Effect of Web-based Clinical Decision Support Systems on Adherence to Venous Thromboembolism Prophylaxis guideline among ICU Nonsurgical Patients: A Prospective Before and After Study

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Abstract

**Background and objective:** There is a gap between expert recommendations and clinical practice in (Venous Thromboembolism) VTE prophylaxis among nonsurgical patients worldwide. Rate of adherence to evidence-based practice is inadequate in the nonsurgical population. Therefore, this study aimed to determine The effect of Clinical Decision Support Systems (CDSS) on the use of the appropriate VTE Prophylaxis in Nonsurgical Patients in the Intensive Care Unit (ICU).

**Method:** We conducted a cross-sectional study (pre and post-implementation CDSS for recommendation VTE prophylaxis order set) to analyze the effect of the CDSS within CPOE on the appropriate VTE prophylaxis in three ICUs of the Nemazee hospital (before intervention from 20 April 2020, to 21 November 2020 and post-intervention duration form 7 April 2021, to 9 July 2021). The pre-intervention and post-intervention phase samples comprised 175 and 27 patients, respectively. P-value is less than 0.05 was considered a significant level. All statistical analysis was performed by SPSS version 24.

**Results:** Adherence to VTE prophylaxis guidelines after introduced CDSS for recommendation VTE prophylaxis within CPOE system in nonsurgical patients in ICUs increase from 48.6% to 77.8% (p-value<01). However, mortality rate (pre-intervention 13.80% vs post-intervention 14.80%(p-value=0.88)) and means of length of stay (pre-intervention 13.66 vs post intervention 13.63(p-value=0.49)) in ICU have not significantly change after introduced CDSS for recommendation VTE prophylaxis order sets.

**Conclusion:** The results indicate that the CDSS for recommendation VTE prophylaxis within CPOE improves adherence to VTE prophylaxis in nonsurgical patients at ICUs, which assist provider to select the most tailored VTE prophylaxis. Further study needs to evaluate implemented CDSS for recommendation VTE prophylaxis in nonsurgical patients at a province and national level.

**Background**

Venous thromboembolism (VTE) is one of the most common complications in nonsurgical critical patients. Incidence of VTE hospitalized ill medical patients have an eight-time higher than the general population(1). The incidence of VTE in ICU is up to 60%(2, 3).

VTE developing in ICU increases hospital length of stay and mortality(4). Annual hospitalization costs of nonsurgical patients with a diagnosis of VTE are from 13.4 to 27.3 billion(5). Although some VTE events are unpreventable, several studies have shown that appropriate VTE prophylaxis in high-risk critical patients reduces the risk of VTE and related complications(6). However, several studies have demonstrated that some hospitalized patients receive inappropriate VTE prophylaxis(7). Inappropriate VTE prophylaxis increases adverse complications(8). VTE guideline recommendations produced by the American College of Chest Physicians (ACCP) are considered to be given appropriate VTE prophylaxis in nonsurgical patients(9).
Multi-faced interventions have been attempted to improve appropriate VTE prophylaxis in different patient populations(10). This intervention strategy includes education intervention, increasing delivery of ordered prophylaxis, reduced use of central venous catheters, enhanced mobility, Audit and feedback, pock guideline distribution, care pathway, checklists, electronic alerts in digital medical records, prescription reminder, pre-established orders, and order sets embedded VTE prevention protocol(10–14). Improving appropriate VTE prophylaxis is multifactorial. clinicians should assess patient risk for VTE and prescribe therapy appropriate for each patients’ risk profile, the patient should accept the prescribed therapy, and nurses must administer the therapy as prescribed. First, an ideal, proper VTE prophylaxis process measure requires; 1-documentation of a standardized VTE risk assessment; 2-prescription of optimal, risk-appropriate VTE prophylaxis; and 3- administration of all risk-appropriate VTE prophylaxis as prescribed(15).

