

## Venous Thromboembolism in Medical Critically Ill Patients: Prevalence and Incidence

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**Abstract-** The objective of this study was to determine the prevalence and incidence of venous thromboembolism among critically ill medical surgical patients. In this cross sectional and retrospective study, we observed 243 patients who were first admitted at the intensive care unit. Patients who were diagnosed with deep venous thrombosis or embolism either by clinical or paraclinical methods were enrolled. Among 243 patients of ICU ward 12 cases of them were confirmed to have thromboembolism (prevalence of 9.4%). But the incidence of venous thromboembolism after 48 hour of ICU admission was 5.2% (6 cases). Among 6 VTE cases 3 of them didn't receive any anticoagulant prophylaxis, 2 patients received LDUH 5000 unit twice a day and one patient received LMWH 60 mg daily but all developed VTE although receiving prophylaxis. We found that the prevalence of proximal lower limb DVT among medical-surgical critically ill patients remaining in the ICU for  $\geq 3$  days is about 9.4% and the incidence of that is about 5.2%. Further studies should be performed in order to assess the benefits and risks of venous thromboprophylaxis in Iranian patients.

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### Introduction

Venous thromboembolism (VTE) is a common and lethal complication in critically ill patients, due to several predisposing factors such as pre morbid conditions (e.g., trauma, major surgeries, malignancy, sepsis), invasive interventions like central venous catheterization, and prolonged immobility (1). Patients in intensive care unit have a higher risk of lower limb deep venous thrombosis (DVT) in comparison with other hospitalized patients (2). Concern about undiagnosed DVT in the medical-surgical ICU setting is underestimated by studies showing that 10% (3) to

100% (4, 5) of DVTs detected by screening ultrasound investigation were clinically unknown, and it is likely that lots of patients under mechanical ventilation with unexpected episodes of tachycardia, hypotension, or hypoxia may have unnoticed pulmonary embolism (PE) (6). Unsuspected PE may also lead to delay weaning patients from mechanical ventilation (4). As well as VTE could be unrecognized in the critically ill patients because of the difficulty in eliciting symptoms and or signs from sedated or intubated patients, because most of them positioned semi recumbent so leg swelling couldn't be detected easily. About the significance of VTE we should emphasize that intensive care unit

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patients, who have reduced cardiopulmonary reserve, are prone to have serious complications of even small pulmonary embolism (7). The incidence of VTE is reported variously in different studies based on the population, prophylactic interventions and screening methods. We hypothesized that unlike some studies conducted in the last decade (3-5) DVT occurrence rates would be lower in a mixed population of medical-surgical ICU patients, due to increased interest to thromboprophylaxis. The aim of this study is to determine the prevalence and incidence of lower extremity DVT detected among medical-surgical critically ill patients.

## Materials and Methods

We conducted a retrospective chart review study at a university affiliated hospital Massih Daneshvari, Tehran, Iran. All consecutive patients admitted to the ICU for the first time from March 2006 to March 2008 were considered. Patients were excluded if they used antithrombotic agents or were diagnosed for VTE before ICU admission; also patients who used Intermittent Pneumatic Compression (IPC) were excluded. We used a trained nurse and a standardized form to collect baseline characteristics of patients including age, sex, ICU admitting diagnosis, illness severity (acute physiologic and chronic health evaluation (APACHE II)), VTE prophylaxis, duration of ICU hospitalization, and patients outcome. Patients received low dose unfractionated heparin (LDUH) every 12 hours or low molecular weight heparin (LMWH) every 24 hours as prophylactic regimens at the time of study. To identify VTE prevalence venous thromboembolism diagnostic tests such as duplex compression ultrasounds, venograms, ventilation perfusion scan of lungs, lung computed tomography (CT) scans were recorded. This study was approved by the Research Ethics Board of Shahid Beheshti University of Medical sciences. All patients or their next of kin provided written informed consent.

## Results

A total of 243 patients were participated in this study ,141 (58%) were male and 102(42%) female. 51 patients didn't have any contraindications to receive anticoagulants and underwent LDUH or LMWH for prophylaxis . Unfractionate heparin (LDUH) 5,000 units were given to 31 patients twice a day, 12 three times a day, and one patient only a single dose. One patient received LDUH (1,000 units) infusion every hour and 6

patients received LMWH. We detected VTE in 12 patients at the time of ICU admission or prevalence of 4.95%. On the other hand 6 patients developed VTE during their ICU stay therefore incidence of 2.5% was recorded. Of these 6 patients 3 were male (50%) and 3 were female (50%), with an age range of 22 to 81 years old (mean age of 60 years). In this group APACHE II score of 15.5, mean ICU stay of 23 days and mortality range of 50% was found. One of them was admitted to the ICU because of OCPD exacerbation and received LMWH 60 mg every day but developed pulmonary embolism 8 days later which was detected by CT of lungs. Other 5 patients were medical/surgical cases ,the two surgical cases and one patient with cirrhotic disease couldn't receive anticoagulant agents and all developed DVT ,diagnosed by duplex ultrasound. Two other patients who received unfractionate heparin 5000 units twice daily were also detected to have DVT at ICU. Only one patient with diagnosis of mediastinal mass and inferior vena cava syndrome developed DVT in both lower extremities and none of the patients who received heparin 5000 units three times a day developed venous thromboembolism. It is likely that heparin prophylaxis three times a day would be more convenient in ICU patients with greater risks to develop VTE, though further study is needed to confirm this theory.

