Venous thromboembolism prophylaxis in hospitalized medical patients

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Abstract

Background: Venous thromboembolism (VTE) is the most common unpredictable cause of in-hospital death. Despite the fact that VTE prophylaxis has been proven to be efficacious and safe it remains underused. The aim is to determine the use of VTE prophylaxis in patients admitted to medical wards of the Division of Internal Medicine of the University Medical Centre Ljubljana.

Methods: On a pre-specified day, all patients hospitalized on the wards of the Division of Internal Medicine were assessed for VTE risk by Padua prediction score. According to the risk of VTE and contraindications for pharmacological prophylaxis the adequacy of VTE prophylaxis was determined by trained data abstractors. Doctors responsible for the patients' treatment were not aware of the study.

Results: 511 patients were enrolled (222 women and 289 men). VTE prophylaxis was not indicated in 245 patients; 17 (6.9 %) patients classified as being at low risk for VTE nevertheless received prophylaxis. A half of 266 (52.1 %) patients at high risk for VTE had a contraindication to pharmacological prophylaxis. In 133 at-risk patients without contraindications, VTE prophylaxis was prescribed correctly in 50 (37.6 %) patients, 11 (8.3 %) patients received wrong doses and 72 (52 %) at-risk patients did not receive any prophylaxis.

Conclusion: On the chosen day, VTE prophylaxis was appropriately used in 81 % of hospitalized patients on medical wards of the Division of Internal Medicine of the University Medical Centre Ljubljana. Since only 37 % of the patients at high risk for VTE received recommended VTE prophylaxis, our data reinforce the rationale to implement measures to improve these results.

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1 Introduction

Venous thromboembolism (VTE), pulmonary embolism (PE) and deep venous thrombosis (DVT) represent a great challenge to health care services and the affected individuals. Despite improved understanding of the disease and recent advances in diagnosis and treatment, the incidence of VTE has been increasing (1). In-patients develop VTE 100 times more often than the general

population (2). According to some estimates, 60 % of PE cases occur in hospitals (3). PE is the most common unpredictable cause of in-hospital deaths and kills as many as 10 % of hospitalised patients (4).

Risk factors for the development of VTE are more frequently present in patients treated in hospitals. The prevalence of VTE is related to the number of risk factors present. A minimum of three risk fractors are present in 19 % of in-patients (5). Asymptomatic VTE develops in nearly all patients with five risk factors, if left untreated (6). VTE was diagnosed in 25 % of patients at internal medical wards, and in as many as 40–60 % of patients with heart failure or stroke (7). Moreover, late sequelae of VTE, such as post-thrombotic syndrome and chronic thromboembolitic pulmonary hypertension, are knlown to increase morbidity rates and the financial burden. Risk-adapted VTE prophylaxis is a safe and simple method of prevention recommended in hospitalised patients (8) Despite clear evidence-based guidelines (9), VTE prophylaxis reportedly remains underused (10). A large-scale international study investigated the adequacy of VTE prophylaxis used at internal medicine and surgical wards. It was found that VTE prophylaxis was provided to only 60 % of patients hospitalised at surgical wards. At internal medicine wards the proportion of treated patients was even as low as 40 % (10). Similar studies conducted in several countries that followed this investigation yielded comparable results (11,13). They increased awareness of this serious issue that can be addressed by implementing the published recommendations. Several computer programmes and electronic reminders have been devleoped to alert the physicians to the need of using VTE prophylaxis (14,15).

Table 1: Padua prediction score (16).

Risk factors	Score
Active cancer	3
Previous VTE (exc. superficial venous thrombosis)	3
Reduced mobility	3
Hereditary or acquired thrombophilia	3
Trauma and/or surgery within 1 month before admission	2
Age (≥ 70 yrs)	1
Heart failure and/or pulmonary diseasse	1
Acute MI and ischaemic stroke	1
Acute infection and/or rheumatic disease	1
Obesity (BMI ≥ 30)	1
Hormonal therapy	1
Assessment for VTE risk factors:	
Low risk	< 4 points
High risk	≥ 4 points

VTE – venous thromboembolism; BMI – body mass index

The aim of this study was to investigate VTE prophylaxis practices at internal medicine wards of the University Medical Centre Ljubljana, and to determine the numberr of patients receiving appropriate VTE prophylaxis and the number of patients in whom VTE prophylaxis is not indicated.

