Venous thromboembolism risk and prophylaxis in the acute hospital care setting-results of the Endorse study in Tunisia

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Risque et prévention de la maladie thrombo-embolique veineuse chez les malades hospitalisés, résultats tunisiens de l'étude ENDORSE

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RÉSUMÉ

Prérequis : Il y a peu d'informations relatives au risque de la MTEV et sa prophylaxie en Tunisie. Les auteurs rapportent les résultants tunisiens d'une étude observationnelle multicentrique internationale.
But : Evaluer les malades à risque de développer une maladie thrombo-embolique veineuse et préciser le pourcentage de ceux qui recevaient une prévention adéquate.
Méthodes : Etude réalisée dans des services hospitaliers médicaux (patients âgés de 40 ans et plus) et chirurgicaux (patients âgés de 18 ans et plus. Huit cents quatre vingt cinq patients issus de cinq hôpitaux ont été évalués dont 212(24%) chirurgicaux et 673(76%) médicaux.
Résultats : Parmi les malades chirurgicaux 95(44,8%) sont à risque et parmi les patients médicaux 313(46,5%) sont à risque. Parmi les patients à risque 167(41%), dont 92 (29,4%) médicaux et 75 (79%) chirurgicaux ont reçu une prophylaxie recommandée. Un risque hémorragique élevé pouvant contre-indiquer l'anti coagulation est retenu chez 25 (8%) des malades médicaux et 10(10,5%) des malades chirurgicaux, ce risque ne peut à lui seul expliquer le faible niveau de prophylaxie. Les Héparines de bas poids moléculaire sont les plus utilisées. La prophylaxie mécanique est inexistante.
Conclusion : Le pourcentage des malades à risque en Tunisie, est comparable à celui des autres pays. La majorité des malades à risque sont des malades médicaux où la prophylaxie est sous-utilisée. Une sensibilisation des praticiens avec une mise en place dans les hôpitaux d'une stratégie de prévention de la MTEV est nécessaire.

Mots-clés

Maladie thrombo-embolique veineuse ; Risque ; Prophylaxie

SUMMARY

Background : There are not information about the risk of venous thromboembolism (VTE) and its prophylaxis in Tunisia.
Aim: To report the Tunisian results of a multinational cross-sectional study, designed to assess the prevalence of VTE risk in the acute hospital care setting and to determine the proportion of at risk patients who receive effective prophylaxis.
Methods: All hospital inpatients aged 40 years or over admitted to a medical ward or these aged 18 years or over admitted to surgical ward, in 5 Tunisian hospitals were assessed for risk of VTE on the basis of hospital chart review. The 2004 American College of chest physicians (ACCP) evidence based consensus guidelines were used to assess VTE risk and to determine whether patients were received recommended prophylaxis.
Results: 885 were enrolled, 212 (24%) were surgical and 673 (76%) were medical. 408 (44, 9%) judged to be at risk, 95 (44, 8%) are surgical and 313 (46, 5%) are medical. LWMH are the most used. Mechanical prophylaxis was never used.
Conclusion: The percentage of at risk patient in Tunisia is comparable to these of other countries. The majority of at risk patient are medical. The prophylaxis was under used. Hospital strategies to assess patient VTE risk and implementation of prophylaxis protocols are needed.

Key-words

Venous Thromboembolism; Risk; Prophylaxis

Venous thromboembolism risk and prophylaxis in the acute Venous thromboembolism (VTE) is a common complication during and after hospitalization for acute medical illness or surgery. Pulmonary embolism accounts for 5-10% of death in hospitalized patients, making VTE the most common preventable cause of in-hospital death. (2-5). In addition to the acute risk of mortality, VTE is associated with long-term risks of post-thrombotic syndrome (6) and chronic thromboembolic pulmonary hypertension (7). These complications contribute substantially to patient morbidity and raise the costs for public healthcare systems.

Evidence-based consensus guidelines for VTE prophylaxis have been available for more than 15 years (8). Despite the existence of these guidelines, VTE prophylaxis remains underused. (9, 10) Existing studies have assessed compliance with prophylaxis guidelines within defined institutions or countries, (11-13) but to date, the proportion of at-risk patients who should receive prophylaxis globally remains unknown.