## Discussion

By use of lower extremity ultrasonographic investigation at the time of ICU stay, among seriously ill medical or surgical patients, we found that 4.9% of them had DVT and 2.5% developed new onset lower extremity DVT. In an earlier observational survey of 100 critically ill medical patients, lower extremity ultrasounds was done twice weekly and at 1 wk post-ICU discharge detected DVT in 40% of those receiving subcutaneous unfractionated heparin, in 32% of patients without prophylaxis, and 33% of patients with mechanical prophylaxis (4). In another trial, among 110 patients mechanically ventilated for  $\geq 1$  week underwent weekly ultrasound investigation, 16% incidence of lower extremity DVT was reported (8). The lower incidence of DVT in our survey compared with previous reports(4,8) maybe owing to one or more of the following: lower specificity of previous ultrasound screening, differences in case mix, various baseline characteristics of the population of the study or a combination of factors. Muscedere *et al.* (1) evaluated VTE incidence among 600 ICU patients during 2001 and 2002 with APACHE II score of 18.5+7.9 and mean ICU stay of 14.8 and

declared incidence of 3% at the ICU and 5.7% during 8 weeks after ICU stay in the ward. In another retrospective study by Patel *et al.* (9) among 12 ICU centers in Canadian hospitals 12338 patients were observed and VTE incidence of 2%(246 patients) was reported, patients had mean ICU stay of 6 days and APACHE II score of 17.6, most cases developed VTE in the first 2 weeks of ICU stay. On the other hand Cook *et al.* (10) evaluate risk factors, diagnostic and prophylactic methods in a Canadian ICU among 93 patients who were enrolled with APACHE II score of 21.1 and mean ICU stay of 3 days incidence of 5.4 was reported. In our study mean APACHE II score was 15.5 with mean ICU stay of 23 days, only one patient had prolonged ICU stay for 58 days and other 5 patients stayed 12 days at the ICU by average and main VTE occurrence was after mean ICU stay of 11 days. Mortality rate of our study was 50% compared with 41% in Patel *et al.* study (9) and 20% in Muscedere *et al.* study (1) and 20.4% in Cook *et al.* study (10). In compared with recent studies (1,9,10) the mean age of our patients was older. In our study among 6 VTE cases 3 of them didn't receive any anticoagulant prophylaxis, 2 patients received LDUH 5000 unit twice a day and one patient received LMWH 60 mg daily but all developed VTE although receiving prophylaxis. Muscedere *et al.* (1) reported that patients who developed VTE received anticoagulant prophylaxis in 78% days of their ICU stay, medical-surgical patients received LDUH, trauma patients received LMWH and in neurosurgical patients pneumatic compression stockings (PCS) was used. According to Patel *et al.* (9) study 65.8% of patients who developed VTE had received prophylaxis in 80% days of their ICU stay and 43% of them received anti thrombotic drugs (including LDUH, LMW, warfarin, and danaproid) however, they developed VTE and two third of the cases were reported to be a cause of prophylaxis failure. Cook *et al.* (5) reported that 64 patients didn't have any contraindications to receive heparin and 40 of them (62.5%) underwent LDUH prophylaxis 5000 units twice a day. Muscedere *et al.* (1) and Patel *et al.* (9) showed that some of the ICU patients develop VTE although they receive anticoagulant prophylaxis which was also obvious in our study. Recurrent VTE is a well known consequence of serious disease; for instant, along with 1,021 patients with acute VTE received heparin subsequently warfarin, four risk factors for recurrent VTE were chronic respiratory disease, cancer, chronic cardiovascular disease, and other clinically essential medical circumstances (7). These four situations are frequent in critically ill patients, causative of the risk of

VTE recurrence in the ICU. A systematic review of various observational trials displays that in comparison with venography the sensitivity of compression ultrasonography for proximal DVTs in symptomatic patients is 97% (95% CI 96–98%) and in asymptomatic patients is 62% (95% CI 53–71%) and the specificity of ultrasound for proximal DVTs in symptomatic patients is 94% (95% CI 90–98%) and in asymptomatic patients is 94% (95% CI 91–98%). (11) As a limitation of this study we should inform that in the critically ill patients, the precision of compression ultrasonography as a screening method for DVT has not been compared with venography. Consequently, it is likely that the proximal DVT rate we reported in this survey is either an overestimate or an underestimate. However, similar to previous observational trails in critically ill medical-surgical patients (3-5,8,12,13), we applied ultrasonography to detect DVT. Nevertheless, according to the American College of Radiology ultrasonography still remains the choice imaging procedure in order to diagnose DVT (14). On the other hand according to surveys of radiologists (15) and intensivists (16) ultrasonography is also the favored screening and diagnostic test for critically ill patients. In another study by Ebrahim *et al.* (8) it was demonstrated that despite the use of prophylaxis, occurrence of VTE is common among patients who required prolonged mechanical ventilation, still, further study should be done in order to determine the relevance between prolonged mechanical ventilation and increased risk of VTE. In conclusion, we found that the prevalence of proximal lower limb DVT among medical-surgical critically ill patients remaining in the ICU for  $\geq 3$  days is about 9.4% and the incidence of that is about 5.2%. Further studies should be performed in order to assess the benefits and risks of venous thromboprophylaxis in Iranian patients.

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