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Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE II study): results of a Mexican national cross-sectional study

Ricardo Martínez-Zubieta

Abstract

Background: It is well known that a significant proportion of hospitalized medical and surgical patients with risk factors for deep vein thrombosis (DVT) are not receiving thromboprophylaxis. We designed this study to evaluate the proportion of at-risk patients and the proportion of those receiving recommended prophylaxis.

Methods: We conducted a multicentric cross-sectional survey that included medical and surgical patients from 43 hospitals throughout Mexico. Patients who were at risk for DVT according to the ACCP 2004 guidelines were included and evaluated for thromboprophylaxis.

Results: Overall, 625 patients were at risk: 308 (49%) surgical patients and 317 (51%) medical patients. There were 179 (58%) surgical patients receiving recommended prophylaxis, whereas medical patients represented 117 (37%) patients.

Conclusions: There is a significant proportion of hospitalized medical and surgical patients at risk for DVT. There is also a significant underutilization of recommended thromboprophylaxis among these patients.

Key words: venous thromboembolism, deep vein thrombosis, pulmonary embolism, prophylaxis.

Introduction

Venous thromboembolism (VTE) is a common complication in medical and surgical patients¹⁻⁸ and is a cause of high morbidity and mortality.⁹⁻¹¹ Pulmonary embolism (PE) is present in >600,000 cases per year in the U.S. and causes or is a contributing factor in 50,000-200,000 deaths per year,¹² being reported as the most common cause of preventable in-hospital deaths.^{8,13} In Mexico, Sigler et al. of the Hospital General (Centro Medico Nacional, Instituto Mexicano del Seguro Social) reported a rate of PE of 15% in 1685 au-

topsies, being the direct cause of death in 28% and indirect cause in 62% of cases.¹⁴ In another study on 1032 autopsies, Sandoval et al. of the Instituto Nacional de Cardiología “Ignacio Chávez” reported an incidence of 22%, being the third cause of mortality.¹⁵

These severe and troublesome figures of hospitalized patients with VTE stand out when there is a significant gap between national and international guidelines and the appropriate use of prophylaxis for this disease. The multinational cross-sectional ENDORSE study showed that VTE prophylaxis in medical or surgical patients is less than that recommended by the guidelines of the American College of Chest Physicians (ACCP) in 2004¹⁶ with greater prophylaxis in the surgical group of patients (58.5%) compared to the group of medical patients (39.5%).¹⁶

Two meta-analyses also highlighted the underutilization of prophylaxis in medical patients.^{17,18} An interesting article by Howard describes two important data:

- Suboptimal use of prophylaxis of medical patients due to inconsistencies and complexity of current guidelines in relation to the stratification of the risks of VTE
- 76% of hospitalized medical patients with one or more risk factors for VTE did not receive appropriate DVT prophylaxis in an audit conducted in 2004 at the John Radcliffe Hospital in Oxford⁸

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Failure of prophylaxis has also been reported in other groups of patients. Bratzler et al. in a retrospective study of 419 surgical patients 65 years of age or older showed that only 38% received prophylaxis. In the group of 250 patients with very high risk of VTE only 39% received some form of prophylaxis, but only 64 of these 97 (66%) received appropriate prophylaxis.¹⁹ Similar results have been reported in other studies of patients 65 years or older with other risk factors (cancer, previous VTE, heart failure, ischemic cerebrovascular disease, infection or sepsis) for VTE due to comorbidities and immobilization.^{20,21}

Materials and Methods

The design was similar to the international ENDORSE registry:¹⁶ national multicentric, observational, cross-sectional, including the guidelines for DVT prophylaxis of the ACCP 2004.²² The primary objectives were as follows:

- Identify the percentage of hospitalized patients at risk for VTE in selected hospitals representative of the country
- Determine the percentage of hospitalized patients at risk who receive effective types of prophylactic treatment for VTE prophylaxis

Secondary objectives were as follows:

- Define the rate of patients who receive an adequate DVT prophylaxis in medical vs. surgical populations
- Define the rate of hospital patients at risk for DVT due to acute disease (i.e., medical and/or surgical)
- Analyze the factors to determine adequate prophylaxis
- Perform the analysis by type of hospital (public and private)

Hospital selection was conducted from a list of representative public and private hospitals in Mexico, which met the following characteristics: 1) bed capacity ≥ 50 and 2) with revenues for treatment of acute illness or exacerbations of chronic diseases and/or who schedule routine major surgeries. Psychiatric, pediatric and rehabilitation hospitals were excluded.

