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Assessment of Venous Thromboembolism Prophylaxis in Neurological Patients with Restricted Mobility – VTE-NEURO Study

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ABSTRACT

The authors present the data of a medical registry which evaluated if the physicians assess VTE risk in stroke patients, during hospitalization period and at hospital discharge and if the thromboprophylaxis is used according to National Guidelines for VTE Prophylaxis. 884 patients with acute ischemic stroke patients were enrolled between June 2010 and December 2011, from 62 centers, 51.4% male and 48.6% female with mean age 70.07 years (68.25 years in the male group and 71.92 years in the female one). There were two co-primary endpoints: the percentage of patients at risk for VTE at hospital admission assessed by the physician, and the percentage of patients with risk factors for VTE that persist at hospital discharge from the total number of patients hospitalized with ischemic stroke. The secondary endpoints were: the percentage of hospitalized patients receiving prophylaxis according to the National Guidelines of VTE Prophylaxis from the total number of patients at risk of VTE, the percentage of hospitalized patients with VTE risk receiving recommendation for thromboprophylaxis at discharge, the duration and the type of VTE prophylaxis in hospitalized patients, the duration and the type of VTE prophylaxis at discharge.

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Results: *879 (99.4%) of the total number of patients at risk of VTE have received prophylaxis during hospitalization. The most frequently types of prophylaxis used during hospitalisation were LMWH in 96.3% of the patients and mechanic method in 16.6% that were in accordance with the National Guidelines of VTE Prophylaxis recommendations.*

Conclusions: *There is a clear improvement in both assessment and thromprophylaxis recommendation in acute stroke patients with restricted mobility at VTE risk and in our country. LMWH is preferred to unfractionated heparin for venous thromboembolism prophylaxis in this high-risk patient population in view of its better clinical benefits to risk ratio and convenience of once daily administration.*

Keywords: venous thrombosis embolism, ischemic stroke, low molecular weight heparins

INTRODUCTION

Venous thromboembolism (VTE) is a common complication in stroke patients. Venous thromboembolism (VTE) encompasses both deep vein thrombosis (DVT) and pulmonary embolism (PE). The incidence of VTE among patients with stroke is high, and PE remains the third-highest cause of case fatality in stroke. Stroke places patients at high risk of VTE (1).

Screening studies performed in cerebrovascular accidents prior to the era of routine prophylaxis have suggested that the prevalence of VTE may approach 10-75% (2). The risk of deep vein thrombosis in stroke hospitalized patients is between 20-50% (3). Pulmonary embolism account for 13-25% of early post stroke mortality. In addition, pulmonary embolism is the most common cause of death between 2 and 4 weeks from stroke onset.

Immobility is generally a key risk factor for VTE and as many as two thirds of patients will be immobile or require assistance with walking immediately after their stroke. One third will be non-ambulatory or require assistance at 3 months (1). Immobility due to stroke may be due to deconditioning and comorbidities including dementia, arthritis, and peripheral vascular disease. Systemic inflammation from cerebral injury (4-6) and infectious complications may also contribute to thrombosis risk (1).

In fact the degree of leg weakness and old age are the most widely documented risk factors for VTE in post stroke patients. In a multivariate analysis, the strongest association of risk factors was detected for the Barthel index (4) of 9 or less, which is correlated with both VTE and proximal deep vein thrombosis (5). In fact, all medical patients are at increased risk of VTE if they have had or are expected to have significantly reduced mobility for 3 days or more (6).

In addition to being a major risk factor for VTE, stroke is also a major risk factor for intracranial bleeding or, in the case of hemorrhagic stroke, hematoma expansion. The weighing of the benefits of thromboprophylaxis against the risks of hemorrhage is an ever-present challenge for the management of post-stroke patients care and necessitates a careful assessment of the available evidence (1).

The benefits of VTE prophylaxis have been seen in patients with acute ischemic stroke; low molecular weight heparin and unfractionated heparin are recommended in guidelines from expert consensus groups (7).

In Prevention of VTE after Acute Ischemic Stroke with LMWH (PREVAIL trial) was demonstrated that the LMWH enoxaparin was superior to unfractionated heparin (UFH) for VTE prevention in patients with acute ischemic stroke. In this trial, use of enoxaparin reduced the risk for VTE in these patients by 43% compared with UFH (10% versus 18%; relative risk, 0.57; 95% CI, 0.44 to 0.76; P 0.0001) and was associated with similar incidence of total bleeding and a small but significant increase in extracranial hemorrhage (1% versus 0%; P 0.015) (7).

