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Adherence to Venous Thromboprophylaxis Guidelines for Medical and Surgical Inpatients of Teaching Hospitals, Shiraz-Iran

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Background: Venous thromboembolism (VTE) exerts a considerable burden on the health care systems. Although many practice guidelines have been developed regarding prophylaxis and treatment of venous thromboembolism, there is a large gap between the recommendations and the medical practice in health care centers. In this study, we tried to assess adherence of the medical team to guidelines for venous thromboprophylaxis in medical and surgical wards of teaching hospitals affiliated to Shiraz University of Medical Sciences.

Materials and Methods: In this cross-sectional descriptive study, a total number of 500 patients were recruited among hospitalized patients in neurosurgery, orthopedics, general surgery, internal medicine, and obstetrics & gynecology departments and surgical and medical intensive care units. Afterwards, adherence to thromboprophylaxis guidelines was assessed by comparing the medical records of patients with proper indications extracted from the American College of Chest Physicians Guidelines for VTE prophylaxis (ACCP, 9th edition). In other words, for each patient a comparison between proper indications of receiving thromboprophylaxis and the regimen used in practice was made.

Results: Out of 472 patients assessed with respect to the appropriateness of the administered prophylaxis, 212 (45.1%) had received proper type of thromboprophylaxis with regard to ACCP guidelines. Orthopedic surgical wards showed the highest rate of appropriateness while neurosurgical wards showed the lowest rate of adherence (76% vs. 1.8%). The overall rate of inappropriateness was 54.9% (260 patients). Inappropriateness was divided into 3 categories: 1) patients had absolute indications to receive thromboprophylaxis but were not provided with any type of prophylaxis in practice (171 patients, 36.2% of total), 2) in presence of absolute indications, incorrect type of prophylaxis was administered (52 patients, 11% of total), 3) in absence of indications for thromboprophylaxis, patients received some forms of prophylaxis (35 patients, 7.4% of total).

Conclusion: The findings of the present study showed that prophylaxis are not properly utilized and physicians' practices vary considerably among different specialties.

Key words: Venous thromboembolism, Thromboprophylaxis, Guideline adherence

INTRODUCTION

Pulmonary embolism (PE) and deep vein thrombosis (DVT), collectively known as VTE, are significant causes of disability and death around the world. VTE is the most common vascular disease following acute myocardial infarction and stroke having an estimated annual incidence of 0.1% and affecting 2% to 5% of the population during their lifetimes (1).

VTE exerts considerable burden on the health care systems (2, 3). As an example, VTE resulted in approximately 300,000 hospitalizations and at least 50,000 deaths per year in the United States in 2005 (4,5). In addition, among patients adequately treated for VTE, thromboembolism may recur in 5% at three months and up to 30% at eight years (6, 7). It has been suggested that, in DVT patients alone, nearly $500,000 in health care costs could be prevented per 100 patients per year if patients were properly screened and treated, emphasizing the importance of timely screening and treatment of VTE (2).

Although many practice guidelines have been developed regarding prophylaxis and treatment of VTE (8), there is a large gap between the recommendations and the medical practice in health care centers (9-11). Even though many strategies have been proposed to improve the practice of VTE prophylaxis and treatment, it remains suboptimal (12-14). In Iran, as in many other developing countries, little information describing adherence to VTE prophylaxis and treatment is available. It seems that strategies to increase the compliance to VTE prophylaxis and treatment guidelines should be evaluated in order to ensure patient safety. To our knowledge, there are few studies on the adherence of medical centers to proper prophylactic and therapeutic practice of antithrombotics in the Iranian hospitals (15,16).

Therefore, the present study was designed as a cross-sectional descriptive study with the aim of evaluating adherence to the 9th edition of ACCP guidelines for VTE prophylaxis in medical and surgical inpatients in teaching hospitals affiliated to Shiraz University of Medical Sciences.