The study, if required, was approved by the Ethics Committees of each hospital, but no informed consent was sought from respondents. In the remaining hospitals there was an academic guarantee from the Mexican Academy of Surgery.

Each hospital had a designated principal investigator who trained for 1 day on how to complete the required forms in the survey. The investigator was also responsible for completing the Hospital Recruitment Form, which included hospital code (code per hospital) and hospital cha-

acteristics (i.e., number of beds, clinical services available and any academic affiliation).

Each principal investigator determined the need for assistance by other physicians and/or nurses who were responsible for completing two forms: a) Patient Recruitment Form (PRF) in each participating hospital that included a list of all patients in the eligible services or wards and included the patient identification number or reason for study exclusion, and b) Case Report Form (CRF) containing the data of patients enrolled such as demographic data, admission diagnosis and diagnoses after admission, risk factors for bleeding and risk factors for VTE, length of hospital stay, type of surgical procedure on admission or within 14 days, and type of thromboprophylaxis indicated on the hospital stay and at discharge.

Patient data were taken from the patient's file and only the first 14 days of the hospital stay were taken into consideration.

Eligible patients were medical patients age 40 years or older admitted for an acute medical illness and surgical patients 18 years or older undergoing a major surgical procedure under general or epidural anesthesia lasting ≥ 45 min or having suffered a major traumatic event without requiring major surgery, including intracranial injury or admission to a surgical service for observation or preoperative evaluation.

Patients selected from the Ob/Gyn hospital were those who were reported to have thromboprophylaxis and who were admitted with other nonobstetric conditions, i.e., with gynecological diseases (cancers, etc.). Excluded were those patients admitted to the following services: emergency, psychiatry, pediatrics, palliative care, maternity and obstetrics, neonatology, burn units, otolaryngology, dermatology, ophthalmology, rehabilitation, admitted for treatment of addiction to alcohol and drugs, admitted for VTE treatment or minor surgical treatment, anesthesia lasting < 45 min or lack of data in the patient's clinical file.

Statistical Analysis

Categorical data are presented in numbers and percentages, both in the number of patients with risk factors for VTE who received thromboprophylaxis and their location by public or private hospital.

Population characteristics including demographics, medical history, nature, duration and severity of the disease, concomitant diseases and treatment (thromboprophylaxis) are presented in complete data sets (average, SD, minimum, maximum and median, 95% CI of quantitative variables). Data sets and percentages were also performed with 95% CI of the population for categorical data. Results were classified according to hospital.

The prevalence of risk for VTE according to risk factors defined by the ACCP (2004) are presented according to hospital and divided by patients according to medical or surgical category with 95% CI. The analysis was performed on populations with a satisfactory level of data. The prevalence of thromboprophylaxis according to hospital as well as patient distribution according to thromboprophylaxis received will be reported.

Results

The survey was conducted in all participating hospitals from June 2 to June 16, 2008. Unlike the original ENDORSE study that analyzed the hospitals by beds assigned to the services included, our study considered patients admitted to these services and not beds assigned by service because most of the hospitals in Mexico, especially private hospitals, do not assign a determined number of beds for each service where surgical patients share space (floor or area) with medical patients.