In Romania there are quite few epidemiological data regarding stroke patients that need to receive or are receiving thromboprophylaxis. In ENDORSE study, in our country were included only 280 neurological patients out of the total number of 5714. Only 28 (2%) of them have received thromboprophylaxis, out of which only 21 (1%) according to ACCP 2004 guidelines (9).

In 2009, in Romania a group of experts has published the updated VTE prophylaxis guidelines (8), with the scientific agreement of Romanian Society of Neurology (the previous version has been published in 2007).

In the present registry was evaluated if the physicians assessed VTE risk in stroke patients, during hospitalization period and at hospital discharge and if the thromboprophylaxis is used according to National Guidelines for VTE Prophylaxis: "in patients with ischemic stroke and restricted mobility prophylactic doses of LMWH or UFH are recommended (grade 1A indication). If pharmacological thromboprophylaxis is contraindicated, mechanic methods are recommended (grade 1B") (8). ❑

METHODS

Patients

Patients were eligible for enrolment if they were 18 years or older with an acute ischemic stroke and restricted mobility (complete immobilization or immobilization with bathroom privileges due to any neurological disease) for 3 days or more. Exclusion criteria were: patients with contraindication to anticoagulant therapy; patients who refused to sign the Informed Consent Form; patients with haemorrhagic stroke. All patients provided written informed consent. The study was done according to the Declaration of Helsinki and local regulations. Approval for the study was obtained from National Ethic Committee and National Agency of Drugs for all sites (9).

(62 sites – the neurological wards from all around country, from university centers, medium and large cities, with maximum 20 patients/site).

Study design

This was a retrospective study for data collection during hospitalisation and a prospective multicentric, non-interventional study for follow up. Two visits were scheduled: V1 – at hospital discharge and V2 (on site or phone contact) - at 1 month after discharge.

There were two co-primary endpoints: the percentage of patients at risk for VTE at hospital admission assessed by the physician, from the total number of patients hospitalized with ischemic stroke and the percentage of patients with risk factors for VTE that persist at hospital discharge from the total number of patients hospitalized with ischemic stroke. The VTE risk factors were considered: restricted mobility (complete immobilization or immobilization with bathroom privileges due to any neurological disease) for 3 days or more, active cancer; age over 60 years; dehydration; known thrombophilia; obesity (BMI >30 kg/m$^{2)}$; one or more significant medical comorbidities (heart failure III/IV NYHA; respiratory failure; acute infectious disease); use of hormone replacement therapy; use of oestrogen-containing contraceptive therapy; varicose veins with phlebitis.

All the data recorded in CRF were performed based on the anamnesis and clinical examination from patients' medical files: demographic data, diagnosis at hospital admission and at discharge, past history related to VTE, VTE risk factors.

The secondary endpoints were the percentage of hospitalized patients receiving prophylaxis according to the National Guidelines of VTE Prophylaxis from the total number of patients at risk of VTE, the percentage of hospitalized patients with VTE risk receiving recommendation for thromboprophylaxis at discharge, the duration and the type of VTE prophylaxis in hospitalized patients, the duration and the type of VTE prophylaxis at discharge.

In this study were also evaluated the risk factors for bleeding: active bleeding; bleeding disorders; concurrent use of anticoagulants (INR >2); thrombocytopenia; uncontrolled systolic hypertension; previous haemorrhagic stroke and renal function.

No study drug was given in this study. The study did not interfere with the patient management, as decided between physician and patient. There was no restriction on pharmacological and other treatments.

Statistical analyses

The sample size calculation was based on the expected incidence of ischemic stroke patients assessed at risk of VTE (according to Shorr et al, Chest 2008;133:149-155 data) by their physicians: with an expected incidence rate of 70%, the inclusion of 884 patients would allow to measure a 95% confidence interval of this incidence with a precision rate of +/- 1.7%; taking into account 5% of non-evaluable patients, it was planned to include 900 patients, 95% CI.

The centers were neurological wards from all around country, from university centers, medium and large cities; there were maximum 20 patients/site.

Descriptive statistical analysis was performed. ❑

RESULTS

A total of 884 patients with acute ischemic stroke patients were enrolled between June 2010 and December 2011, from 62 centers, 51.4% male and 48.6% female with mean age 70.07 years (68.25 years in the male group and 71.92 years in the female one). Table 1 shows the diagnosis at hospital admission.

