along with those with pregnancy, congenital coagulation disorders and terminal illness.

**Results:** The incidence of DVT was 0.8% (95% confidence interval: 0.78-0.81) in mixed populations (1.6% in medical and 0.5% in surgical). The higher DVT score (DVT (+) 10.75 ± 2.06/DVT (−) 8.75 ± 1.7 P = 0.0264), Acute physiology and chronic health evaluation (APACHE) IV score (DVT positive patient - DVT (+) 59.25 ± 15.06/DVT negative patients - DVT (−) 44.01 ± 13.74 P = 0.0292), length of ICU stay (DVT (+) 26.75 ± 12.87 days/DVT (−) 5.19 ± 6.18 P < 0.010), and inotropes (DVT (+) 50%/DVT (−) 12.3% P = 0.023) were associated with DVT.

**Conclusion:** The incidence of DVT was 0.8% with prophylaxis. High DVT and APACHE IV score were associated with DVT. Prolonged ICU stay and vasopressors were the risk factors.

**Key words:** Acute Physiology and Chronic Health Evaluation, cardiothoracic vascular surgery, central venous catheter, computed tomography pulmonary angiogram, deep vein thrombosis, pulmonary embolism, venous thromboembolism

Introduction

Epidemiological data on the incidence of deep venous thrombosis (DVT) and venous thromboembolism (VTE) in Asian populations is ambiguous. The Indian data from ENDORSE study revealed that despite a similar proportion of patients at risk in India and other participating countries, there is major underutilization of prophylaxis (17.4%) in India as compared to prophylaxis globally (50.2%).[1] VTE remains one of the most common unsuspected autopsy findings in critically ill patients.[2] In view of conflicting data from other countries in Asia, we decided to have a prospective study on the incidence of DVT in high-risk Intensive Care Unit (ICU) patients with proper DVT prophylaxis, in India.
Material and Methods

This prospective observational study was conducted in medical and surgical ICUs of a tertiary care referral hospital, after prior approval was obtained from Institutional Review Board, and the study was registered with CTRI (No: 2012/06/002735).

After taking informed consent, patients who were admitted in ICUs between the periods of November 01, 2011 to October 30, 2012, were more than 18 years old and were expected to stay in ICU for more than 48 h, were prospectively assessed and enrolled into the study.

The exclusion criteria were:

Patients excluded from the study were those receiving anticoagulants such as; 1. Admitting diagnosis of DVT, 2. Postoperative cardiac surgical patients, pulmonary embolism (PE)/DVT, acute coronary syndrome, 3. Cerebrovascular accident (CVA) (thrombolysed within 48 h), 4. Pregnant patients, 5. Congenital coagulation disorders, 6. Terminally ill patients.

All patients were examined clinically and radiologically (Doppler) for lower limb DVT within 48 h of the ICU admission, twice weekly and if VTE was clinically suspected. Bilateral lower extremity duplex venous ultrasound at groin and popliteal fossa was performed with Sonosite, using 13-6 MHz, 6 cm; vascular probe [Figure 1]. One co-investigator was dedicated to the physical assessments throughout the study and was blinded to the patient’s history and ultrasound results. DVT screening was continued twice weekly until the patient remained in ICU.

Independent variables included, were baseline factors such as, age, gender, body mass index (BMI), medical or surgical status, pre-ICU location, personal or family history of DVT/VTE, known thromboiphilia disorder, smoking, alcohol, oral contraceptive, recent hospitalization, and activity level, admitting diagnosis (sepsis, trauma, malignancy, chronic cardiac, respiratory, peripheral vascular disease, renal, or central nervous system disease), Acute Physiology and Chronic Health Evaluation (APACHE IV) score, and DVT risk factors on ICU admission were recorded at baseline and with evolving or resolving illnesses, events, and exposures.

Other independent factors recorded were daily ICU variables; vasopressors, mechanical ventilation, central venous line, dialysis, surgical interventions, hemoglobin, platelet count, serum creatinine, international normalized ratio, partial thromboplastin time, and activated partial thromboplastin time.

We used a computerized clinical information system for data collection of physiologic variables.