The number of respondents was 2133 patients in 44 participating hospitals, excluding 506 patients who met one or more exclusion criteria, leaving 1627 patients for the analysis (Figure 1). Of these 1627 patients, 715 were surgical (43.9%) and 777 (47.8%) were males, with a mean age of 57.15 years (± 17 years), mean weight 69.5 kg (± 15.4 kg) and mean height of 162.2 cm (± 9.81 cm). According to the guidelines of the ACCP, 625 (38.4%) patients were at risk for VTE, 311 (40.0%) patients were males and 317 (44.3%) were nonsurgical patients (Table 1).

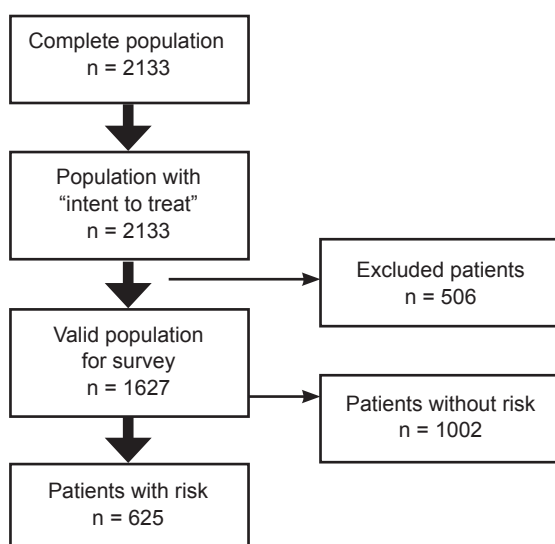


Figure 1. Flow diagram in the selection of patients.

Table 1. Total number and percentage of patients at risk for VTE

Type of illness	Number/total patients	%
Medical	715/1627	43.9
With risk for VTE	317	44.3
Without risk for VTE	398	55.7
Surgical	912/1627	56.1
With risk for VTE	308	33.8
Without risk for VTE	604	66.2
Female	850/1627	52.2
With risk for VTE	314	36.9
Without risk for VTE	536	63.1
Male	777/1627	47.8
With risk for VTE	311	40.0
Without risk for VTE	466	60.0

VTE, venous thromboembolism.

Other demographic data are presented in Table 2, with an average BMI in the overweight category observed. Table 3 shows the risk factors present for VTE before patient admission to the hospital. In both groups of patients, obesity was the most common risk factor. In the group of medical patients it was followed by chronic pulmonary disease, peripheral vascular disease, long-term immobilization, and chronic heart failure. In the surgical group of patients the presence of venous insufficiency and long-term immobilization followed obesity.

Among other premorbid conditions prior to hospitalization, the following stand out: cardiovascular diseases unrelated to heart failure (18.1%), endocrine and metabolic problems (16.7%) and hepatobiliary and gastrointestinal problems (10.6%). At the time of admission, gastrointestinal and hepatobiliary problems (18%) nonpulmonary infections (17.1%) are predominant. The most frequently reported events after hospitalization were pulmonary infection (20%) followed with the same frequency by non-respiratory infection and noninfectious respiratory disease (12.92%). The most frequent risk factors for VTE in both groups of patients during hospitalization were the presence of central venous catheter (CVC) and complete or limited immobilization (Table 4).

In relation to the limitation of pharmacological thromboprophylaxis, the use of NSAIDs was present in 40.3% of patients, followed by significant renal damage in 20.4%, and thrombocytopenia in 14.0% of the patients (Table 5). Of the 625 (38.4%) patients at risk for VTE, only 295 (47.2%) received prophylaxis according to ACCP guidelines. In the surgical group at risk for VTE (308 patients,

Table 2. Average BMI of patients at risk for venous thromboembolism

Parameter	Patients				
	(n)	Minimum	Maximum	Average	SD
Age (years)	1627	18.0	105.0	57.15	17.1
Male	501	18.0	94.0	54.8	17.5
Female	574	18.0	94.0	57.3	16.1
Weight (kg)*	1185	34.0	142.0	69.5	15.4
Male	501	35.0	142.0	74.6	14.8
Female	574	34.0	130.0	64.6	14.1
Length (cm)*	1082	103.0	194.0	162.2	9.81
Male	501	103.0	194.0	168.5	8.5
Female	574	134.0	188.0	156.8	7.3
BMI (kg/m ²)	1075	12.47	58.44	26.27	5.1
Male	501			26.27	
Female	574			26.32	

Average body mass index (BMI) was in the range of overweight.