MATERIALS AND METHODS

In this cross-sectional descriptive study, the duration of study was 4 months from February 2014 to May 2014. The study protocol was approved by the Ethical Committee of Shiraz University of Medical Sciences.

A total number of 500 patients were recruited among hospitalized patients in neurosurgery, orthopedics, general surgery, internal medicine and obstetrics & gynecology departments and surgical and medical intensive care units. The number of study subjects for enrollment was based on the objectives of our study with consideration of previous reports and presumption of a 5% error, 80% power and 10% quantity of effect. Subjects were selected using convenience sampling. The inclusion criteria were:

- Hospitalization more than 3 days in a certain ward.
- Negative history of receiving oral or intravenous anticoagulation therapy with indications other than thromboprophylaxis.

Patients with the following criteria were excluded:

- Patients under 16 years of age.
- Patients who had received recent fibrinolytic therapy.

Overall, 472 individuals were considered eligible for enrollment.

Measurements and Data Collection

Two data gathering forms with three parts were designed in order to obtain data from records of the studied individuals in surgical and non-surgical wards. In the first part, demographic characteristics of the studied individuals were recorded including age, sex, previous medical conditions, ward admission and duration and cause of hospitalization. In the second part, information regarding previous history of thromboembolic events and indications/contraindications for current prophylactic administration of anticoagulants, along with type of anticoagulants and possible complications of treatment was recorded. The third part included a thromboembolic risk assessment score and risk factors for major bleeding complications. Surgical wards included neurosurgery, orthopedics and general surgery while obstetrics & gynecology, internal medicine and intensive care units (surgical and non-surgical) were considered as non-surgical wards.

Data collection forms were completed by the first author during the study period. Medical records and clinical status of all patients were reviewed and data regarding VTE risk development for each patient was extracted. Using the Caprini's risk assessment score (appendix 1) and considering the risk factors for major bleeding complications in surgical patients (appendix 2), Pauda's VTE risk assessment score in non-surgical patients

(appendix 3) and a bleeding risk assessment score in non-surgical patients (appendix 4), each patient was evaluated in terms of being a candidate for receiving thromboprophylaxis. All admitted patients were assessed for VTE risk in accordance with 2012 ACCP guidelines (9th edition). The risk for VTE was considered in presence of predisposing conditions or clinical characteristics. Any type of prophylaxis (mechanical or pharmacologic) as indicated according to the ACCP guidelines was defined as proper VTE prophylaxis compliance.

Afterwards, adherence to thromboprophylaxis guidelines was assessed through comparing medical records of patients and proper indications extracted from the latest ACCP guidelines.

Statistical Analysis

Abstracted data were coded and entered into statistical Package for Social Sciences version 18 (SPSS Inc., Chicago, IL, USA) and all analyses were performed using this package. Summary statistics including frequency, percentage, means and standard deviations were calculated to summarize the data. Data were presented as mean ± standard deviation (SD). The 95% confidence intervals for the mean values of data were calculated and the significance of differences between independent variables was assessed using independent t-test. Normally distributed continuous variables were compared using t-test. Categorical variables were compared using the Chi-squared test or Fisher's exact test. A two-sided P value <0.05 was considered statistically significant.

RESULTS

A total of 472 patients (221 males and 251 females) with a mean age of 52.6 ± 18.5 years (range 18 to 95 years) were included. Distribution of studied patients in different wards was as follows: internal medicine: 124 patients, 26.3%, general surgery: 92 patients, 19.5%, obstetrics and gynecology: 69 patients, 14.6%, orthopedics: 76 patients, 16.1%, neurosurgery: 56 patients, 11.9% and the intensive care unit: 55 patients, 11.7%.