Recently a multinational, observational, cross-sectional Epidemiologic International day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care setting (ENDORSE) study (1) was conducted between August, 2006 and January, 2007. A chart audit of medical and surgical patients in a large sample of hospitals worldwide. The study assessed the number of patients at risk for VTE in the acute care hospital setting in 358 hospitals across 32 countries and established the proportion of patients who received thrombo prophylaxis according to the recommendations of the American College for Chest Physicians (ACCP) guidelines, evidence-based consensus guidelines (2). Tunisia took part in this study. This paper presents the country-specific data from the 5 Tunisian hospitals participating in the ENDORSE study.

METHODS

Procedures:

Detailed procedures have been described in the primary ENDORSE report (1). Briefly, hospitals with >50 beds, admitting patients with acute medical illnesses and exacerbations of chronic diseases, and scheduled routine major surgical procedures were included in the study. Non-acute and single specialty hospitals were excluded. Hospitals were selected at random from authoritative lists of acute care hospitals in 32 participating countries. In Tunisia, Five hospitals were selected from the Tunisian government health authority's list. According to the national rules, the approval of the Ethics Committee was obtained for the study in Tunisia. Signed patient consent was not required.

Hospital wards were eligible if they were occupied by acute medical and surgical patients (eg, internal medical, respiratory, or cardiac wards, and general surgical and orthopaedic wards). Psychiatric, paediatric, eye, ear, nose and throat, dermatology, alcohol/drug treatment, rehabilitation, accident and emergency, maternity, chronic, and palliative care wards were excluded. Patients' data, including demographics, admission and post-admission diagnoses, risk factors associated with VTE, bleeding risk factors for, the duration of a stay and the type of VTE prophylaxis, were collected from a review of hospital charts on standard case report forms by trained physicians. For inclusion, each patient had to be hospitalized in an eligible ward on the predetermined day of survey. In large hospitals it was possible to survey one ward or floor on any particular day. Each ward was assessed on one pre specified day to allow complete and systematic processing of patient data. For inclusion, each patient had to be an inpatient in an eligible ward on the day it was surveyed. Data abstraction from all eligible charts in selected wards at each hospital was completed within 14 days.

Patients:

Patients aged 40 years or more in eligible medical wards or 18 years or more in eligible surgical wards were screened. Patients were ineligible or excluded from the study if their chart was unavailable, they would normally have been admitted to an ineligible ward, were admitted solely for the treatment of VTE. Enrolled patients were assessed for risk for VTE in accordance with the 2004 ACCP guidelines, which included acutely ill medical patients and those admitted for major trauma or undergoing a major surgical procedure requiring general or epidural anesthesia for at least 45 min (2, 14). Surgical patients were first assessed for age, type of surgery, and duration of anesthesia, and then classified as being at highest, high, moderate, or low risk for VTE as per the ACCP guidelines. The use of recommended types of VTE prophylaxis received by at-risk patients was defined according to specific recommendations from the 2004 ACCP guidelines for the different types of patients at risk. When assessing whether prophylaxis was compliant with the ACCP guideline recommendations, only the type of prophylaxis was considered. Data regarding the dose administered were collected; however, such data are not presented because of different dosing recommendations in different countries and because of variations in the drugs approved in different countries; furthermore, the ACCP does not give global recommendations for dosing schedules. Duration of dose could not be assessed because of the cross-sectional nature of the study.

Patients were considered to have a sufficient risk for bleeding to present a contraindication to anticoagulant prophylaxis if they presented with, or developed during hospitalization, any of the following: intracranial hemorrhage; hepatic impairment; bleeding at hospital admission; active gastro duodenal ulcer; or a known bleeding disorder.

Statistical analysis:

Statistical analyses are discussed in detail in the global primary ENDORSE report (1). Briefly, quantitative data were summarized as median (IQR) and the number of non-missing data were summarized into number and percentage of the population. Rates were calculated from individual patient data. To assess the true occurrence of VTE risk at 25% with a margin of error of 4%. SAS version 9.1 was used for all statistical analysis.

RESULTS

Among the 5 hospitals 4 are academic (Hospitals of La Rabta, Habib Thameur and Abdurrahman Memi à l'Ariana inTunis and hospital Hedi Chaker in Sfax) and one county hospital (Mahares). The number of beds assessed, and reasons for exclusion from assessment, together with the number of assessable medical and surgical patients are shown in figure 1.