DVT prophylaxis was started within 24 h of ICU admission according to the DVT risk score and continued till the patient remained in ICU. We adhered to strict DVT prophylaxis protocols and monitored DVT scores in all patients. Different measures were used alone or in combinations as per the DVT risk scores. Early mobilization, limb physiotherapy, low molecular weight heparin (LMWH) Enoxaparin Sodium S/C in doses of 40 or 60 mg once daily/unfractionated heparin (UFH) 2500-5000 units TID as per age/weight/bleeding risk, sequential pneumatic compression device (SCD), antiembolic stockings were used for prophylaxis. Patients with active bleeding, high-risk of bleeding, suspected or proven heparin-induced thrombocytopenia (HIT) received SCD. Patients with contraindications to both heparin and SCD received only antiembolic (DVT) stockings. When thrombolytic therapy and therapeutic anticoagulation were contraindicated, inferior vena cava filter was inserted. DVT positive patients were given therapeutic doses of intravenous UFH or subcutaneous LMWH for the treatment of DVT.

Primary outcome

The primary outcome was the diagnosis of DVT by duplex ultrasound. We visualised the veins and noted flow, compressibility and filling defect in the veins. DVT was diagnosed with nonvisualization, lack of compressibility, flow and filling defect in the veins.

Patients with a positive or indeterminate duplex ultrasound had to undergo extensive bilateral lower extremity Doppler ultrasound by the radiologist.

Patients diagnosed or suspected with VTE had to undergo repeat Doppler and computed tomography pulmonary

Figure 1: Doppler ultrasound showing normal and thrombosed veins
angiography (CTPA), and treatment regime of VTE was given simultaneously. Patients with negative CTPA were shifted again to prophylaxis regimen.\(^{[11]}\)

**Statistical analysis**

The quantitative data for each parameter was expressed in terms of sample size, mean and standard deviation. The categorical data were expressed as percentages. The comparison of parameters for the two groups was tested for its significance using the two-sample independent \(t\)-test. Software used: SPSS, version 20.0, IBM. A \(P\)-value <0.05 was considered statistically significant.

**Results**

Over 1 year of the study period, 500 ICU patients were enrolled into the study. Of these only 4 patients developed DVT during the stay in ICU. The incidence of DVT was 0.8%. Two had proximal (right femoral), and two had distal (popliteal) DVT. None of them had clinical signs and symptoms and were only diagnosed with duplex ultrasound.\(^{[12]}\) These were confirmed by detailed venous Doppler of limbs by an experienced radiologist.

One of these patients was operated for large middle cerebral artery infarction and SCD was applied till the neurosurgical clearance. Initially, the patient received Enoxaparin and SCD. Postoperatively the patient was on SCS and developed DVT by the 3\textsuperscript{rd} week on the 43\textsuperscript{rd} day of ICU stay. The patient was started on therapeutic doses of Enoxaparin and followed by Doppler for recanalization.

In the other 2 patients, there were no such contraindications, and they received enoxaparin sodium in doses of 40-60 mg subcutaneous once daily as pharmacological prophylaxis and SCD like other patients. Both were diagnosed to have DVT by 2\textsuperscript{nd} and 7\textsuperscript{th} week during their 13 and 50 days stay in ICU respectively.

One post total knee replacement patient was on enoxaparin 60 mg S/C daily for 2 days before surgery and after 12 h of surgery had SCD started immediately postoperatively. The patient developed DVT postoperatively by the end of the 1\textsuperscript{st} week, despite all these and was shifted on therapeutic doses of enoxaparin and stayed in ICU for 21 days.

The enrolled 500 patients had an average age of 62.80 ± 12.09 years, APACHE IV score of 44.36 ± 13.91, 103 patients (20%) were mechanically ventilated, 63 patients (12.60%) required inotropes, 35 patients (7%) died, and 3 patients (0.6%) left the hospital against medical advice (LAMA).

All patients were prescribed DVT prophylaxis as per their risks and protocols, that is, there was 100% compliance to DVT prophylaxis protocol. Of these, 368 patients received LMWH (73.60%), 497 patients (99.40%) received SCDs, 116 patients (23.20%) received DVT stockings alone or in combinations as per their risk scores and contraindications. No patient developed heparin induced thrombocytopenia (HIT).

All patients were screened with duplex ultrasound as per protocol. DVT developed at a mean time of 2.75 weeks (19.5 days) during the stay in ICU.