At hospital discharge the diagnosis was almost the same. Table 2 shows the diagnosis at discharge.

Primary endpoint

The first co-primary endpoint was to evaluate the percentage of patients assessed by the physician at risk for VTE at hospital admission from the total number of patients hospitalized with ischemic stroke and restricted mobility.

All the patients (884-100%) were assessed for VTE risk at hospital admission and considered at risk by their physicians. The following risk factors for VTE have been identified: restricted mobility (complete immobilization or immobilization with bathroom privileges due to any neurological disease) for 3 days or more in 90.7% of the patients, age over 60 years old in 84.2% of them, dehydration in 25.7% ; neoplasia – active cancer 3.6%; history of VTE 8.1%; hormone replacement therapy / use of oestrogen-containing contraceptive therapy 1.0%; chronic cardiac failure class III / IV NIHA 19.8%; respiratory failure 4.0%; severe acute infection / sepsis 5.3%; obesity (BMI >30 kg/m^2) 25.1%; inherited / acquired thrombophilia 2.6%; venae varicose 24.5% and central venous catheter in 0.5%. Figure 1 shows this distribution of risk factors in these patients at hospital admission.

The patients were also assessed for risk factors for bleeding. The following risk factors for bleeding have been identified at hospital admission: active bleeding in 0.2% of the patients, treatment with oral anticoagulants (INR >2) in 1.4%, thrombocytopenia <100000 / mm^3 in 0.3%, uncontrolled systolic hypertension in 8% of the patients, previous haemorrhagic stroke in 0.7% of them; no patients have had coagulation disorders.

The renal function has been evaluated in 870 patients and the mean value of serum creatinine was 0.9806 mg/dl.

The second co-primary endpoint was to evaluate the percentage of patients at risk for VTE at hospital discharge from the total number of patients hospitalized with ischemic stroke.

From the total number of 884 evaluated patients, 780 patients (88.2%) have been considered at risk of VTE based on the investigators assessment at hospital discharge. The following risk factors for VTE have been identified at hospital discharge: restricted mobility (complete immobilization or immobilization with bathroom privileges due to any neurological disease) for 3 days or more in 70% of the patients, age over 60 years old in 84.2% of them, dehydration in 7.9%, neoplasia – active cancer 4.2%, history of VTE 8%, hormone replacement therapy / use of oestrogen-containing contraceptive therapy 0.3%, chronic cardiac failure class III / IV NIHA 19.6%, respiratory

Diagnosis	N	%
Ischemic stroke	587	66.4%
Transient Ischemic Attack (TIA)	164	18.6%
Hemiplegia of non-determined etiology	133	15%

TABLE 1. Diagnosis at hospital admission.

Diagnosis	N	%
Ischemic stroke	594	67.2%
Transient Ischemic Attack (TIA)	179	20.2 %
Hemiplegia of non-determined etiology	111	12.6%

TABLE 2. Diagnosis at hospital discharge.

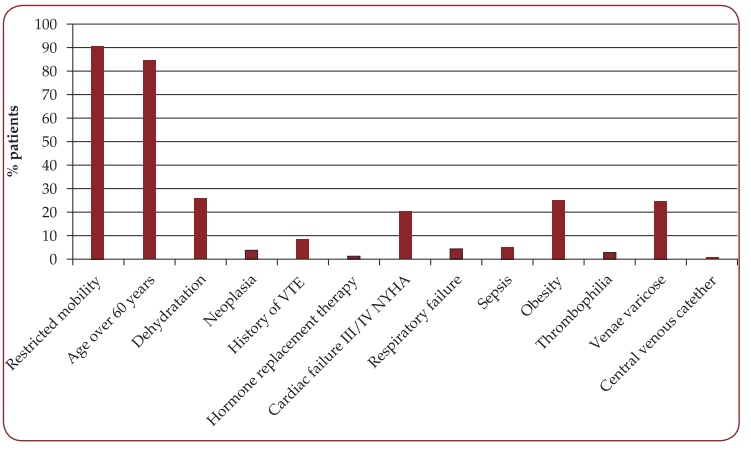

FIGURE 1. Risk factors distribution at hospital admission.

Restricted mobility means complete immobilization or immobilization with bathroom privileges due to any neurological disease for 3 days or more, neoplasia means active cancer; we also have included hormone replacement therapy and use of oestrogen-containing contraceptive therapy, severe acute infection and sepsis 5.3%, obesity means BMI >30 kg/m^2, thrombophilia inherited / acquired.