2 Participants

All patients treated at the wards of the Division of Internal Medicine, University Medical Centre Ljubljana on a pre-specified day were included in the study. Data were retrieved from their medical records, as well as from examination results, when necessary. Also included in the study were patients admitted and patients discharged on the pre-specified day. Data were collected by independent data abstractors. Physicians responsible for the patients' treatment were blinded

to the time period of the study. The collected patient data included age, weight, height, BMI and length of hospital stay. The leading diagnoses were as follows: heart failure (functional class III or IV), respiratory infection, other acute heart disorders, acute non-infectious respiratory disease, other infections, active cancer, systemic inflammatory rheumatic disease, haematological disorder, neurological disease, renal disease, endocrine metabolic disorder, gastrointestinal/hepatobiliary disease and other medical diseases.

The study was approved by the Medical Ethics Committee of the Republic of Slovenia.

3 Methods

All patients were assessed for VTE risk factors. The Padua prediction score (Table 1) was used to identify medical in-patients at high risk (10 %) and those at low risk (< 0.5 %) of VTE (16). In patients with a hospital stay of < 3 days, the level of mobility related to their disease and the intended treatment was assessed.High-risk patients with a Padua risk score of ≥ 4 were candidates for VTE prophylaxis, provided that it was not contraindicated. Table 2 presents therapy that was considered appropriate prophylaxis for these patients.

Justifications for omission of thromboprophylaxis and several contraindications to its administration were investigated in all patients at high risk of VTE who received no therapy. Contraindications to the use of prophylaxis included current conditions or conditions which may develop during hospital stay and may increase the risk of bleeding, such as : intracranial haemorrhage, acute renal failure, bleeding on admission, known blood clotting disorder, thrombocytopenia (50×10^9 /L), blood pressure of > 230/120 mmHg, acute stroke, major intervention with moderate or high bleeding risk performed within the previous 24 hours or planned for the next 24 hours, and anticoagulant therapy administered for other reasons (10,17,18).

Considering indications and contraindications to thromboprophylaxis the patients were assigned to two groups, i.e. a group receiving appropriate prophylaxis and a group with incorrect prophylaxis. In some cases the prescri-

Table 2: Thromboprophylaxis dosage.*

Active ingredient	Dose	Dose with oGF < 30 mL/min
Unfractionated heparin	5000 IU s.c./12 h or 5000 IU s.c./8 h	unchanged
Dalteparin (Fragmin)	5000 IU s.c. /24 h	unchanged
Nadroparin (Fraxiparine)	0.6 ml s.c./24 h > 70 kg body weight 0.4 ml s.c./24 h < 70 kg body weight	tapered by 30 %
Enoxaperin (Clexane)	0.4 ml s.c./24 h	0.2 ml/24 h
Fondaparin (Arixtra)	2.5.mg s.c./24 h	contraindications
Mechanical prophylaxis	intermittent pneumatic compression device – both legs until normal mobility is achieved	

* all other doses are inappropriate

Table 3: Demographics of medical in-patients on a pre-specified day.

Ward	N	Age (yrs)		Hospital stay (days)		BMI (kg/m^2)	
		$\bar{x} \pm SD$	Min.–max. value	$\bar{x} \pm SD$	Min.–max. value	$\bar{x} \pm SD$	Min.–max. value
DIIM	10	75,6 ± 8.9	56.2–83.7	3.2 ± 4.4	0–14	25.7 ± 3.7	21.1–30.7
DEDMD	40	66.1 ± 15.7	37.0–95.6	8.2 ± 9.9	0–48	28.6 ± 6.1	18.2–41.8
DG	85	65.4 ± 17.4	19.4–95.4	8.0 ± 8.3	0–33	25.1 ± 5.1	15.6–37.5
DH	36	61.7 ± 15.9	18.5–88.0	21.0 ± 19.3	0–77	25.8 ± 4.5	16.0–37.9
DHyp	33	76.3 ± 10.7	46.0–91.3	12.8 ± 12.4	0–54	25.8 ± 4.1	18.5–32.4
MEU	6	86.6 ± 5.5	79.3–93.0	0.3 ± 0.8	0–2	24.3 ± 3.4	18.5–27.7
DC	136	68.5 ± 14.5	25.6–90.4	7.6 ± 9.9	0–70	27.5 ± 4.6	17.3–43.4
DVD	61	71.8 ± 12.0	33.3–92.1	8.5 ± 7.9	0–33	26.7 ± 3.9	20.4–38.1
DN	29	69.8 ± 12.7	42.8–87.5	12.0 ± 15.4	0–69	26.9 ± 4.7	13.1–35.7
TPU	21	76.6 ± 13.2	48.0–96.5	6.9 ± 7.2	0–26	28.5 ± 6.0	20.0–44.1
DPDA	12	71.0 ± 18.6	20.1–89.8	3.8 ± 7.2	0–26	24.7 ± 5.6	16.1–33.6
DR	25	67.6 ± 17.1	28.9–89.3	6.8 ± 6.4	0–20	24.0 ± 4.0	17.1–32.6
GMU	17	83.3 ± 9.1	62.8–99.1	5.6 ± 7.0	0–26	27.0 ± 8.2	13.4–49.3
Total*	511	69.5 ± 15.2	18.5–99.1	9.0 ± 11.1	0–77	26.5 ± 5.0	13.1–49.3