*Weight and length unavailable in all study patients.

SD, standard deviation.

49.3%) only 179 received thromboprophylaxis (58.1% of patients), whereas in the medical group of 317 patients (50.7%), 117 (36.9%) received thromboprophylaxis (Figure 2). Pharmacological prophylaxis in medical patients was used in 81/317 patients (25%) and 97/308 (31.5%) of surgical patients. Mechanical prophylaxis was used in 57 medical patients (18.0%) and 120 surgical patients (39.0%). No patient received antiplatelet therapy as VTE prophylaxis.

Low molecular weight heparin (LMWH) was the most commonly used pharmacologic prophylaxis in patients prior to admission, at admission and during the subsequent 14 days of hospitalization (Table 6). LMWH enoxaparin was the most widely used (98.8%). In relation to mechanical prophylactic methods, graduated compression stockings were the most frequently used (>90% of cases).

Of the patients surveyed, 1129 (69.4%) were from public hospitals. According to type of patient at risk of VTE and type of hospital, 433 (69.2%) were in public hospitals and

Table 3. Pre-morbid risk factors for venous thromboembolism present at admission

Previous medical condition	Medical illness (317)		Surgical illness (308)		General	
	n	%	n	%	n	%
Obesity	114	35.9	179	58.1	293	46.8
Previous VTE	29	9.1	18	5.8	47	7.5
COPD	61	19.2	29	9.4	90	14.4
Thrombophilia	5	1.5	3	0.97	8	1.2
Long-term immobilization	46	14.5	49	15.9	95	15.2
Contraceptive use	2	0.63	8	2.5	10	1.6
Venous insufficiency	60	18.9	66	21.4	126	20.1
Pregnancy	5	1.5	10	3.2	15	2.4
Chronic cardiac failure	42	13.2	27	8.7	69	11.0
HRP	2	0.63	3 (0.97%)		5	0.8

VTE, venous thromboembolism; COPD, chronic obstructive pulmonary disease; HRP, hormone replacement therapy.

Table 4. Risk factors for VTE present prior to admission, at the time of admission and in the 14 days following hospital admission

	Medical illness						Surgical illness					
	Pre-admission		Admission		Post-admission		Pre-admission		Admission		Postadmission	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Admitted to ICU	11	4.9	35	9.26	12	9.30	20	8.5	67	14.19	62	17.61
CVC	43	19.2	67	17.7	50	38.7	30	12.8	83	17.5	95	26.9
MV	10	4.4	28	7.4	19	14.7	19	8.1	59	12.5	50	14.2
Inmobilization with bathroom privileges	54	24.1	152	40.2	18	13.9	60	25.6	131	27.7	79	22.4
Complete immobilization	56	25.0	85	22.4	19	14.7	77	32.9	131	27.7	63	17.9
Chemotherapy	49	21.8	11	2.91	10	7.7	27	11.5	0	0.0	1	0.2
Heparin-induced thrombocytopenia	1	0.45	0	0.0	1	0.78	1	0.43	1	0.21	2	0.5

ICU, intensive care unit; CVC, central venous catheter; MV, mechanical ventilation.

192 (30.8%) were patients in private hospitals. The frequency of medical patients was higher in public hospitals and on a reciprocal basis was observed with surgical patients.

Discussion

ENDORSE II is a supplement to the International ENDORSE Registry¹⁶ and the results are preferentially compared with this registry, taking special consideration of the per-

centages of patients at risk of VTE and the use of thromboprophylaxis in medical and surgical patients.