Thromboprophylaxis was indicated for more than 92% (n=436) of the patients. There was a statistically significant difference between the studied wards in terms of presence of indications for thromboprophylaxis administration. Patients in obstetrics and gynecology ward had a lower likelihood of requiring thromboprophylaxis whereas those admitted to the neurosurgery wards and intensive care units had a higher likelihood of requiring thromboprophylaxis (Table 1). According to the ACCP guidelines, among the studied individuals, 226 had indications for low molecular weight heparin (LMHW), 93 for unfractionated heparin (UFH), 49 for mechanical thromboprophylaxis, 36 for either UFH or LMHW, six for concurrent UHF and mechanical thromboprophylaxis, 26 for concurrent LMHW and mechanical thromboprophylaxis and 36 had no indication for prophylaxis of VTE. There was a statistically significant difference between the studied wards in terms of type of indicated thromboprophylaxis (Table 2).

Table 1. Presence of VTE prophylaxis indication in different wards

Ward	Prophylaxis indicated number/ total (%)
Internal medicine	114/124(91.9%)
General surgery	86/92(93.5%)
Obstetrics and gynecology	57/69(82.6%)
Orthopedics	70/76(92.1%)
Neurosurgery	56/56(100%)
ICU	53/55(96.3%)
Total (%)	436/472(92.4%)

Table 2. Indicated type of VTE prophylaxis in different wards

Ward	Indicated thromboprophylaxis number (%)		
	LMWH	UFH	Others*
Internal medicine	31(25.0%)	56(45.2%)	37(29.8%)
General surgery	49(53.3%)	14(15.2%)	29(31.5%)
Obstetrics and gynecology	42(60.9%)	9(13.0%)	18(26.1%)
Orthopedics	70(92.1%)	0(.0%)	6(7.9%)
Neurosurgery	9(16.1%)	0(.0%)	47(83.9%)
ICU	25(45.5%)	14(25.5%)	16(29.1%)
Total	226(47.9%)	93(19.7%)	153(32.4%)

*Other types of indicated thromboprophylaxis were mechanical, concurrent UFH and mechanical, concurrent LMHW and mechanical or no indications at all.

LMWH and UFH were the two most widely used medications for prevention of VTE in the teaching hospitals administered for 186 (39.5%) and 116 (24.6%)

patients, respectively. Meanwhile, mechanical thromboprophylaxis alone or in conjunction with medical prophylaxis was not apparently used in the studied wards (Table 3).

Table 3. Administered type of thromboprophylaxis in different wards

Ward	Administered VTE prophylaxis n (%)		
	UFH	*LMWH*	*None*
Internal medicine	74(60.2)	13(10.6)	37(29.3)
General surgery	18(19.6)	28(30.4)	46(50)
Obstetrics and gynecology	4(5.8)	50(72.5)	15(21.7)
Orthopedics	1(1.3)	67(88.2)	8(10.5)
Neurosurgery	0(0.0)	1(1.8)	55(98.2)
ICU	19(34.5)	27(49.1)	9(16.4)
Total	116(24.6)	186(39.5)	170(35.9)

There were 36 (7.6%) patients who did not have indications to receive either regimens and should not have been treated; however, 170 (35.9%) patients did not receive prophylactic regimens in practice.

Out of 472 patients analyzed for appropriateness of the administered prophylaxis, 212 (45.1%) had received proper type of thromboprophylaxis according to the ACCP guidelines. The overall rate of inappropriateness was 54.9% (260 patients). Inappropriateness was divided into three categories (Table 4).

1. Patients had absolute indications to receive thromboprophylaxis but were not provided with any type of VTE prophylaxis in practice (170 patients, 35.9% of total).
2. In presence of absolute indications, incorrect type of prophylaxis was administered (54 patients, 11.4% of total).
3. In absence of indications for thromboprophylaxis, patients received some type of VTE prophylaxis (36 patients, 7.6% of total).

Of the studied wards, orthopedics followed by ICU and obstetrics/gynecology wards had the highest rate of appropriateness (77.6%, 65.5% and 54.4%, respectively). On the other hand, neurosurgical (98.2%) and general surgical wards (51.6%) had the highest proportion of patients who did not receive medical or mechanical prophylaxis although indications were present. Meanwhile, internal medicine wards (25%) and ICUs (14.5%) had the highest proportion of patients receiving the incorrect type of thromboprophylaxis. Finally, the appropriateness of the administered prophylactic regimens was not similar among the studied wards (P=0.000).