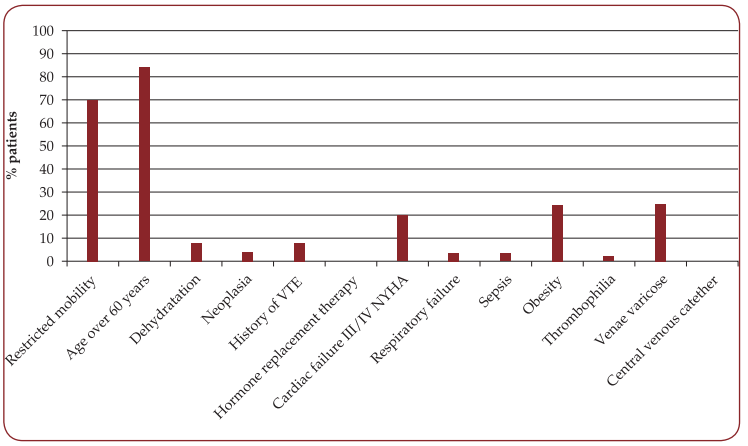

FIGURE 2. Risk factors distribution at hospital discharge.

Restricted mobility means complete immobilization or immobilization with bathroom privileges due to any neurological disease for 3 days or more, neoplasia means active cancer; we have also included hormone replacement therapy and use of oestrogen-containing contraceptive therapy, severe acute infection and sepsis 5.3%, obesity means BMI >30 kg/m^2, thrombophilia inherited / acquired.

Type of VTE prophylaxis		Patients number	Patients %
Mechanic methods	No	737	83.4%
	Yes	147	16.6%
UFH	No	876	99.1%
	Yes	8	0.9%
LMWH	No	33	3.7%
	Yes	851	96.3%
Vitamin K antagonists	No	839	94.9%
	Yes	45	5.1%
Other (ASA, etc.)	No	850	96.2%
	Yes	34	3.8%

TABLE 3. VTE prophylaxis recommended during hospitalization.

UFH – unfractioned heparin, LMWH – low molecular weight heparin, ASA – acetylsalicylic acid

failure 3.8%, severe acute infection / sepsis 3.5%, obesity (BMI >30 kg/m^2) 24.2%, inherited / acquired thrombophilia 2.4%, venae varicose 24.8% and central venous catheter in 0.1%.

Secondary endpoints

The percentage of hospitalized patients receiving prophylaxis according to National Guidelines of VTE Prophylaxis from the total number of patients at risk of VTE.

879 patients (99.4%) have received VTE prophylaxis during hospitalization period.

The duration and the type of VTE prophylaxis in hospitalized patients

The mean duration of VTE prophylaxis during hospitalization period was 10.65 days. The methods of prophylaxis recommended are shown in Table 3.

76.8% of the patients have received one method of thromboprophylaxis, 21.9% a combination of two methods and 0.7% of three methods. 0.6% of the patients did not received VTE prophylaxis during hospitalization period.

The percentage of patients at VTE risk receiving recommendation for thromboprophylaxis at discharge

The total number of patients who received recommendation of VTE prophylaxis at hospital discharge was 786 (88.9%).

The duration and the type of VTE prophylaxis recommended at patient discharge.

The mean duration of VTE prophylaxis recommended at hospital discharge was 17.27 days. The methods of prophylaxis that had been recommended are shown in Table 4.

89.8% of the patients have received recommendation for one VTE prophylaxis method, 10.0% a combination of two methods and 0.2% of three methods.

718 patients (81.2%) have received VTE prophylaxis during the one month follow-up period after hospital discharge. The methods of prophylaxis used are mentioned in Table 5.

In 71.6% of the patients have been used one VTE prophylaxis method, 8.7% a combination of two methods and 0.1% of three methods. 19.6% of the patients did not received VTE prophylaxis during one month period after hospital discharge.

The mean duration of VTE prophylaxis performed by the patients after hospital discharge was 16.13 days. ❑

DISCUSSION

We have observed that 100% of patients hospitalized with ischemic stroke have been assessed by the physician for the VTE risk at hospital admission. We must also mention that 90.7% of them had restricted mobility (complete immobilization or immobilization with bathroom privileges due to any neurological disease) for 3 days, or age over 60 years old in 84.2% or dehydration in 25.7%. So they associated important cumulative risk factors.