Our survey population with risk factors (ACCP guidelines—2004) was comprised of 625 patients (38.4%), lower than the percentage of patients at risk from the International ENDORSE Registry (52%)¹⁶ and the percentage found in patients surveyed only in Mexico in the same study (57%) (477/838 patients) (Martínez ZR, personal communication).

Moreover, VTE prophylaxis was low (47.2%), similar to the average of the International ENDORSE Registry (50%) and that of Mexico as part of it (45%). Results of this cross-sectional survey confirm data reported in other studies with a high incidence of at-risk patient for VTE and low thromboprophylaxis.^{8,16-18} Few studies have shown a higher percentage of thromboprophylaxis in medical patients at risk, reaching 60%.²³

It is noted in the International ENDORSE Registry that the possible explanation for this discrepancy could be a broader definition of the prophylactic methods for VTE and a population of patients in academic centers being surveyed. The latter information was not collected in our survey.

Regarding types of patients, the surgical group was more protected (58.1%) than the medical group (36.9%). As in previous comparisons, these data are similar to that reported in the international ENDORSE study, with prevention in the surgical group of 58.1%, and in the medical group of 39.6%.

These data can be related to a greater awareness of the problem of VTE in surgical patients who frequently have more risk factors (surgery, immobilization, trauma, neo-

Table 5. Number and percentage of conditions limiting pharmacological prophylaxis in patients at risk for VTE

Condition	<i>n</i> (625)	%
Renal damage	128	20.4
Intracranial hemorrhage	51	8.16
Thrombocytopenia	88	14.0
Known hemorrhagic condition	25	4.0
Hepatic damage	40	6.4
Hemorrhage at hospital admission	72	11.5
Active GI ulcer	26	4.1
Aspirin	78	12.4
NSAIDs	252	40.3

GI, gastrointestinal; NSAIDs, nonsteroidal antiinflammatory drugs.

Table 6. Number, percentage of illnesses and type of pharmacological prophylaxis used in VTE

Pharmacological prophylaxis	Preadmission		Admission		Postadmission (1 or more days)	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
LMWH	25	64.1	55	93.2	422	90.9
Nonfractionated heparin	3	7.6	3	5.0	34	7.3
Vitamin K antagonists	7	17.9	1	1.6	5	1.0
Fondaparinux	0	0.0	0	0.0	1	0.2
Other anticoagulants	4	10.2	0	0.0	2	0.4

VTE, venous thromboembolism; LMWH, low molecular weight heparin.

plasms, etc.).²⁴ Regarding this point, Howard states that the discrepancies and contradictions between the various current guidelines are an important reason in their lower use in the group of medical patients.⁸ An example of these inconsistencies is described by the same author in the SIGN guidelines, where aspirin is mentioned as a prophylactic VTE agent, which differs from the ACCP guidelines.^{8,22} Our survey reported an invalid use of antiplatelet drug as a prophylactic measure for VTE, more in keeping with the ACCP guidelines of 2004 and 2008.^{22,25} Cohen et al. also mention that this difference simply is an assessment of surgical patients.¹⁶ Like the international ENDORSE study, our survey

used the 2004 ACCP guidelines for defining patients at risk and effective thromboprophylaxis, thus avoiding bias in the stratification of patients and adequacy of prophylaxis.

In our survey, obesity was an important risk factor for VTE (35.9% in the group of medical patients and 58.1% in the surgical group of patients), numbers well above those reported in international ENDORSE study¹⁶ and in conjunction with the high incidence of obesity in the Mexican population. This factor has been implicated as an independent risk factor for VTE.^{5,26} Venous insufficiency and immobilization were the most frequent risk factors present before admission and during the hospital stay. Chronic heart failure