*- the number exceeds the number of beds because of admission and discharge on the same day; BMI – body mass index, DIIM – Dept.of Internal Medicine; DEDMD – Dept. of Endocrinology, Diabetes and Metabolic Disorders; DG – Dept. of Gastroenterology; DH – Dept.of Haematology; DHyp – Dept. of Hypertension; MEU – Medical Emergency Unit; DC – Dept.of Cardiology; DVD – Dept.of Vascular Diseases; DN – Dept.of Nephrology; TPU – Toxicology and Pharmacology Unit; DPDA – Dept.of Pulmonary Diseases and Allergy; DR – Dept.of Rheumatology; GMU – Geriatric Medicine Unit.

bed thromboprophylaxis was deemed unnecessary.

3.1 Statistical methods

The arithmetic mean, standard deviation and range data were calculated for demographics. For other data proportion of the whole was calculated.

4 Result

The study involved 511 patients, 222 women and 289 men. Patient demographics are shown in Table 3.

The majority of patients were admitted to hospital because of heart disorders, followed by infections and gastrointestinal diseases (Table 4).

Table 5 indicates the presence of risk factors based on the Padua prediction score.

Table 6 shows patients with contraindications to thromboprophylaxis. The most common contraindication was anticoagulant therapy for other causes, and past or planned major interventions associated with a moderate or high bleeding risk (19). The most frequent interventions included diagnostic or therapeutic arterial puncture for coronaro-

Table 4: Leading diagnoses on the pre-specified day

Diagnosis	No.of patients (%)
Heart failure (Class III or IV)	52 (10.2)
Other acute heart diseases	126 (24.6)
Acute non-infectious respiratory disease	29 (5.7)
Respiratory disease	29 (5.7)
Other infections	22 (4.3)
Active cancer	8 (1.6)
Systemic inflammatory disease (rheumatologic)	17 (3.3)
Haematological disease	36 (7.0)
Neurological disease	1 (0.2)
Nephrological disease	14 (2.7)
Endoctine metabolic disorder	21 (4.1)
Gastrointestinal/ hepatobiliary disease	78 (15.3)
Other medical diseases	78 (15.3)
Total	**511 (100)**

graphy and peripheral angiography with or without intervention.

Table 7 shows thromboprophylaxis practices at different departments. Appropriate therapy, which took into account all indications and contraindications, was administered to 414 patients (81 %). Thromboprophylaxis was omitted in 364 patients (71.2 % of all patients) because of reservations regarding therapy, or because of low VTE risk.

VTE prophylaxis was deemed necessary in 266 at-risk patients (52.1 %) with risk factors for VTE, but it was not used in half of these patients (133) because of contraindications to the therapy. In the other half without contraindications, appropriate thromboprophylaxis was provided to 50 of patients (37.6 %). Therapy with inadequate doses was administered to 11 of 133 patients (8.3 %). Thus, thromboprophylaxis was omitted in 72 of the 133 patients who should have received it (52 %) (Figure 1). It was prescribed to 17 of the 245 patients (6.9 %) who did not need it.

5 Discussion

This cross-sectional study was the first to investigate the appropriateness of thromboprophylaxis for VTE in patients hospitalised at the wards of the Division of Internal Medicine, University Medical Centre Ljubljana on a pre-specified day. Considering indications and contraindications to prophylaxis, appropriate therapy was administered to 81 % of patients. In 47.0 % of patients thromboprophylaxis was found to be unnecessary. Of the 52.1 % of patients who required thromboprophylaxis, one half were not eligible for the therapy because of contraindications to therapy. In another half appropriate prophylaxis was administered to solely 37.6 % of patients. The therapy proved unnecessary in 6.9 % of patients. The proportions, however, varied slightly from one ward to another.It should be pointed out that patient data were not comparable because of differences between the wards.

Table 5: No. of patients at risk for thromboembolism assessed by Padua Prediction Score.