Table 4. Appropriateness of practiced thromboprophylaxis in different wards

Ward	Appropriateness		Inappropriate categories*		
	Appropriate N(%)	Inappropriate N(%)	1 N(%)	2 N(%)	3 N(%)
Internal medicine	48(38.7%)	76(61.3%)	36(29.0%)	31(25.0%)	9(7.3%)
General surgery	31(34.1%)	61(65.9%)	47(51.6%)	8(7.9%)	6(6.6%)
Obstetrics & gynecology	37(54.4%)	32(45.6%)	15(22.1%)	5(6.1%)	12(17.6%)
Orthopedics	59(77.6%)	17(22.4%)	8(11.6%)	2(2.6%)	7(8.1%)
Neurosurgery	1(1.8%)	55(98.2%)	55(98.2%)	0(.0%)	0(.0%)
ICU	36(65.6%)	19(34.4%)	9(16.4%)	8(14.5%)	2(3.6%)
Total	212(45.1%)	260(54.9%)	170(35.9%)	54(11.4%)	36(7.6%)

* Inappropriate categories were defined as:

1- Patients had absolute indications to receive thromboprophylaxis but they did not receive any type of VTE prophylaxis in practice

2- In presence of absolute indications, incorrect type of prophylaxis was administered

3- In the absence of indications for thromboprophylaxis, patients received some VTE prophylaxis

Of 472 patients studied, 290 were analyzed regarding risk level of thromboembolic events considering the Caprini's risk assessment score. Study subjects hospitalized in general surgical, orthopedics, neurosurgery and obstetrics and gynecology wards were analyzed and 19 (6.6%) patients were marked as low risk, 108 (37.2%) as medium risk and 163 (56.2%) as high risk. A statistically significant difference was noted between the study wards in terms of distribution of medium and high-risk patients (P=0.000). More than 93% of neurosurgery and general surgery patients were medium to high risk compared to a value of 85% in obstetrics. Appropriateness of thromboprophylaxis increased among the studied individuals as the Caprini's risk increased i.e. 21.2% of low risk, 33.33% of medium risk and 55.2% of the high risk patients received appropriate prophylaxis (P=0.000).

DISCUSSION

VTE prophylaxis has shown to be the number one patient safety intervention in patients at risk. Thromboprophylaxis reduces adverse patient outcomes, is safe and decreases the overall costs (17).

As mentioned earlier, more than 90% of the studied patients had indications to receive thromboprophylaxis according to the ACCP guidelines, which indicates that a relatively high-risk patient population was studied here. Other studies have reported a range of 75–80% for patients at risk of VTE (18, 19). In a multinational study by Cohen et al, approximately 51% of all hospitalized patients were at risk of VTE based on the 2004 ACCP guidelines (10). This relatively high proportion of patients at risk in our study may have two reasons: First, difference in definition of at risk patients in our study in comparison to the mentioned studies, second, our university hospitals are large referral centers covering the entire southern population of the country.

Despite high percentage of patients at risk, only 45.1% were prescribed with appropriate prophylaxis indicating a relative underutilization of thromboprophylaxis in our university hospitals. Broken down by wards, appropriateness of the administered thromboprophylaxis regimen ranged from 1.8% in neurosurgical patients to 76% in orthopedic wards.