A systematic review and meta-analysis study have indicated that introducing CDSS increases VTE-appropriate prophylaxis in surgical patients(16). Mandatory computerized CDS tool for VTE prophylaxis in trauma patients significantly improves compliance with VTE prophylaxis guidelines(17). CDSS for VTE prophylaxis in surgical patients increase compliance to the guideline but did not significantly alter VTE outcome(18). Prior knowledge-translation (KT) interventions applying “high-tech” approaches, such as electronic alerts, electronic CDSS, and computerized provider order entry(CPOE) systems, have improved compliance with clinical guidelines(19). A computerized alert system improves appropriate VTE prophylaxis and improves risk assessment documentation. However, the Adoption computerized alert system for improving VTE prophylaxis rates is uncertain(20).

there is a gap between expert recommendations and clinical practice in VTE prophylaxis in nonsurgical patients worldwide, yet (9, 21–24). Thus, the rate of adherence to evidence-based practice of VTE prophylaxis is inadequate in the nonsurgical population. Consequently, the rate of VTE in nonsurgical patients is high. Yet, hospital-acquired VTE is a global challenge(25).

CDS tools improve evidence-based medicine to patient care(26), especially improve the implementation of VTE prophylaxis guidelines. Nevertheless, there is not research investigate the effect of CDS for recommendation prophylaxis on appropriate VTE prophylaxis in nonsurgical ICU patients in Iranian hospital. despite CDS clear advantages in the world, the effects of CDSS within the CPOE system on appropriate prophylaxis for nonsurgical ICU patients remain uncertain. In addition, our previous study indicates that CDS for recommendation VTE prophylaxis has reached high priority to implementation within CPOE in ICU, based on CDS committee consensus in Iran(27). Still, there is a gap between expert recommendations and clinical practice in VTE prophylaxis in a nonsurgical ICU patient in Iranian hospital. Therefore, we conducted a study aimed at assessing the impact of real-time computerized CDSS on the use of appropriate prophylaxis for VTE among nonsurgical ICU patients in a southern Iran.

Methods
All methods were conducted accordance with (Strengthening the Reporting of Observational studies in Epidemiology) STROPE guidelines for this study. This is a cross-sectional study to assess the effect of a real-time CDSS for recommendation VTE prophylaxis within CPOE on adherence to VTE prophylaxis guideline in nonsurgical patients. This study was conducted at the three ICUs (General ICU, Central ICU, and Emergency ICU) of Nemazee hospital, which is located in Shiraz, and is the largest academic hospital in southern Iran. Data related to before intervention have been collected from April 20, 2020, to 21 November 2020 and post-intervention have been collected form 7 April 2021, to 9 July 2021. It is a teaching hospital, with 850 beds. Three ICUs of Nemazee hospital uses the homegrown electronic medical record (EMR) with a CPOE system since 2015. The Homegrown EMR implemented in Nemazee hospital has not equipment the VTE prophylaxis CDSS. In three ICUs serviced by one medical team, with similar services. All ICUs was administered by intensivists with a closed system. The inclusion criteria included nonsurgical patients aged over 18 years and having been hospitalized in General ICU, Central ICU, and emergency ICU of Nemazee hospital. another hand pregnancy, and surgical patients and patients’ current use of anticoagulation were excluded because surgical and pregnancy populations were used different guidelines.

For Real-Time computerized clinical decision support systems on the use of Appropriate Prophylaxis for VTE in nonsurgical patients’ intervention

**First step:**

modified VTE prophylaxis guidelines nonsurgical for use at ICU in Iran. Intensivists (three individuals), clinical pharmacy (one individual), and health informatics (two individuals) from Shiraz University of Medical Science(SUMS) were invited to attend the panel. In three sessions panel members discuss VTE prophylaxis guideline use in Iran. VTE risk assessment model and appropriate prophylaxis in nonsurgical patients at ICU in Iran country and contraindication of VTE prophylaxis was modified and established by this panel. Local VTE prophylaxis guidelines based on American College of Chest Physicians (ACCP) prophylaxis in nonsurgical patients are being in the supplementary file. Appendix 1.