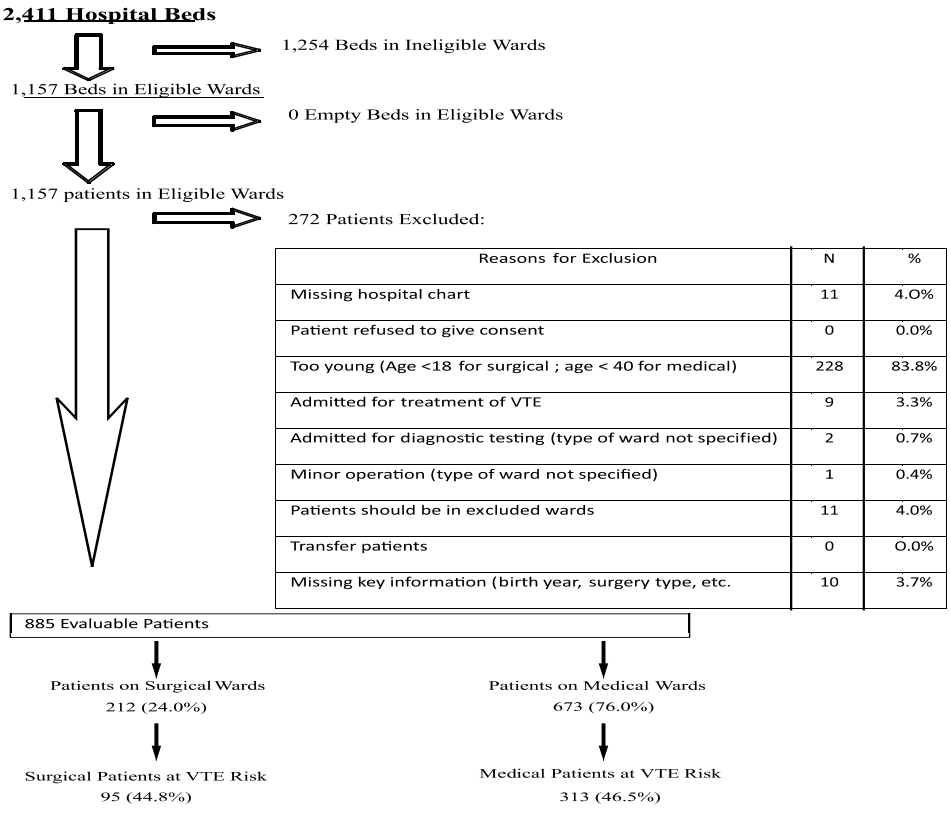
A total number of 885 patients were enrolled, 673 (76.0%) on medical and 212(24.O%) on surgical wards. 408 (46.1%) of the enrolled evaluable patients were deemed to be at risk for VTE. 95 (44.8%) surgical patients were at risk, as were 313 (46.5%) medical patients. General characteristics of at- risk patients are shown in table 1. Of the at risk patients in medical wards, 190(61.7%) are men, the median age is 62 years and the median BMI is 24.7kg/m2 and the median length of hospital stay up to survey date was 7.0 days. Of the at risk patients in surgical wards 54(57.4%) are men, the median age is 55 years, the median BMI is 23.9 kg/m2 and the median length of hospital stay up to survey date was 5.0 days.

Risk factors for VTE that were present before admission and the post admission factors are shown in table 2. In medical patients the most common VTE risk factors present prior to hospital admission were chronic pulmonary disease (32.5%), chronic heart failure (11.9%) and obesity. In surgical patients the most common VTE risk factors prior to hospital admission were obesity (8.9%) and chronic heart failure (6.7%). In medical patients the most common VTE risk factors present during hospital admission were cardiovascular disease (40.0%), pulmonary infection (36.1%) and acute non infectious disease. In surgical patients the most common risk factors present during hospital admission were gastro-intestinal and hepatobiliary conditions (27.4%), non respiratory infections (20.0%), cardiovascular disease (13.7%) and active malignancy (12.6%). The type of first major operation during the current admission is shown in table 3.

Table 1 : General characteristics of patients

Patients Characteristics	Surgical Risk (N=95)	Medical Risk (N=313)	All Risk (N=408)
Male	54 (57.4%)	190 (61.7%)	244(60.7%)
Female	40 (42.6%)	118 (38.3%)	158 (39.3%)
Age, Years (median)	95 (55.0)	313 (62.0)	408 (61.0)
Weight, kg (median)	33 (64.0)	225 (67.0)	258 (66.0)
Height, cm (median)	31 (167.0)	205 (165.0)	236 (165.0)
BMI, kg/m^2 (median)	30 (23.9)	198 (24.7)	228 (24.6)
Hospital admission to survey day, days (median)	95 (5.0)	311 (7.0)	406 (7.0)