We compared both groups i.e. DVT positive and negative patients in Table 1.

All DVT positive patients were started therapy with UFH or therapeutic doses of LMWH.\(^{[13]}\) Patients were followed with Doppler for recanalization. Two patients, recanalized well while one of them died due to sepsis and one went LAMA.

One patient was suspected of VTE, underwent CTPA, which was negative. His screening Doppler was also negative. He was given VTE regime and was later converted to standard prophylaxis.\(^{[11]}\)

Factors associated with the incidence of DVT on multivariate analyses were high APACHE IV score \((P = 0.029)\), high DVT risk score \((P = 0.026)\) use of vasopressors \((P = 0.023)\), central venous catheter (CVC) \((P < 0.01)\), and prolonged ICU stay \((P < 0.01)\).

Use of early pharmacological prophylaxis (before ICU admission) did not decrease the incidence of DVT \((P < 0.01)\).

None of the patients had bleeding or HIT due to pharmacological prophylaxis.

We compared surgical and medical patients within DVT positive group in order to find out different risk factors within this subgroup but did not find any association as the number was too small for analysis.

In subgroup analysis between surgical and medical patients, the incidence of DVT was higher in medical patient (1.6%) compared to surgical (0.5%) and mixed ICU (0.8%) study population. The incidence was higher in medical patients as less number of patients received pharmacological prophylaxis because of thrombocytopenia and contraindication to heparin. In the medical patients, ventilator days were more and hence mechanical ventilation (ventilator days) seemed to be a significant risk factor associated with the development of DVT in addition. We compared both groups in Table 2.
Discussion

In our study, the incidence of DVT in mixed ICU populations was low 0.8%, compared to other studies with DVT prophylaxis. In our study, we used duplex ultrasound to detect DVT as in previous observational studies. Ultrasonography is the preferred screening and diagnostic method for detecting DVT in critically ill patients.

DVT may be silent clinically because thrombus that does not cause a net venous outflow obstruction is often asymptomatic and hence remains undiagnosed or even if symptomatic, the clinical signs are nonspecific like; pain, edema, and tenderness. In ICU patients’ edema is universally present due to hypoalbuminemia, right-sided heart failure, fluid overload, hepatic, renal insufficiency, or due to surgery.

In our study, neither the patients with clinical signs of DVT had DVT nor did the DVT positive patients have clinical signs of DVT. Of the DVT positive patients, none of them was having history of congenital or acquired hypercoagulable state.

Until a few decades ago, DVT was the disease of West and less frequent in India or Eastern countries. Various studies were done in different Asian countries, including India showed different incidence rates. Most of these studies were done on a selective (high-risk) group of patients and prophylaxis was given to only those with increased risk because of fear of bleeding. However, the studies done in the last decade have shown the incidence of DVT in Indian patients as high as Western patients. Various studies done in recent past have shown a drastically lower incidence of DVT with proper prophylaxis e.g. Cook et al. 9.6%, Turpie et al. 1.7% and Sharma et al. 3%.

Our study is unique in this regard because we have given DVT prophylaxis to all ICU patients who were in ICU for 48 h or more with no selection bias of low risk vs high-risk.

The incidence of DVT was less in our study, perhaps due to the strict adherence to DVT protocol and not studying the high-risk group only.

Though CVC is a risk factor for DVT ($P = 0.01$) but no DVT was associated with CVC in our study. The probable reason may be the strict adherence to CVC bundles.

In the subgroup analysis, the incidence of DVT was relatively higher in medical patient (1.6%) compared to surgical (0.5%) and the mixed ICU study population (0.8%). Although the