**The second step**

design, development, and implement CDS for recommendation VTE prophylaxis within the CPOE system. Common UML (unified model language) diagrams included use case, activity diagram, and sequence diagram were designed for the VTE prophylaxis CDSS (as can be seen in UML diagrams in supplementary file2 appendix 2). The knowledge base of VTE prophylaxis CDSS in nonsurgical patient consists of 26 rule sets. After that, the VTE prophylaxis CDSS was developed in CPOE (as can be seen in Screen of this CDSS in supplementary file3 appendix 3). In the next step, chairman of the ICU and CDSS committee in the hospital was assessment and tested the VTE prophylaxis CDSS. All major bugs or changes in functionality or content have been fixed after the testing system. After approval VTE prophylaxis system by the CDS committee, all end-users (clinicians) have been trained to use the VTE
prophylaxis CDSS in class and one by one. Finally, the VTE prophylaxis CDSS has been installed in three ICUs of Nemazee hospitals. The physician has completed the VTE risk factors checklist and contradiction document for the nonsurgical patient, then CDSS based on VTE risk score, contraindication VTE prophylaxis, patient weight, and renal functions recommended VTE prophylaxis order sets. The content of VTE prophylaxis CDS was changed by consensus of the CDS committee includes three ICU attending, a clinical pharmacist, and two health information management specialists. The unexpected bug in the VTE prophylaxis CDSS resolves each day.

The third step

The researcher’s measurement clinician adherence to VTE prophylaxis guidelines in nonsurgical patients after implemented VTE prophylaxis CDS. The pharmacist in the research team evaluated adherence to VTE prophylaxis guidelines in nonsurgical patients.

A VTE risk assessment model for hospitalized nonsurgical patients, the Padua Score, has been established and recommended using the 2012 ACCP evidence-based clinical practice guideline for VTE prevention in nonsurgical patients (9). This tool includes 11 risk factors including age, Body Mass Index (BMI), history of VTE, a surgical procedure during present hospitalization, acute myocardial infarction or ischemic stroke, presence of malignancy, heart or respiratory failure, and hormonal treatment. The score of each VTE risk factor in nonsurgical patients recommended VTE prophylaxis based on VTE score, and contraindication of each VTE prophylaxis is presented in the supplementary file. appendix 1. A Padua Prediction Score was calculated for each patient. The patient was identified as high risk if they had a calculated score > 3.

Variables that were collected from the patients' interviews and completed from the medical file for all patients from the adult ICU included demographics (age, and sex), ICU length of stay, mortality in ICU, and risk factors of VTE.

For the baseline period, researchers reviewed each patient’s medical record to collect the following VTE-related variable: provider documentation of Padua risk stratification, patient VTE risk factors, contraindications to pharmacological prophylaxis, and written orders for prophylaxis within 24 h of admission. For the post-implementation period, these variables were extracted directly from the EMR and CPOE system. Compliance with appropriate best practice VTE prophylaxis guidelines was defined as adherence to local VTE prevention algorithm. The primary outcome was appropriate VTE prophylaxis or adherence to the local VTE prophylaxis algorithm. The secondary outcome was ICU mortality and ICU length of stay.

Continuous variables are summarized with means and standard deviation, and categorical variables are summarized with numbers and proportions. Adherence to VTE prophylaxis guidelines in the group without VTE prophylaxis CDS compared to the group using CDSS for recommendation VTE prophylaxis, by using the 2-sided $X^2$ test for categorical variables and Student t-test was used to the evaluated effect
of CDS on appropriate VTE prophylaxis and patient’s outcome. Value of $P < 0.05$ was considered statistically significant. All statistical analysis was performed by SPSS version 24.