These risk factors are mentioned in all risk scores for hospitalized medical patients. In the most recent ACCP guidelines (10) (2012, 9th edition) for estimating baseline risk and for low- and high-risk strata it is recommended the Padua Prediction Score (Table 6).

99.4% (879) of the total number of patients at risk of VTE (884) have received prophylaxis

during hospitalization. The most frequently types of prophylaxis used during hospitalisation were LMWH in 96.3% of the patients and mechanic method in 16.6% of them that were in concordance with National Guidelines of VTE Prophylaxis recommendations (8). The actual ACCP guidelines states that "In patients with acute stroke and restricted mobility, we suggest the use of prophylactic-dose heparin or intermittent pneumatic compression devices (grade 2B) and suggest against the use of elastic compression stockings (grade 2B). In patients with acute ischemic stroke and restricted mobility, we suggest prophylactic-dose LMWH over prophylactic-dose UFH (grade 2B)"(11).

A meta-analysis provided estimates of the relative effects of prophylactic-dose anticoagulation for VTE prophylaxis in patients with acute ischemic stroke and restricted mobility (2,17). Heparin prophylaxis, in comparison with no heparin prophylaxis, results in 33 fewer symptomatic DVTs, five fewer pulmonary emboli, and five additional major hemorrhages (three intracranial and two extracranial) per 1.000 treated patients. The overall quality of the evidence is moderate due to imprecision. Patients with additional risk factors for venous thrombosis are more likely to benefit from heparin thromboprophylaxis, whereas patients with risk factors for bleeding are less likely to benefit. Prophylactic-dose heparin is treatment with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) at a lower dose than what is typically used for therapeutic anticoagulation. The definition for prophylactic dose was adapted from a review of pharmacologic prophylaxis of VTE in stroke patients (17). Prophylactic-dose UFH was defined as 10,000 to 15,000 units/day and prophylactic-dose LMWH as 3,000 to 6,000 International Units/day. Prophylactic-dose heparin therapy is typically initiated within 48 h after onset of stroke and continued throughout the hospital stay or until the patient regains mobility. Prophylactic-dose heparin should not be used within the first 24 h after administration of thrombolytic therapy.

Compared with UFH, the use of LMWH in patients with restricted mobility, reduces VTE events (eight fewer PE and seven fewer symptomatic DVTs per 1,000 patients treated) without an influence on mortality and bleeding complications (11).

Trials that compared intermittent pneumatic compression devices to no treatment have shown an approximate 50% reduction in DVT detected by a systematic method such as venography (11).

Type of VTE prophylaxis		Patients number	Patients %
Mechanical methods	No	571	72.6%
	Yes	215	27.4%
UFH	No	786	100.0%
LMWH	No	326	41.5%
	Yes	460	58.5%
Vitamin K antagonists	No	655	83.3%
	Yes	131	16.7%
Other (ASA etc.)	No	713	90.7%
	Yes	73	9.3%

TABLE 4. VTE prophylaxis recommended at patients discharge.

UFH – unfractioned heparin, LMWH – low molecular weight heparin, ASA – acetylsalicylic acid

Type of VTE prophylaxis		Patients number	Patients %
Mechanical methods	No	530	73.8%
	Yes	188	26.2%
UFH	No	717	99.9%
	Yes	1	0.1%
LMWH	No	299	41.6%
	Yes	419	58.4%
Vitamin K antagonists	No	593	82.6%
	Yes	125	17.4%
Other (ASA, etc.)	No	661	92.1%
	Yes	57	7.9%

TABLE 5. VTE prophylaxis used at hospital discharge.

UFH – unfractioned heparin, LMWH – low molecular weight heparin, ASA – acetylsalicylic acid

Risk factor	Points
Active cancer[a]	3
Previous VTE (with the exclusion of superficial vein thrombosis)	3
Reduced mobility[b]	3
Already known thrombophilic condition[c]	3
Recent (<1 month) trauma and/or surgery	2
Elderly age (>70 y)	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI >30)	1
Ongoing hormonal treatment	1

TABLE 6. Risk Factors for VTE in Hospitalized Medical Patients.

In the Padua Prediction Score risk assessment model, high risk of VTE is defined by a cumulative score >4 points. In a prospective observational study of 1,180 medical inpatients, 60.3% of patients were low risk and 39.7% were high risk. Among patients who did not receive prophylaxis, VTE occurred in 11.0% of high-risk patients vs. 0.3% of low-risk patients (HR, 32.0; 95% CI, 4.1-251.0). Among high-risk patients, the risk of DVT was 6.7%, nonfatal PE 3.9%, and fatal PE 0.4%.HR=hazard ratio.