Some differences between various wards may be explained by physicians' knowledge of appropriate thromboprophylaxis as demonstrated by Bikdeli et al, in PROMOTE study (20). In addition, 1.8% appropriateness in neurosurgical wards may be caused by the fact that these patients had indications to receive mechanical thromboprophylaxis in most cases (84%), yet our university hospitals were incapable of providing intermittent pneumatic compression devices due to limited resources. In neurosurgery patients who should have received pharmacologic prophylaxis (16%), the treating physicians' concern about the risk of bleeding after surgical interventions may be the cause of inappropriate practice. This issue may further be confirmed by the relatively lower rate of appropriateness in surgical wards (34%) comparing to the intensive care units (65%), internal medicine (38%) and obstetric wards (54%). Similarly, reports around the world also show that mechanical thromboprophylaxis is not widely used (21); although ACCP recommendations suggest that mechanical methods be used in patients in whom there is a contraindication for anticoagulant prophylaxis (22). An international study revealed that the availability of intermittent compression device was very low, and it was rarely used in participating centers outside of the United States (21).

We propose that considering the reassuring meta-analyses and randomized control trials (23-25), which demonstrate little or small increases in the absolute risk of major bleeding with the use of LMWH, this concern of surgeons should be eliminated by continuous education. Finally, it should be mentioned that the latest ACCP guidelines have declared that in high risk spine and skull surgeries, VTE thromboprophylaxis can be undertaken until proper hemostasis is achieved by the third or fourth day following the surgery (as proper practice) (26) and LMWH can be administered afterwards. Therefore, neurosurgeons were somehow correct, not prescribing

pharmacologic thromboprophylaxis. However, our neurosurgery patients did not receive prophylaxis even after the fourth day of surgery leading to low rate of appropriateness.

We reported an overall appropriateness rate of 45.1%, which is within the reported range of 3%-91% in different studies around the world (10,11, 15-16, 27-30). Excluding those studies with a very low or very high rate of appropriateness, most of the reports are within a range of 30-60% for VTE prophylaxis appropriateness (10) including our own study.

Other studies have also declared that the most common reason for under prescription of thromboprophylaxis appears to be lack of awareness of both the disease and evidence-based guidelines (31, 32). Many practitioners believe that VTE is not a common diagnosis (based on their own clinical experience) and prevention may not be indicated in the majority of cases. Yet, one should consider that the majority of VTE events are clinically silent and the condition remains under diagnosed.

LMHW was the most commonly used form of pharmacologic prophylaxis in total (39.3%), followed by UFH (24.6%) and no prophylaxis (39.5%). However a comparison between the studied wards revealed that, only in the internal medicine wards, patients had received UFH more commonly compared to LMWH (60.2% vs. 10.6%). Overall, these findings are compatible with the existing literature and are suggestive of a safety benefit with LMWH compared with UFH (33, 34). The relatively lower cost of UFH compared to LMHW explains why UFH was prescribed more commonly in the internal medicine wards. For the remaining surgical wards including orthopedics, LMWH was practiced more commonly than UFH as the ACCP guidelines recommend the use of LMWH for orthopedic surgery prophylaxis, emphasizing that the risk of heparin-induced thrombocytopenia is lower with LMWH prophylaxis than with UFH prophylaxis (35). It should be mentioned that in surgical wards and specifically orthopedics we could not monitor the post operation status of patients regarding receiving thromboprophylaxis after being discharged from the hospital. It seems that duration of prophylaxis was not long enough in these patients.

Appropriateness of VTE prophylaxis in different risk levels is another important aspect of our findings yet to be discussed. We indicated that high-risk patients had a greater rate of appropriateness compared to individuals in lower risk levels (55.2% vs. 22.1%). We hypothesize that this finding is mainly due to the fact that the majority of these high risk patients were older individuals with cancer diagnosis, having surgical interventions and these clinical scenarios had enough impact on physicians making them prescribe some forms of thromboprophylaxis. Still, a large group of high-risk individuals did not receive proper VTE prophylaxis (44.8% of high risk patients) indicating that confusion still exists among the practitioners in administering proper agents. It is evident that a critical gap exists between the strong evidence in support of thromboprophylaxis in high-risk groups and its implementation in practice. Other studies have also shown that only 35 to 42% of patients in the highest risk groups receive prophylaxis (36-38). The complexity of the existing guidelines may also lead to the underuse of prophylaxis; we propose that educational initiatives should be taken into consideration to increase the awareness and understanding of management guidelines in our teaching hospitals (26).

