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# Do appropriate thromboprophylaxis and routine physiotherapy prevent venous thromboembolism in intensive care unit?

*Yoğun bakım ünitesinde uygun tromboprofilaksi ve rutin fizyoterapi venöz tromboemboliyi önler mi?*

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***ABSTRACT***

***Background:*** This study aims to investigate the prevalence and incidence of venous thromboembolism in intensive care unit (ICU) patients receiving thromboprophylaxis.

***Methods:*** Seventy-four consecutive patients (34 females, 40 males; mean age 55.8±19.4 years; range 20-86 years) admitted to the medical-surgical ICU, who were ≥18 years old and expected to stay in ICU for ≥72 hours, were included. Demographic data, Acute Physiology and Chronic Health Evaluation II scores, baseline and time-dependent deep vein thrombosis (DVT) risk factors were recorded. Bilateral lower extremity compression ultrasound was performed twice weekly, and one week after discharge from ICU. If DVT was suspected at any time during ICU stay, compression ultrasound was repeated. All patients were administered low molecular weight heparin or mechanical thromboprophylaxis. Also, passive extremity exercises were applied by physiotherapist to all patients every day.

***Results:*** Mean Acute Physiology and Chronic Health Evaluation II score was 17±6.1. The prevalence of DVT was 2.7% (CI 95% 3.3-9.42) on ICU admission. Of the patients, 89.1% were administered low molecular weight heparin, and 10.9% were administered mechanical thromboprophylaxis. We did not detect new DVT or pulmonary embolism during the ICU stay.

***Conclusion:*** Although DVT prevalence in ICU was 2.7%, appropriate and effective thromboprophylaxis prevented the development of new DVT during ICU stay.

***Keywords:*** Deep vein thrombosis; intensive care unit; physiotherapy; pulmonary embolism; thromboprophylaxis.

***ÖZ***

***Amaç:*** Bu çalışmada tromboprofilaksi uygulanan yoğun bakım hastalarında venöz tromboembolizm prevalansı ve insidansı araştırıldı.

***Çalışma planı:*** Medikal-cerrahi yoğun bakım ünitesine kabul edilen ≥18 yaşında ve ≥72 saat yoğun bakımda kalması planlanan 74 ardışık hasta (34 kadın, 40 erkek; (ort. yaş 55.8±19.4 yıl; dağılım 20-86 yıl) çalışmaya dahil edildi. Demografik veriler, Akut Fizyolojik ve Kronik Sağlık Değerlendirmesi II skoru, başlangıç ve zaman bağımlı derin ven trombozu (DVT) risk faktörleri kaydedildi. İki taraflı alt ekstremite kompresyon ultrasonografi haftada iki kez ve yoğun bakımdan çıktıktan bir hafta sonra uygulandı. Yoğun bakım yatışı süresince DVT şüphesi olduğunda, kompresyon ultrasonografi tekrarlandı. Hastaların tümüne düşük molekül ağırlıklı heparin veya mekanik tromboprofilaksi uygulandı. Ayrıca, her gün fizyoterapist tarafından tüm hastalara pasif ekstremite egzersizleri uygulandı.

***Bulgular:*** Ortalama Akut Fizyolojik ve Kronik Sağlık Değerlendirmesi II skoru 17±6.1 idi. Yoğun bakıma kabulde DVT prevalansı %2.7 (CI %95; 3.3-9.42) idi. Hastaların %89.1'ine düşük molekül ağırlıklı heparin, %10.9'una mekanik tromboprofilaksi uygulandı. Yoğun bakım yatışı süresince yeni DVT veya pulmoner emboli saptanmadı.

***Sonuç:*** Yoğun bakım ünitesinde DVT prevalansı %2.7 olmasına rağmen, uygun ve etkili tromboprofilaksi yoğun bakım yatışı süresince yeni DVT gelişimini önledi.