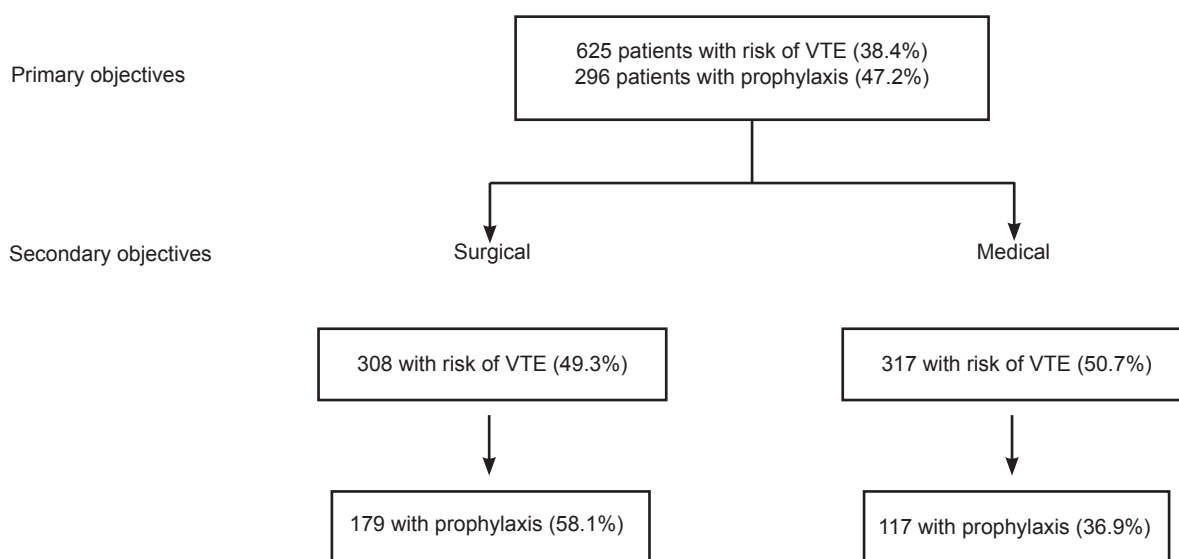


Figure 2. Number and percentage of the total population at risk for venous thromboembolism (VTE) who received thromboprophylaxis (Guidelines of the ACCP, 7th ed.) and distribution according to group of surgical patients and medical patients.

and chronic lung disease had a lower incidence in relation to the international ENDORSE registry.¹⁶ All these factors have been described extensively in the literature as factors that should be considered when deciding to initiate thromboprophylactic methods.^{9,13,19-20,24}

Using the same methodology of inquiry as the international ENDORSE registry, we found the same limitations. It is likely that the survey population does not adequately represent the population of medical and surgical patients of other hospitals. Our country has a large number of hospitals with <50 beds (not included in the survey) where there is a high probability of not following any guidelines to stratify patients at risk of VTE and at least receive some form of prophylaxis. The population also varies significantly in cultural and economic terms and the possibility of not receiving appropriate pharmacologic thromboprophylaxis is high. Due to the cross-sectional design of the survey, we were not able to analyze whether thromboprophylaxis was continued beyond the day of data collection.

Our results with a high number of at-risk patients for VTE and low use of thromboprophylaxis are consistent with the suggestion of several authors to recognize this as a public health problem. VTE is the most important preventable complication of increased mortality and its development (DVT and/or PE) implies an increase in days of hospitalization, cost and mortality.^{8,27} With the same vision worldwide, organizations dedicated to the development of guidelines on patient safety and quality of care such as the U.S. Joint Commission for Hospital Accreditation (Joint Commission) have established guidelines on the monitoring of policies on prevention of VTE. This information should ultimately lead to a commitment in each hospital to develop strategies to implement the rational use of thromboprophylaxis (with management guidelines), both mechanical and/or pharmacological.²⁸

In conclusion, as in the international ENDORSE study, the frequency of medical and surgical patients at risk for VTE is high and its prophylaxis is low. Surgical patients received VTE prophylaxis more frequently than medical patients with results similar to those observed in the international ENDORSE study. These findings highlight the urgent need to improve monitoring of this prophylactic measure in patients at risk for VTE.

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