Strengths and Limitations

Our study was the first cross-sectional descriptive study conducted in the Southern part of Iran regarding the appropriateness of VTE prophylaxis and adherence to guidelines. We studied a variety of different medical and surgical wards and made a comparison among these wards. Moreover, three different hospitals were included in the analysis, which increased the impact of our findings.

There were a number of potential limiting factors in our study. Relatively small number of studied subjects compared to the Western studies can be mentioned as the most important limitation. We did not investigate

specifically appropriate duration of thromboprophylaxis. Considering the small number of individuals with thromboembolic events, we could not draw associations between appropriateness of VTE prophylaxis and rate of DVT and further studies are required. Finally, it was not possible to determine the exact reasons underlying the lack of prescription of thromboprophylaxis for patients in whom prophylaxis was indicated.

CONCLUSION

The findings of the present study show that prophylaxis is not properly utilized and physicians' practices vary considerably among different specialties. It is evident that current practice could be improved through implementation of current evidence-based guidelines in hospitals. In addition, discussion and consensus with physicians along with continuing medical education and providing physicians with feedback on prescribing patterns could be appropriate corrective actions.

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Appendix 1

Caprini VTE risk assessment score

1 Point	**2 Points**	**3 Points**	**5 Points**
- Age 41-60 years - Minor surgery - Swollen legs - Varicose veins - Pregnancy or postpartum - History of unexplained or recurrent Spontaneous abortion - Oral contraceptives or hormone Replacement therapy - Sepsis (<1 month) - Serious lung disease, including Pneumonia (<1 month) - Abnormal pulmonary function - History of inflammatory bowel disease - Medical patient at bed rest	- Age 61-74 years -Arthroscopic surgery - Major open surgery (>45 minutes) - Laparoscopic surgery (>45 minutes) - Malignancy - Confined to bed (>72 hours) - Immobilizing plaster cast - Central venous access	- Age≥75 years - Family history of VTE	- Stroke (<1 mo) - Elective arthroplasty - Hip, pelvis, or leg fracture - Acute spinal cord injury (<1month)

Appendix 2

Risk factors for major bleeding complications

Active bleeding
Previous major bleeding
Known, untreated bleeding disorder
Severe renal or hepatic failure
Thrombocytopenia
Uncontrolled systemic hypertension
Lumbar puncture, epidural, or spinal anesthesia within previous 4 hours or next 12 hours
Procedure-specific risk factors
Abdominal surgery
Male sex, preoperative hemoglobin level, <13 g/dL, Malignancy,
Pancreaticoduodenectomy
Sepsis, pancreatic leak, sentinel bleed
Hepatic resection
Primary liver malignancy
Lower preoperative hemoglobin level, and platelet counts
Use of aspirin
Nonselective surgery
Older age, renal insufficiency
Thoracic surgery
Procedures in which bleeding complications may have especially severe consequences
Craniotomy, spinal surgery, spinal trauma, reconstructive procedures involving free flap

Appendix 3

Pauda's VTE risk assessment model for non-surgical patients

Cancer (3 points)
Previous history of thromboembolism (3 points)
Immobility (3 points)
Hypercoagulability state (3 points)
History of trauma and surgery in preceding month (2 points)
Age over 70 (1 point)
Cardiovascular or respiratory insufficiency (1 point)
Acute myocardial infarction or acute ischemic stroke (1 point)
Acute infection or rheumatologic disease (1 point)
BMI over 30 (1 point)
Acute or critically ill patient (1 point)

Appendix 4

Risk factors for major bleeding complications in non-surgical patients

Active peptic ulcer disease
History of gastrointestinal bleeding in recent 3 months
Platelet count less than 50,000 per microliter
Age over 80 years
Hepatic failure (INR over 1.5)
Renal failure (GFR less than 30 mL/min)
Hospitalization in intensive care units
Presence of a central venous catheter
Rheumatologic disorders
Presence of cancer
Male gender