***Anahtar sözcükler:*** Derin ven trombozu; yoğun bakım ünitesi; fizyoterapi; pulmoner emboli; tromboprofilaksi.

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Critically ill patients run a high risk of developing deep vein thrombosis (DVT) compared with other hospitalized patients,[1] and DVT and pulmonary embolism (PE) cause increased morbidity and mortality in this patient group.[2] In addition, critically ill patients commonly have asymptomatic thromboembolic events and are often unable to report their symptoms because of sedation and mechanical ventilation.

The vast majority of patients admitted to an intensive care unit (ICU) usually have at least one major risk factor for venous thromboembolism (VTE), and most generally have multiple risk factors,[3,4] some of which precede ICU admission while others develop during the course of their ICU stay. Advanced age, serious medical illnesses, recent surgical procedures, trauma, sepsis, heart failure, previous VTE, and immobilization (stroke, spinal cord injury, bed rest, etc.) are the most common risk factors present before ICU admission, whereas mechanical ventilation, paralysis, the use of sedatives, immobilization, central venous lines (especially femoral vein catheters), surgical procedures, sepsis, and platelet transfusions are often seen during the patients' stay in the ICU.[2] Sudden episodes of hypotension, tachycardia, or hypoxia in mechanically ventilated patients may be due to undetected PE, and unsuspected PE may be the cause of difficult weaning.[5,6] Therefore, VTE is one of the major complications that occur in critically ill patients in the ICU, especially for those with impaired cardiac and respiratory functions. Consequently, routine DVT prophylaxis is recommended for all ICU patients.[7]

According to current data, the incidence of DVT identified by screening ultrasound among patients in the medical-surgical ICUs ranges between 10% and 100%.[6-8] This large range may be the result of the different methods used to detect DVT in previous studies. For patients who do not receive thrombophylaxis routinely, VTE is inevitable.[2] On the other hand, critically ill patients may still be at risk for DVT even after receiving universal thromboprophylaxis.[9]

Therefore, in this study, we aimed to determine the prevalence and incidence of VTE in ICU patients who were receiving effective, appropriate thromboprophylaxis as well as routine daily physiotherapy.

## PATIENTS AND METHODS

This prospective, observational, cohort study was performed in a 21-bed, closed, university-affiliated medical-surgical ICU at İstanbul University, İstanbul Medical Faculty in the Department of Anesthesiology and Intensive Care. Between September 2009 and March 2010, 278 patients who were admitted to the ICU were assessed, and 74 patients (34 females, 40 males; mean age 55.8±19.4 years) who were ≥18 years old that were expected to be in the ICU for >72 hours were included in the study. The patients who had undergone a routine postoperative follow-up of <72 hours as well as those with active VTE or a high risk of bleeding (PLT <100,000/μL, INR >1.5) were excluded from the study along with those for whom this was their second admission to the ICU, those who were pregnant, and those who were receiving anticoagulant treatment. In the end, a total of 204 patients were excluded. Twenty of these were younger than 18 years old, 85 had stayed in the ICU for less than 72 hours, 20 had been admitted to the ICU a second time, 50 had received anticoagulant therapy when they were admitted to the ICU, 24 had low platelet levels (<100,000/μl), and five were pregnant. This study was approved by the institutional review board, and written informed consent was obtained from either the patients or their relatives.

We recorded the patient's demographic data (age and gender) along with their diagnosis at admission and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores.[10] In addition, we obtained the patients' baseline and time-dependent DVT risk factors and also recorded the duration of their mechanical ventilation and ICU and hospital stays.

Bilateral lower extremity compression ultrasound (CUS) was performed within 48 hours of admission to the ICU to evaluate the prevalence of DVT. When present, CUS was also performed twice weekly as well as one week after being discharged from the ICU to determine the incidence rate of the DVT. If VTE was suspected at any time during their ICU stays, CUS was then performed again, and if it was suspected clinically, CUS was performed on that same day. Investigation of sites other than the lower extremities was performed only if there was a clinical suspicion of DVT. Helical computed tomography (CT) was also performed if there was laboratory or clinical suspicion of PE.