**Results**

Two hundred two patients have participated in the study (175 individuals in the pre-implementation group, 27 individuals in the post-implementation group). Table 1 presents characteristics of patients who are admitted in ICUs in pre-intervention and post-intervention groups over study periods. The mean age of the population in the pre-intervention group was $52.61 \pm 20.21$. While the mean age of the population in the post-intervention group was $55.11 \pm 16.17$. The mean of VTE risk scores in the pre-intervention group was lower than the post-intervention group (2.59 vs 3.67). Detail of patient baseline demographic data in pre and post-implementation groups are represented in Table 1.

| Baseline data                             | Pre-intervention | Post-intervention |
|-------------------------------------------|------------------|-------------------|
| All admission in the study period (N;%)   | 175(86.6%)       | 27(13.4%)         |
| Age (Mean; SD)                            | $52.61 \pm 20.21$| $55.11 \pm 16.17$|
| Gender (Female %)                         | 75(42.90%)       | 16(59.3%)         |
| Gender (Male %)                           | 100(57.10%)      | 11(40.7%)         |
| Weight (Mean; SD)                         | $72.74 \pm 16.53$| $79.11 \pm 11.27$|
| Height (Mean; SD)                         | $168.72 \pm 8.56$| $167.89 \pm 7.17$|
| Creatinine (Mean; SD)                     | $1.43 \pm 0.97$  | $1/52 \pm 0/84$   |
| VTE risk score (Mean; SD)                 | $2.59 \pm 2.75$  | $3.67 \pm 2.69$   |

Figure 1 presents the frequency of each VTE risk factor in the pre-implementation and post-implementation groups. Reduced mobility, heart and/or respiratory failure, and age over 70 years were three top common VTE risk factors in the pre and post-implementation group.

Table 2 shows the frequency of VTE prophylaxis orders pre and post-implementation CDSS for recommendation VTE prophylaxis within CPOE in Adult ICUs of a large academic hospital. The results show that most patients received heparin in the pre-intervention group (CPOE without CDSS for recommendation VTE prophylaxis) (56.9%). While in the post-intervention group (CPOE with CDSS for recommendation VTE prophylaxis) a large percentage of patients received Enoxaparin (59.2%).
Table 2
Frequency VTE prophylaxis pre and post-intervention (CDSS for recommendation VTE prophylaxis within CPOE) in adult ICUs of large Academic Hospital

| VTE prophylaxis                  | Group                  | Pre-Implementation | Post-Implementation |
|----------------------------------|------------------------|--------------------|---------------------|
| Early Ambulation                 | 1(0.6%)                | 0(0.0%)            |
| Sequential Compression Device (SCD) | 6(3.4%)               | 0(0.0%)            |
| Heparin 5000 units BID           | 88(50.3%)              | 10(37.0%)          |
| Heparin 5000 units TID           | 11(6.3%)               | 1(3.7%)            |
| Enoxaparin 40 mg QID             | 9(5.1%)                | 7(25.9%)           |
| Enoxaparin 40 mg BID             | 1(0.6%)                | 0(0.0%)            |
| Enoxaparin 60 mg QID             | 9(5.1%)                | 8(29.6%)           |
| Enoxaparin 60 mg BID             | 6(3.4%)                | 0(0.0%)            |
| None                             | 44(25.1%)              | 0.0%               |
| Enoxaparin 60 mg QID & SCD       | 0(0.0%)                | 1(3.7%)            |
| Total                            | 175(100%)              | 27(100%)           |

The results show that the proportion of patients receiving appropriate VTE prophylaxis was an increase after introduced CDSS for recommendation VTE prophylaxis within CPOE. Table 3 summarizes how the CDSS for recommendation VTE prophylaxis within CPOE effect on guideline compliance rate in ICU. The total VTE prophylaxis recommends by the CDSS was 27 smart VTE prophylaxis order sets. The percentage of no adherence to VTE prophylaxis guidelines in nonsurgical patients after implementation of CDSS for recommendation VTE prophylaxis declined from 51.4–22.2%. In contrast, the adherence rate to VTE prophylaxis guidelines after the implementation CDSS for recommendation VTE prophylaxis increased by 29.2%. Detail of performance of CDS for recommendation VTE prophylaxis is represented in Table 3.
Table 3
Performance of a CDSS for recommendation VTE prophylaxis within CPOE in ICUs of a large academic hospital