Padua prediction score	0	1	2	3	4	5	6	7	8	9	10
No.of patients	34	91	60	60	97	97	44	19	8	0	1
Low risk < 4 points: 245 patients											
High risk ≥ 4 points: 266 patients											

Table 6: No.of patients with contraindications to thromboembolism on the pre-specified day

Contraindication	Petient no. (%)
Intracranial haemorrhage	0 (0)
Liver disease	7 (1.4)
Bleeding on admission	21 (4.1)
Diagnosed blood clotting disorder	1 (0.2)
Thrombocytopenia (< 50 × 109/L)	26 (5.1)
Blood pressure > 230/120 mmHg	0 (0)
Acute stroke	0 (0)
Major intervention associated with moderate or high bleeding risk performed within the past 24 hours or planned for the following 24 hours	35 (6.8)
Anticoagulant therapy for other reasons	117 (22.9)
Other	2 (0.4)
Total	**209 (40.9)**

According to the results of the ENDORSE study, which involved 358 hospitals across 32 countries, thromboprophylaxis was required in 40 % of all medical patients, of whom only 40 % were appropriately managed. The results are comparable to our data, but the ENDORSE study, published in 2008, was designed to assess prophylaxis practices and to enhance the use of thromboprophylaxis (10). Some countries published their national data, collected as part of the ENDORSE survey: in Poland (20) appropriate therapy was administered to 32 %of patients, in Hungary (21) to 28 %, and in Germany (22) to 70 % of all patients who required thromboprophylaxis.

A cross-sectional study, similar to ours, was conducted in several Swiss hospitals. The results showed that after exclusion of patients who were reciving therapeutic doses of anticoagulants, thromboprophylaxis was required in 58.7 % of patients,. The therapy was provided to 55.1 % of the patients needing VTE prophylaxis. In 17 % of all patients in the observed group the prescribed prophylaxis was not necessary (23). In a small Brazilian study, thromboprophylaxis was required in 42 % of patients. Appropriate therapy was given to 82.7 %. As many as 33.7 % of patients were treated unnecessarily (24), a significantly higher proportion compared to our study. In some surveys thromboprophylaxis was followed for a longer period of time. In a study conducted in Canada, prophylaxis was given to only 16 % of the 1,702 patients who required it (25). In an Italian study, which incuded 1,761 patients, thromboprophylaxis was administered to 80.5 % of all patients deemed to be at increased VTE risk. Among them 20.4 % were at high risk of bleeding. Bleedings occurred in only 0.9 % of patients and were not related to prophylaxis (26). Based on the Padua predicton score, a Padua study provided a systematical estimate of VTE risks and determined the role of risk factors in the development of VTE in hospitalised patients. The results of the study showed that thromboprophylaxis was required in 42.3 % of the 1,108 patients. Appropriate therapy was provided to 39.7 % of those patients (12).

In our study VTE risk was assessed on the basis of the Padua prediction score (16) as recommended by the current guidelines (9). Despite slight differences between the available risk assessment tools, they mostly deal with the same risk factors. Unfortunately, an ideal scoring system which would assess both, risks for VTE, as well as risks for bleeding related to thromboprophylaxis, is not yet available (27). However, the predictive value of risk assessment tools is superior to that of clinical judgement alone (28). In our study, we had reservation about the use of thromboprophylaxis in pati-

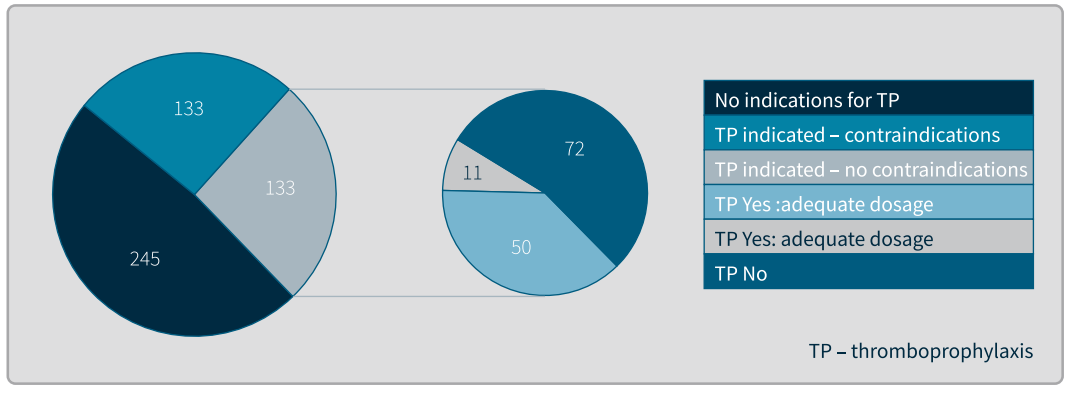

Figure 1: Appropriateness of VET prophylaxis provided to the studied in-patients. Patients with contraindications to prophylaxis assessed by the Padua prediction score (no.of patients)