[a]Patients with local or distant metastases and/or in whom chemotherapy or radiotherapy had been performed in the previous 6 months.

[b]Anticipated bed rest with bathroom privileges (either because of patient's limitations or on physician's order) for at least 3 days.

[c]Carriage of defects of antithrombin, protein C or S, factor V Leiden, G20210A prothrombin mutation, antiphospholipid syndrome.

The vitamin K antagonists and aspirin are not mentioned for VTE prophylaxis in hospitalized or outcome patients in actual ACCP guidelines (11) or National one (8). The contribution of platelet activation to the pathogenesis of venous thrombosis is less clear than for arterial thrombosis. Although the use of acetylsalicylic acid (ASA) for VTE prevention is appealing because of its low cost, oral administration, and low bleeding rates, the effectiveness of ASA or other antiplatelet drugs to prevent VTE has been studied in relatively few hospitalized medical patients (nine trials, total of 555 patients) with a small number of reported outcome events (10).

Based on the investigators assessment, risk factors for VTE have persisted at hospital discharge in 88.2% of the patients hospitalized with ischemic stroke (70% with restricted immobility). 99.4% (775) of the total number of patients at risk of VTE at hospital discharge (780) have received recommendation for thromboprophylaxis with LMWH in 58.5% patients, mechanical method in 27.4% and vitamin K antagonists in 16.7 %

The mean duration of VTE prophylaxis during hospitalization period was 10.65 days and the mean duration of VTE prophylaxis recommended at hospital discharge was 17.27 days.

Optimal duration for VTE prophylaxis in stroke patients with prolonged immobility is not well defined. According to actual ACCP guidelines: "For acutely ill hospitalized medical patients at increased risk of thrombosis, we suggest against extending the duration of thromboprophylaxis beyond the period of patient immobilization or acute hospital stay (grade 2B)" (10). But epidemiological data have shown that deep vein thrombosis is reported in the stroke rehabilitation population in up to 10 % to 30%; 20 % of cases may occur after 12 weeks post-stroke onset (12). Pulmonary embolism may occur up to 4 months post-stroke (13). Some advocate continued prophylaxis for patients with persistent immobility (14-15). In spinal cord injured patients with complete paraplegia, by 6 months post-injury the risk of DVT declines to that of the general population (16). Whether the risk of VTE declines similarly in stroke patients is unknown and requires further study.

In the previous National Guidelines (8) the recommendation was to individualize the optimal duration of thrombophylaxis in medical patients correlated with persistence of actual and previous risk factors. Usually the duration was 10-14 days for outcome patients. So we can consider that in the study the physicians had taken in consideration the guidelines recommendations.

The Extended Prophylaxis for Venous Thromboembolism in Acutely Ill Medical Patients With Prolonged Immobilization (EXCLAIM) study is the only published RCT of extended duration thromboprophylaxis in hospitalized medical patients (18). The study population consisted of 6,085 hospitalized patients aged 40 years with acute medical illness (e.g., heart failure, respiratory insufficiency, infection) and reduced mobility. All patients received initial open-label enoxaparin (40 mg daily for 10 ± 4 days), and were then randomized to receive extended duration enoxaparin (40 mg daily for 38 ±4 days) or placebo. Extended-duration enoxaparin, compared with placebo, reduced the incidence of overall VTE (composite of asymptomatic and symptomatic events) (RR, 0.62; 95% CI, 0.45-0.84) and symptomatic proximal DVT (RR, 0.25; 95% CI, 0.09-0.67) but failed to exclude benefits or harm for fatal PE (RR, 0.34; 95% CI, 0.01-8.26) and overall mortality (RR, 1.00; 95% CI, 0.7-1.43). The risk of major bleeding was significantly increased with extended-duration enoxaparin (RR, 2.51; 95% CI, 1.21-5.22), and there were four intracranial bleeding events (one fatal) in the extended enoxaparin group compared with none in the placebo group. In terms of absolute effects, extended-duration enoxaparin prevented six fewer symptomatic proximal DVT per 1,000 (95% CI, from three fewer to seven fewer) at a cost of five more major bleeding events per 1,000 (95% CI, from one more to 14 more).