Based on the American College of Chest Physicians (ACCP) guidelines for the prevention of VTE, all patients received low-molecular-weight heparin (LMWH)-enoxaparin sodium (Na) 4000 IU once daily or LMWH-enoxaparin Na 6,000 IU once daily if they had a body weight of > 100 kg-, used intermittent pneumatic compression (IPC) devices, wore elastic compression stockings, or had any combination of these characteristics.[11] Sixty-six patients were given LMWH while eight received mechanical thromboprophylaxis

(three patients used an IPC device, two wore elastic compression stockings, and three patients used both an IPC device and wore elastic compression stockings). The LMWH doses were checked by doctors using the nurses' records and recorded to a checklist, and the LMWH dosage was adjusted according to the creatinine clearance in patients with renal pathology. Furthermore, an ICU physiotherapist helped the patients perform daily routine lower extremity exercise training when there were no contraindications. Since leaving patient without thromboprophylaxis is not ethical, our study did not include control group.

The primary goal of our study was to determine the prevalence and incidence of DVT in critically ill patients as diagnosed by bilateral lower extremity CUS. Doppler US examinations were performed using a Sonasite TITAN® portable US unit (Sonosite, Inc, Bothell, WA, USA) with C60/5-2 MHz and L38/10-5 MHz convex probes. The lower extremity was scanned in B mode to locate the external iliac, common femoral, superficial and deep femoral, popliteal, tibialis anterior, and tibialis posterior veins. These veins were then compressed using the probe, and acute DVT was diagnosed if an expanded, non-compressible segment was detected. Color Doppler US was also used to detect filling defects in the lumen. In addition, if no spontaneous flow was found, the augmentation (compression of the calf veins to increase the flow in the proximal segments) maneuver was performed. To ensure uniformity of screening, the skilled radiologist who performed all of the tests was blinded to the patient's history and physical examination results.

### Statistical analysis

IBM SPSS Statistics version 21.0 for Windows software program (IBM, Armonk, NY, USA) was used for statistical analyses. The data was expressed as frequencies and percentages (categorical variables) or median ($25^{th}$-$75^{th}$ percentile) (continuous variables). Variables with normal distribution t test was used in independent groups, variables without normal distribution Mann-Whitney U test was used. $P<0.05$ was statistically significant in all analyses.

## RESULTS

The mean APACHE II score in our study was 17±6.1. In addition, 65 (87.8%) of the patients were mechanically ventilated (Table 1).

The most common baseline risk factors for DVT were immobilization (n=45), age (n=24), malignancy (n=19), renal failure (n=19), and surgery (n=18) (Figure 1), and 60% had more than four risk factors for DVT. Renal replacement therapies were performed on 15 patients, with nine of them receiving hemodialysis and six undergoing continuous veno-venous hemofiltration (CVVH) because of renal failure.

Sixty-six patients (89.1%) received LMWH. According to the nurses' records and doctor's checklist, no gaps in the thromboprophylaxis were detected. Anti-embolism stockings and/or intermittent pneumatic compression devices were used by eight patients (10.9%) due to a contraindication for anticoagulants. Of these eight patients, five received non-pharmacological thromboprophylaxis due to thrombocytopenia. For two of these patients, this

**Table 1. Clinical characteristics of the intensive care unit patients**

| | n | % | Mean±SD | Median | Percentile |
|---|---|---|---|---|---|
| Age (years) | | | 55.8±19.4 | | |
| Females | 34 | 45.9 | | | |
| Males | 40 | 54.1 | | | |
| APACHE II score (mean) | | | 17±6.1 | | |
| Number of medical patients | 56 | 75.6 | | | |
| Number of surgical patients | 18 | 24.4 | | | |
| Number with central venous catheters | 67 | 90.5 | | | |
| Number with femoral arterial catheters | 19 | 25.6 | | | |
| Number receiving hemodialysis/hemofiltration | 15 | 20.2 | | | |
| Number of sedated patients | 61 | 82.4 | | | |
| Number receiving platelet transfusions | 7 | 9.4 | | | |
| Number receiving mechanical ventilation | 65 | 87.8 | | | |
| Days of mechanical ventilation (median; $25^{th}$-$75^{th}$ percentile) | | | | 8 | 4.14 |
| Days in ICU (median; $25^{th}$-$75^{th}$ percentile) | | | | 13.5 | 8.24 |
| Days in hospital (median; $25^{th}$-$75^{th}$ percentile) | | | | 24.5 | 10.54 |

APACHE: Acute Physiology and Chronic Health Evaluation; ICU: Intensive care unit.