ents receiving anticoagulant therapy for other causes, which greatly reduced risks of VTE. Other contraindications included invasive interventions done on the day of assessment, or interventions planned for the following day. The majority of similar studies have not defined invasive procedures as possible contraindications to the initiation of prophylaxis. In a recently reviewed scoring system inva-

Table 7: Prescribed thromboprophylaxis (by wards)

ward*	N	Prescribed thromboprophylaxis(N)		No hromboprophylaxis (N)		Appropriate N (%)	Inappropriate N (%)	Padua (N)	
		appropriate	inappropriate	appropriate	inappropriate			<4	≥4
DIIM	10	2		7	1	9 (90)	1 (10)	4	6
DEDMD	40	10	4	18	8	28 (70)	12 (30)	38	2
DG	85	10		65	10	75 (88)	10 (12)	57	28
DH	36			33	3	33 (92)	3 (8)	11	25
DHyp.	33	4	3	23	3	27 (82)	5 (18)	16	17
MEU	6	2		3	1	5 (83)	1 (17)	6	0
DC	136	5	3	104	24	109 (80)	27 (20)	63	73
DVD	61	11		47	3	58 (95)	3 (5)	30	31
DN	29		11	16	2	16 (55)	13 (45)	23	6
TFU	21	4	3	10	4	14 (67)	7 (33)	13	8
DPDA	12			11	1	11 (92)	1 (8)	9	3
DR	25	2	3	19	1	21 (84)	4 (16)	22	3
GMU	17		1	8	8	8 (47)	9 (53)	10	7
Total	**511**	**50**	**28**	**364**	**69**	**414**	**97**	**302**	**209**
%	**100**	**9.8**	**5.5**	**71.2**	**13.5**	**81**	**19**	**59.1**	**40.9**

*for abbreviations see Table 3

sive procedures are not included as contraindications to thromboprophylaxis because of the associated bleeding risk (17).In our study we had reservations about using prophylaxis in patients undergoing procedures associated with low bleeding risk, such as arterial puncture. This policy is arguable considering the low risk of bleeding (< 0.5 %) associated with thromboprophylaxis (7,26). Omitting prophylaxis may be sensible in major interventions with high bleeding risk. In our study, 81 % of patients were appropriatedly managed with all contraindications to prophylaxis being taken into account. These results are good compared to other reports, yet it should be pointed out that appropriate therapy was given to only 37.6 % of our patients who required prophylaxis without contraindications. The same results were reported in the ENDORSE study ten years ago (10). Even then some European countries boasted twice as many appropriately managed patients (22), and other countries reported considerable improvement, achieved by adopting appropriate prophylaxis strategies (12,13). Thromboprophylaxis is the basic treatment provided to hospitalised patients, yet according to several studies it tends to be omitted if there is no reminder system for clinicians. Electronic alerts to prevent VTE (29) have proved very effective. Risk assessment using an approved risk prediction system is imperative in all patients and should be done at regular intervals during hospital stay, i.e.on admission and when the patient's condition changes (12,13,30). Teaching using the lecture format has not proved effective (31), and neither have educational sessions conducted for clinicians on admission wards (15).

In this institution, no systematic training programme addressing prophylaxis practice has been conducted so far, and most likely, risk assessment scores are not regularly used. Given the importance of VTE prophylaxis, it would be sensible to adopt appropriate strategies used in hospitals with better results. Also, the introduction of electronic alert system and regular assessments of the achieved results are recommended.

This study has some limitations. Because of the cross-sectional study design the results presented reflect the situation at a single point of time (a pre-specified day) and it is not possible to infer from these results what was happening with the patients throughout the hospital stay. The appropriateness of the given prophylaxis was assessed by 13 experts. Before the appraisal they were given clear instructions in how to achieve uniformity of performance and adherance to established standards, yet a possible subjective bias in assessing appropriateness of VET prophylaxis cannot be completely ruled out.

6 Conclusion

In conclusion, this study showed that appropriate therapy was provided to only 37 % of all our patients requiring thromboprophylaxis. Our data agree with those reported by other authors a decade ago and reinforce the rationale to implement strategies to improve these results.

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