A limitation of our study could be the low number of centers distributed especially in university centers where both assessment and treatment of VTE prophylaxis are frequently done because doctors are aware about the importance of thromboprophylaxis and clinical evidences. This could also explain the high percentage of prophylaxis use and the accordance with international guidelines. Because of that maybe it is necessary a further study in order to evaluate the assessment of VTE in a higher number of non university hospitals. ❑

CONCLUSIONS

We can conclude that in comparison with ENDORSE study results there is a clear improvement in our country in both assessment and thromprophylaxis recommendation in acute stroke patients with restricted mobility at VTE risk.

The recommended methods for VTE prophylaxis are according to National and International guidelines but still there are few cases that had received vitamin K antagonists and acetylsalicylic acid which are no more mentioned in VTE prophylaxis treatment. We need further studies to define the optimal duration of treatment.

LMWH is preferred to unfractionated heparin for venous thromboembolism prophylaxis in this high-risk patient population in view of its better clinical benefits to risk ratio and convenience of once daily administration.

VTE is a major public health issue: it is an easily preventable disease with a substantial risk of morbidity and mortality in patients hospitalized for acute stroke. Our data show that a large proportion of hospitalized individuals are at risk for VTE, and that recommended VTE prophylaxis is in accordance to guidelines but could be improved.

Hospital-wide strategies to assess patients' VTE risk should be implemented, together with measures that ensure that at-risk patients receive appropriate VTE prophylaxis.

Conflict of interests: none declared.

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References

1. **Field T, Hill M –** Prevention of Deep Vein Thrombosis and Pulmonary Embolism in Patient With Stroke, Clinical and Applied Thrombosis.*Hemostasis* 2012; 18:5-192
2. **Shorr AF, Jackson WL, Sherner JH, et al. –** Differences between low-molecular-weight and unfractionated heparin for venous thromboembolism prevention following ischemic stroke: a metaanalysis. *Chest* 2008; 133:149-155
3. **Geerts WH, Bergqvist D, Pineo GF, et al. –** American College of Chest Physicians. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133(6 suppl):381S-453S
4. **Mahoney FI, Barthel D –** Functional evaluation: The Barthel Index. *Maryland State Medical Journal* 1965; 14:56-61
5. **Kase SC, Pineo GF –** Prevention of venous thromboembolism after ischemic stroke. *Curr Opin Pulm Med.* 2008; 14:389-396
6. NICE clinical guideline 92, January 2010; www.nice.org.uk/guidance/CG92
7. **Sherman DG, Albers GW, Bladin C, et al. –** On behalf of the PREVAIL Investigators* The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischemic stroke (PREVAIL Study): an open-label randomized comparison. *Lancet* 2007; 369:1347-55
8. **Gherasim L, Tulbure D, Antonescu D –** Ghid de preventie a tromboembolismului venos, Editia a II-a. *Medicina Interna* 2009; 6:29-56
9. Sanofi internal data
10. **Kahn SR, Lim W, Dunn AS, et al. –** Prevention of VTE in Nonsurgical Patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th Edition: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141(2)(Suppl):e195S–e226S
11. **Lansberg MG, O'Donnell MJ, Pooja K, et al. –** Antithrombotic and Thrombolytic Therapy for Ischemic Stroke Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141(2)(Suppl):e601S-e636S
12. **Harvey RJ –** Prevention of venous thromboembolism after stroke. *Top Stroke Rehabil.* 2003; 10:61-69
13. **Wijdicks EF, Scott JP –** Pulmonary embolism associated with acute stroke. *Mayo Clin Proc.* 1997; 72:297-300
14. **Muir KW –** The PREVAIL trial and low-molecular-weight heparin for prevention of venous thromboembolism. *Stroke* 2008; 39:2174-2176
15. **Kamphuisen PW, Agnelli G, Sebastianelli M –** Prevention of venous thromboembolism after acute ischemic stroke. *J Thromb Haemost.* 2005; 3:1187-1194
16. **Lamb GC, Tomski MA, Kaufman J, et al. –** Is chronic spinal cord injury associated with increased risk of venous thromboem-bolism? *J Am Paraplegia Soc.* 1993; 16:153-156
17. **Kamphuisen PW, Agnelli G –** What is the optimal pharmacological prophylaxis for the prevention of deep-vein thrombosis and pulmonary embolism in patients with acute ischemic stroke? *Thromb Res* 2007; 119:265-274
18. **Hull RD, Schellong SM, Tapson VF, et al. –** EXCLAIM (Extended Prophylaxis for Venous Thromboembolism in Acutely Ill Medical Patients With Prolonged Immobilization) study . Extended-duration venous thromboembolism pro-phylaxis in acutely ill medical patients with recently reduced mobility: a randomized trial. *Ann Intern Med* 2010; 153:8-18.