| Group                                         | Pre-Implementation | Post-Implementation | P-Value |
|-----------------------------------------------|--------------------|---------------------|---------|
| Adherence to VTE Prophylaxis Guideline in nonsurgical patients | No | 90 (51.4%) | 6 (22.2%) | 0.005 |
|                                                | Yes | 85 (48.6%) | 21 (77.8%) |       |
| Total                                         |     | 175 (100.0%) | 27 (100.0%) |       |

Table 4 represents how the CDSS for recommendation VTE prophylaxis affects the patient outcome in ICUs. The results show that the mortality rate in ICU, and length of stay in ICU was not significantly changed after implemented the CDSS for recommendation VTE prophylaxis within the CPOE system (p-value = 0.88, and 0.49).

Table 4
Comparison of patient outcome pre and post-intervention (CDSS for recommendation VTE prophylaxis within CPOE) in ICU of large academic Hospital

| Patient Outcome measurement | Pre-intervention | Post-intervention | P-value |
|-----------------------------|------------------|-------------------|---------|
| The mortality rate in ICU (N;%) | 20 (13.80%) | 4 (14.80%) | P value = 0.88 |
| Length of stay in ICU (mean; SD) | 13.66 ± 13.66 | 13.63 ± 9.81 | P value = 0.49 |

Discussion

It was the main purpose of the study to draw attention to the effects of VTE prophylaxis CDSS for recommendation VTE prophylaxis on guideline compliance rate in nonsurgical patients at ICU. Our results describe for the first time the effects of a web-based CDSS for recommendation VTE prophylaxis within the CPOE system on guideline compliance rate in nonsurgical patients at ICU in Iran. This is an important finding in the understanding of the effects of web-based CDSS for recommendation VTE prophylaxis order set within CPOE system in nonsurgical patients at ICU of the large academic hospital in southern Iran can avert inappropriate prophylaxis prescription without effects on patient’s outcomes. Also, the main finding indicates that the CDSS for recommendation VTE prophylaxis within the CPOE system improves clinician adherence to VTE prophylaxis guidelines in nonsurgical patients at ICU.

These results agreed with other studies which have shown that VTE prophylaxis CDSS for recommendation prophylaxis order set within CPOE system can improve appropriate VTE prophylaxis in nonsurgical patients at ICU, but the incidence of adherence to VTE prophylaxis guideline is a variety from country to country(29–33). In contrast to some reports in the literature, Eijgenraam and their colleagues
found that after the introduction of VTE prophylaxis CDS did no significantly improve adherence in guideline VTE prophylaxis in nonsurgical patients(34).

This finding was quite unexpected that the CDSS for recommendation VTE prophylaxis within the CPOE system has not affected ICU mortality rate and ICU length of stay. These results consist with other studies which have shown that CDSS for recommendation VTE prophylaxis within CPOE system improves tailored prophylaxis order in nonsurgical patients without effect on patient outcome (18, 30, 35). An important implication of this finding is that an electronic CDSS for recommendation VTE prophylaxis within CPOE System can improve appropriate prophylaxis without effects on patient outcome. Despite the CDSS improve adherence to clinical guidelines, it is maybe a negative effect on physician skills, for example, physician excessive confidence in the CDSS(36). Recommender system in medicine potential to engage users to change their behavior(37). A recent study found that drug recommender systems assist healthcare professionals in select accurate medication(38). Health recommender systems have emerged as high-tech approaches to assist clinicians to make better prevention-related decisions(38). Overall this system improves clinical management and filtered VTE prophylaxis order set based on context, as considered facilitator factor to clinician acceptance medication-related CDSS(39).