Figure 1 : Selection of study population and reasons for exclusion



Reasons for Exclusion	N	%
Missing hospital chart	11	4.O%
Patient refused to give consent	0	0.0%
Too young (Age <18 for surgical ; age < 40 for medical)	228	83.8%
Admitted for treatment of VTE	9	3.3%
Admitted for diagnostic testing (type of ward not specified)	2	0.7%
Minor operation (type of ward not specified)	1	0.4%
Patients should be in excluded wards	11	4.0%
Transfer patients	0	O.0%
Missing key information (birth year, surgery type, etc.	10	3.7%

Table 2 : Risk factors of VTE

Conditions present PRIOR to hospital admission	Surgical Risk (N=95)	Medical Risk (N=313)	All Risk (N=408)
Previous venous thromboembolism	2 (2.2%)	9 (3.1%)	11 (2.9%)
Thrombophilia (laboratory, documented)	0 (0.O%)	4 (1.4%)	4 (1.0%)
Varicose veins or venous insufficiency	2 (2.2%)	12 (4.1%)	14 (3.6%)
Post-menopausal hormone replacement therapy	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic pulmonary disease	3 (3.3%)	96 (32.5%)	99 (25.7%)
Long term immobility	1 (1.1%)	22 (7.5%)	23 (6.0%)
Pregnancy (within 3 months)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Obese (based on physician's note)	8 (8.9%)	31 (10.5%)	39 (10.1%)
Contraceptives	1 (1.1%)	2 (0.7%)	3 (0.8%)
Chronic heart failure	6 (6.7%)	35 (11.9%)	41 (10.6%)
Other Conditions present DURING hospital admission			
Acute heart failure (NYHA Class III or IV)	1 (1.1%)	45 (14.4%)	46 (11.3%)
Ischemic stroke	1 (1.1%)	1 (0.3%)	2 (0.5%)
Hemorrhagic stroke	1 (1.1%)	2 (0.6%)	3 (0.7%)
Other cardiovascular disease	12 (12.6%)	80 (25.6%)	92 (22.5%)
Hematologic disease	0 (0.0%)	8 (2.6%)	8 (2.0%)
Acute non-infectious respiratory disease	2 (2.1%)	71 (22.7%)	73 (17.9%)
Pulmonary infection	7 (7.4%)	113 (36.1%)	120 (29.4%)
Malignancy (active)	12 (12.6%)	27 (8.6%)	39 (9.6%)
Infection (non-respiratory)	19 (20.0%)	32 (10.2%)	51 (13.0%)
Rheumatologic or inflammatory	0 (0.0%)	16 (5.1%)	16 (3.9%)
Neurologic	2 (2.1%)	5 (1.6%)	7 (1.7%)
Renal	5 (5.3%)	13 (4.2%)	18 (4.4%)
Endocrine/Metabolic	7 (7.4%)	42 (13.4%)	49 (12.0%)
GI/Hepatobiliary	26 (27.4%)	13 (4.2%)	39 (9.6%)
Other medical condition	8 (8.4%)	14 (4.0%)	22(5.4%)
Admitted to ICU/CCU	34 (35.8%)	86 (27.5%)	120 (29.4%)
Central venous catheter	9 (9.5%)	11 (3.5%)	20 (4.9%)
Mechanical ventilation	5 (5.3%)	6 (1.9%)	11 (2.7%)
Immobile with bathroom privileges	13 (13.7%)	91 (29.1%)	104 (25.5%)
Complete immobilization	44 (46.3%)	25 (8.0%)	69 (16.9%)
Cancer therapy	2 (2.1%)	5 (1.6%)	7 (1.7%)
Heparin induced thrombocytopenia	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3 : Type of 1st major operation during the current hospital admission

Type of 1st major operation	Surgical Risk (N=95)	Medical Risk (N=313)	All Risk (N=408)
Hip replacement	0 (0.0%)	N/A	N/A
Knee replacement	0 (0.0%)	N/A	N/A
Hip fracture	0 (0.0%)	N/A	N/A
Curative arthroscopy	0 (0.0%)	N/A	N/A
Other ortho trauma	0 (0.0%)	N/A	N/A
Colon/Small bowel	9 (9.5%)	N/A	N/A
Rectosigmoid	4 (4.2%)	N/A	N/A
Gastric	5 (5.3%)	N/A	N/A
Hepatobiliary	16 (16.8%)	N/A	N/A
Urologic	6 (6.3%)	N/A	N/A
Vascular	5 (5.3%)	N/A	N/A
Thoracic	17 (17.9%)	N/A	N/A
Gynecologic	4 (4.2%)	N/A	N/A
Other major surgery	23 (24.2%)	N/A	N/A
Admitted with major trauma but surgery not performed	6 (6.3%)	N/A	N/A

The most common contraindication to pharmacological prophylaxis (Table4) is bleeding at hospital admission (4.5%) in medical patients and (4.2%) in surgical patients. 25 (8.0%) of at risk medical patients and 10 (10.5%) of at risk surgical patients were considered to have a high bleeding risk, sufficient to present a contraindication to pharmacological prophylaxis.