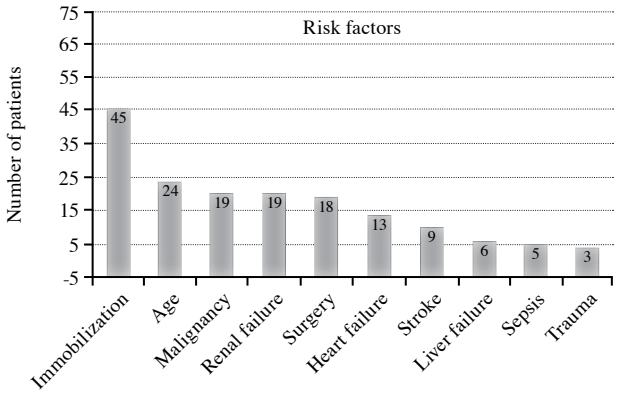


**Figure 1.** Baseline risk factors for deep vein thrombosis.

was related to chemotherapy, and for another, it was in conjunction with a liver transplant. Additionally, it was connected to liver failure caused by mushroom intoxication in two others. The remaining three patients received non-pharmacological thromboprophylaxis due to active bleeding. Furthermore, all seven patients with thrombocytopenia had a platelet transfusion, and no heparin-induced thrombocytopenia or major bleeding were detected as a complication in the patients who were given the LMWH thromboprophylaxis.

Two of the patients (2.7%) had DVT [95% confidence interval (CI) 3.3-9.42) upon admission to the ICU. One was 75 years old and was transferred from the emergency department. This patient had prolonged immobilization and chronic renal failure as risk factors and had thrombus at the right iliac, femoral, and popliteal veins. The second patient with DVT was 69 years old and morbidly obese obesity. Moreover, prolonged immobilization and congestive heart failure were also risk factors in this patient along with thrombus at the left femoral and popliteal veins. This patient was also transferred to the ICU from the emergency department. In this study, we detected no new DVT in any patient during their ICU stays, and none had PE. However, 38 patients underwent thoracic CT during the follow-up period because of a clinical suspicion of PE or clinical and laboratory deterioration. However, we did not find any radiological signs that pointed to the presence of PE.

## DISCUSSION

Among critically ill medical and surgical patients who received routine thromboprophylaxis and lower extremity exercise training, the prevalence of DVT at ICU admission was 2.7% (95% CI 3.3-9.42), and none of the patients had DVT or PE during their ICU stays.

The prevalence of DVT in our patients was similar to the results found in other studies.[9,12] However, unlike those studies, we provided complete protection against DVT or PE with appropriate and effective thromboprophylaxis.[7-9,12] In the study by Hirsh et al.[8] 61% of 100 ICU patients received low-dose heparin or intermittent pneumatic compression for thromboprophylaxis, and the incidence of DVT was 33%. They also examined upper extremity DVT and found that 15% of the cases were associated with central venous catheters. We believe that the reason for the high incidence in their study was the lower thromboprophylaxis rate (61%). In our study, 89.1% of patients received LMWH, and 10.9% used anti-embolism stockings and/or intermittent pneumatic compression devices for thromboprophylaxis. In the study by Marik et al.[7] that featured a higher rate of thromboprophylaxis (92% of 102 medical-surgical patients), the patients who were given low-dose heparin or intermittent pneumatic compression had an incidence rate of 12%. Furthermore, in a study by Cook et al.,[9] 81.7% of the patients (n=261) received subcutaneous unfractionated heparin for thromboprophylaxis, 6.8% had therapeutic intravenous anticoagulation with unfractionated heparin, 4% were given LMWH, 0.4% received warfarin, and 7.2% wore anti-embolism stockings with or without pneumatic compression devices. They also found a DVT incidence rate of 9.6% even when thromboprophylaxis was applied to all of the patients. In addition to these studies that demonstrated a high DVT incidence rate in spite of thromboprophylaxis, Wilasrusmee et al.[13] showed a similar incidence of DVT in the patients who received no thromboprophylaxis.