The main strength of our study was that web-based CDSS for recommendation VTE prophylaxis integrated into homegrown EMR. End-user involved in developing the content of CDSS for recommendation VTE prophylaxis engine for nonsurgical ICU patients improve successful CDSS system. these results demonstrated that CDSS for recommendation prophylaxis order engine within CPOE in nonsurgical ICU patient improve appropriate and tailored medication and VTE prophylaxis. To our best knowledge, our study was the first time to address the effect of the CDSS for recommendation VTE prophylaxis engine within CPOE in nonsurgical ICU patients of academic general hospital in Iran. However, the study had some relevant limitations. The most important limitation related to the sample size because this system was executed in a single center. In addition, this system was not integrated into EHR, because there is no EHR in Iran currently. Thus, this CDSS for recommendation VTE prophylaxis engine within CPOE cannot retrieve patient medication and disease history from EHR. Thus, medication and disease history was not uploaded to the current system at the patient admission time in the ICU of Nemazee hospital. We also have to take into account that our study could have been affected by location bias and suffered from a lack of randomized study.

Finally, the web-based CDSS for recommendation VTE prophylaxis engine within CPOE was tested and validated in ICU at a single general teaching hospital in a developing country; therefore, the implementation of the CDSS for recommendation VTE prophylaxis engine easily can be generalized to healthcare center which admitted nonsurgical patients at a province or national level.

**Conclusion**

This paper has clearly shown that the introduced CDSS for recommendation VTE prophylaxis within CPOE in ICUs assists providers to select the most tailored VTE prophylaxis for nonsurgical patients in ICU.
In addition, introduced CDSS for recommendation VTE prophylaxis improve adherence to VTE prophylaxis guidelines in nonsurgical ICU patients. The findings have approved the great potential of the CDSS inappropriate treatment. Therefore, it can be useful for using the CDSS at point of care. Further study needs to evaluate introduced CDSS for recommendation VTE prophylaxis in nonsurgical patients in the province and national level. Furthermore, the evaluated effect of an expert VTE prophylaxis system on appropriate VTE prophylaxis in nonsurgical patients would be of interest.

**Abbreviations**

VTE = Venous Thromboembolism, ICU = Intensive Care Unit, EMR = Electronic Medical Record, APACHE = Acute Physiology and Chronic Health Evaluation, SPSS = Statistical Package for the Social Sciences, ACCP = American College of Chest Physician, DVT = deep vein thrombosis, IRB = Institutional Review Board, AHRQ = Healthcare Research and Quality, CVA = Cerebral Vascular Accident, SUMS = Shiraz University of Medical Science.

**Declarations**

**Ethics approval**

The study was approved by the local Institutional Review Board and ethics committee of Shiraz University of Medical Science (SUMS) ([Approval ID: IR.SUMS.REC.1398.1046](#)). The safety and security of the CDSS are assurance. Only authorized providers can access the CDSS. All user was training for use system.

**Informed consent:**

Not applicable.

**Confidentiality**

According to the SUMS agreement, anonymity of patients is maintained by de-identification data. Only researchers or authorized personnel can access the data. To comply with SUMS and Nemazee hospital data security regulations, only research team can access patients and providers’ information. SUMS and Nemazee Hospital security approved the investigation protocol.

**Data Availability Statement**

All relevant data are presented in the article, further required can be directed to the corresponding author (sharifianr@sums.ac.ir).
Competing Interests
The authors declared no potential conflicts of interest to the research.

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Author’s Contribution
MK: conceptual and design study, data acquisition, data analysis, drafted and revision paper. FZ: contributed to conceiving and design of the study, interpretation of data, commented on drafts, and made significant revisions to the paper. AV: contributed to design of the study, interpretation of data, commented on the draft, and made significant revisions to the paper. NB: contributed to the design of the study, statistical analysis, commented on drafts, and made significant revisions to the paper. RSH: contributed to the design of the study, interpretation of data, commented on drafts, and made significant revisions to the paper.

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Figures
Figure 1

frequency of VTE risk factors in pre and post implementation CDSS for VTE prophylaxis recommendation groups

Supplementary Files

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