Table 1: Comparison of DVT positive and negative patients

| Parameter                                      | DVT positive (n = 4) (%) | DVT negative (n = 496) (%) | $P < 0.05$ (significant) |
|------------------------------------------------|--------------------------|-----------------------------|--------------------------|
| Mean age (SD)                                  | 62±9.13                  | 62.80±12.12                 | 0.8966                   |
| Gender (male)                                  | 3 (75)                   | 200 (40.32)                 | 0.1585                   |
| Obesity (BMI ≥20)                              | 1 (25)                   | 46 (9.27)                   | 0.2846                   |
| H/O; DVT                                       | —                        | 4 (0.80)                    | 0.8572                   |
| H/O; varicose vein                             | —                        | 1 (0.2)                     | 0.9283                   |
| H/O; thrombocytopenia                          | 1 (25)                   | 29 (5.84)                   | 0.1074                   |
| H/O pharmacological prophylaxis*               | 1 (25)                   | 10 (2.02)                   | 0.001                    |
| H/O; abnormal coagulation disorder             | —                        | —                           | —                        |
| Medical (n=122) (24.4%)                        | 2 (50)                   | 120 (24.20)                 | 0.2263                   |
| Surgical (n=378) (75.6%)                       | 2 (50)                   | 376 (75.81)                 | 0.7566                   |
| DVT pumps (SCD)                                | 4 (100)                  | 493 (99.39)                 | 0.8729                   |
| DVT stockings                                  | 1 (25)                   | 115 (23.19)                 | 0.9283                   |
| LMWH                                           | 3 (75)                   | 365 (73.59)                 | 0.9522                   |
| DVT clinical signs                             | —                        | 4 (0.81)                    | 0.8572                   |
| Contraindications to LMWH                      | 1 (25)                   | 90 (18.15)                  | 0.7263                   |
| DVT risk scores                                | 10.75±2.06               | 8.75±1.79                   | 0.0264*                  |
| APACHE IV means (SD)                           | 59.25 (15.06)            | 44.01 (13.74)               | 0.0285*                  |
| Ventilator days                                | 9.00±6.00                | 2.40±7.46                   | 0.0784                   |
| Vasopressors                                   | 2 (50)                   | 61 (12.30)                  | 0.0238*                  |
| CVC                                            | 2 (50)                   | 42 (8.46)                   | 0.0035*                  |
| ICU stay (LOS)                                 | 26.75 (12.87)            | 5.19 (6.18)                 | <0.01*                   |
| Mortality                                      | 1 (25)                   | 34 (6.85)                   | <0.001*                  |

*Significant, BMI = Body mass index, CVC = Central venous catheter, SD = Standard deviation, DVT = Deep vein thrombosis, SCD = Sequential pneumatic compression device, LMWH = Low molecular weight heparin, APACHE = Acute physiology and chronic health evaluation, ICU = Intensive Care Unit, LOS = Length of stay
The pharmacological prophylaxis were not strictly adhered to in medical group because medical ICU patients usually have deranged coagulation profile, thrombocytopenia and unrecognized drop in hemoglobin, deranged renal profile and may undergo different interventions such as bronchoscopy and endoscopy. In these situations, pharmacological prophylaxis is likely to be delayed.

Use of SCD is also feared in patients with peripheral vascular disease, congestive heart failure, and suspected DVT. Because of these reasons the use of DVT stocking was significantly higher (P < 0.01) in this group of the population.

Other factors such as; family history, obesity, H/O previous DVT, varicose vein, trauma, malignancy, postoperative, and chronic diseases like diabetes mellitus, hypertension, chronic kidney disease, coronary artery disease, and chronic obstructive airway disease (COAD) were not found to be associated with DVT in our study compared to others.\cite{17,19,24}

In the study population, 360 patients received blood transfusions in the form of packed red cells and 26 patients received platelets, but there was no correlation with DVT.\cite{25,26}

In our study, a small number of patients developed DVT compared to previous studies despite being at risk. The possible reasons may be genetic variation, climatic variation, and strict prophylaxis to protocols.\cite{17,20}

The risk factors within subgroup could not be compared because of the few DVT positives in both the groups (surgical and medical). Emphasis was given to enrolment of eligible patients, Doppler screening of lower limbs, and DVT prophylaxis for all patients.

Conclusion

The incidence of DVT was 0.8% with prophylaxis in mixed ICU population. The risk was highest at 19.25 days. Prolonged ICU stay and use of vasopressors were significant risk factors for DVT in our study. There was association between high DVT and APACHE IV scores. Adequate prophylaxis balancing the risk of thrombosis and bleeding, DVT/VTE can be prevented in ICU patients. With the use of Doppler screening, one can diagnose asymptomatic DVT and prevent VTE and related complications. Further larger studies are required to reach more conclusive finding.

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Conflicts of interest
None.

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