ANNEX I

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Neagu Daniela	"Sf. Ioan cel Nou" Emergency County Hospital, Suceava, Romania
Toldişan Ilidico	Emergency County Clinical Hospital, Constanta, Romania
Popi Silvia	Emergency County Clinical Hospital, Constanta, Romania
Bucşe Florentina	Emergency County Clinical Hospital, Constanta, Romania
Hâncu Anca	Emergency County Clinical Hospital, Constanta, Romania
Marin Marieta	Emergency County Clinical Hospital, Constanta, Romania
Docu Axelerad Any	Emergency County Clinical Hospital, Constanta, Romania
Buleu Mariana	"Sf Pantelimon" Emergency County Clinical Hospital, Focsani, Romania
Voinea Daniela	"Sf Pantelimon" Emergency County Clinical Hospital, Focsani, Romania
Gavriliu Ileana	Emergency County Clinical Hospital, Bacau, Romania
Lazar Doina	Emergency County Clinical Hospital, Bacau, Romania
Vargulescu Doinita	Emergency County Clinical Hospital, Bacau, Romania
Chiriac Luiza Maria	Emergency County Clinical Hospital, Bacau, Romania
Miclausanu Alexandru	"Sf Apostol Andrei" Emergency County Clinical Hospital, Galati, Romania
Lungu Mihaela	"Sf Apostol Andrei" Emergency County Clinical Hospital, Galati, Romania
Scutelnicu Dorina	Emergency County Clinical Hospital, Timisoara, Romania
Petrica Maxim	Emergency County Clinical Hospital, Timisoara, Romania
Chirileanu Ruxandra	Emergency County Clinical Hospital, Timisoara, Romania
Gaina Adriana	Emergency County Clinical Hospital, Timisoara, Romania
Albu Cecilia	"Dr. Alexandru Simionescu" Hospital, Hunedoara, Romania
Boros Liviu	Emergency County Clinical Hospital, Arad, Romania
Terfaloaga Alexandrina	Emergency County Clinical Hospital, Resita, Romania
Tudorica Valeria	Clinical Hospital of Neuropsychiatry, Craiova, Romania
Stanca Diana	Clinical Hospital of Neuropsychiatry, Craiova, Romania
Parscoveanu Denisa	Clinical Hospital of Neuropsychiatry, Craiova, Romania
Petria Florin	Military Hospital, Pitesti, Romania
Stanciu Marian	Emergency County Hospital, Pitesti, Romania
Costache Marinela	Emergency Hospital, Ploiesti, Romania
Dascalescu Luiza	Ploiesti, Romania
Grapa Stefan	County Hospital, Targoviste, Romania
Guran Monica	Targoviste, Romania
Moldovan Florina	Emergency County Clinical Hospital, Cluj-Napoca Romania
Dunca Alice	Emergency County Hospital, Baia Mare, Romania
Anitas Marioara	County Hospital, Satu Mare, Romania
Sabau Monica	Clinical Hospital of Neurology and Psychiatry, Oradea, Romania
Marceanu Manuela	Hospital of Psychiatry and Neurology, Brasov, Romania
Toma Luminita	Emergency County Clinical Hospital, Tg. Mures, Romania
Petrutiu Hortensia Sanda	Emergency County Clinical Hospital, Tg. Mures, Romania
Frasineanu Armand Daniel	Colentina Clinical Hospital, Bucharest, Romania
Nica Sanda	Colentina Clinical Hospital, Bucharest, Romania
Plesa Cristina	"Prof. Dr. Dimitrie Gerota" Emergency Hospital, Bucharest, Romania
Dospra Gabriela	"Prof. Dr. Dimitrie Gerota" Emergency Hospital, Bucharest, Romania
Roceanu Adina	Emergency University Hospital, Bucharest, Romania
Ene Amalia	Emergency University Hospital, Bucharest, Romania
Cristina Nica	Emergency University Hospital, Bucharest, Romania
Craciunoiu Adina	Emergency University Hospital, Bucharest, Romania
Dragomir Andreea	Emergency University Hospital, Bucharest, Romania