Boddi et al.[12] showed a significant decrease in the incidence of DVT from 11.9% to 4.5% after an education program that focused on the implementation of DVT prophylaxes. Before and after the education program, all patients received LMWH (daltaparin 5000 IU once daily) and/or mechanical prophylaxis via elastic compression stockings. After the completion of the education, there was a significant decrease in the length of mechanical ventilation (9 vs 3 days), but there was an increase in the use of elastic compressive stockings combined with pharmacological therapy. The LMWH dosage was the same before and after the education program, but the percentage of those receiving pharmacological prophylaxis was not reported in this study. Hence, it is unknown whether there was an increase in the use of LMWH after the end of the education program or how this increase might have affected the incidence of VTE. Their study included an education course for clinicians as well as a

checklist for thromboprophylaxis. In addition, they paid careful attention to the active and passive mobilization of patients and daily sedative administration control. We also consider these same parameters in our ICU, which might also explain our results.

If there is a contraindication for pharmacological thromboprophylaxis, mechanical thromboprophylaxis should be used. Kurtoglu et al.[14] reported no VTE among high-risk trauma and surgical patients for whom thromboprophylaxis was applied via elastic stockings and/or intermittent pneumatic compression. Moreover, Dirimese et al.[15] did not detect any DVT in high-risk postoperative patients who were given thromboprophylaxis in the form of knee-length and thigh-length anti-embolism stockings. Similarly we did not find any DVT in our patients who received only mechanical prophylaxis.

Cook et al.[9] found that patients with end-stage renal disease and those receiving platelet transfusions had an increased risk of VTE in spite of the application of thromboprophylaxis. In our study, neither the patients with end-stage renal diseases (12%) nor those who received platelet transfusions (9.4%) had DVT. Although Boddi et al.[12] found a correlation between DVT and the length of mechanical ventilation, but this relationship did not exist in our cases.

One characteristic of our study was that approximately 90% of the patients received LMWH while just 10% received mechanical prophylaxis. In previous studies, pharmacological thromboprophylaxis was generally carried out with unfractionated heparin.[7-9] Additionally, in our ICU, all of the patients received lower extremity exercise training for early ambulation. In addition, about half of the patients had more than four risk factors for DVT. However, we found that the number of patients receiving mechanical ventilation and the length of ICU stays were relatively higher in our study compared with others.[9,12]

Most of our patients were severely ill. Despite these troubles, DVT did not develop during their ICU stays or one week after they were discharged. On the other hand, we excluded patients with active VTE, those that had been admitted to the ICU a second time, and those who were pregnant, which was contrary to other studies. Screening for DVT was done very often during the ICU stays in addition to one week after the patients were discharged from ICU. Daily lower extremity exercise training to prevent DVT is a routine application in our ICU unit, which was another positive component of our study. According to Sud et al.[16] appropriate prophylaxis is more important than routine screening for DVT; thus, resources should be targeted to optimize the efficacy of thromboprophylaxis. We do our best to put this into practice with our patients.

Our study also had some limitations. First, the accuracy of the CUS for screening DVT was not compared with venography. However, venography is an invasive technique, and we did not suspect missing thrombus when CUS was used to detect DVT. Furthermore, we performed venous US for the upper extremities only if there was a clinical suspicion of DVT. Therefore, we may have missed silent thrombi and could have underestimated the overall rate of DVT in our ICU patients. Finally, the number of patients included in the study was small, which was related to the short study period (six months).

**Conclusion**

The prevalence of DVT at ICU admission was only 2.3% in our study, and none of the other patients had DVT and/or PE during their ICU stays. Our findings compare quite favorably with other studies that have reported DVT incidence rates of between 10 and 100%. The difference in our study was that we used a combination of appropriate pharmacological or mechanical thromboprophylaxis along with routine lower extremity exercise training. This resulted in complete protection against DVT and/or PE.

**Declaration of conflicting interests**

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