Table 4 : Risk factors for bleeding present at current admission

	Surgical Risk (N=95)	Medical Risk (N=313)	All Risk (N=408)
Significant renal impairment	8(8.4%)	22 (7.0%)	30 (7.4%)
Intracranial hemorrhage	2 (2.1%)	1 (0.3%)	3 (0.7%)
Low platelet count (<100,000 /ml)	1 (1.1%)	8 (2.6%)	9 (2.2%)
Known bleeding disorder (congenital or acquired)	0 (0.0%)	4 (1.3%)	4 (1.0%)
Hepatic impairment (clinically relevant)	3 (3.2%)	6 (1.9%)	9 (2.2%)
Bleeding at hospital admission	4 (4.2%)	14 (4.5%)	18 (4.4%)
Active gastro duodenal ulcer	3 (3.2%)	2 (0.6%)	5 (1.2%)
Aspirin on admission	3 (3.2%)	60 (19.2%)	63 (15.4%)
NSAID on admission (excluding aspirin)	0 (0.0%)	11 (3.5%)	11 (2.7%)

167 (41, 0%) patients deemed to be at risk for VTE received ACCP-recommended types of prophylaxis, of whom 92 (29,4%) were medical patients and 74 (79%) were surgical patients. The rate of prophylaxis is low even in medical patients with high risk such as congestive heart failure (22%) and malignancy (29,6%) which is noted in other studies (18,19).

Anticoagulants were the sole form of VTE prophylaxis; low-molecular –weight heparin was the most commonly used (Table 5). The mechanical prophylaxis was never used.

Table 5 : Anticoagulant VTE Prophylaxis ordered during hospital admission

	Surgical Risk (N=95)	Medical Risk (N=313)	All Risk (N=408)
Low molecular weight heparin	73(76.8%)	88 (28.1%)	161 (39.5%)
Unfractionated heparin	2 (2.1%)	4 (1.3%)	6 (1.5%)
Vitamin-K antagonist	2 (2.1%)	2 (0.6%)	4 (1.0%)
Fondaparinux	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other anticoagulants	0 (0.0%)	1 (0.3%)	1 (0.2%)
Mechanical Prophylaxis given			
Intermittent pneumatic compression (IPC)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Foot pump (AVI)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Graduated compression stockings	0 (0.0%)	0 (0.0%)	0 (0.0%)

DISCUSSION

This first Tunisian survey which is a part of an international cross-sectional study(1) shows that about half (46%) of all hospitalized patients are at risk for VTE, then worldwide 52% of hospitalized patients were at risk for VTE. 41% in Tunisia then 51% worldwide of the at risk patients received an ACCP-recommended prophylaxis. The use of prophylaxis in at risk surgical patients (78%) is higher than worldwide but the recommended prophylaxis is poor in the at risk medical patients (29%). The low use of prophylaxis have been related in other studies IMPROVE (13) 60% and CURVE (17) (16%).The difference between surgical and medical patients is seen worldwide this fact could result from several factors. First, the benefits of prophylaxis in the surgical setting have been accepted for many years, while trials in medical patients have been more recent and physician awareness for VTE risk is lower in this population. Second, assessment of VTE risk in surgical patients is easier than in medical patients, the principal criteria is the type of surgery rather than a range of illnesses and risk factors as presented in medical patients. Eight per cent in at risk medical patients and 10, (5%) in at risk surgical patients have a contraindication to pharmacological prophylaxis but this fact is not sufficient to justify the low rate of prophylaxis. In another hand these patients could have received the ACCP recommended mechanical prophylaxis but mechanical methods aren't used in Tunisia probably because a low physician awareness and the cost.

This study have some limitations, the small country- specific size and participating hospitals might not be representative of all hospitalized patients for example there are no orthopedic patients. Some excluded patients may have been at VTE risk. The Cross sectional design without follow-up so the assessment is limited to duration of hospital stay and cannot evaluate whether prophylaxis duration complies with ACCP recommendations .The use of the 2004 ACCP Guidelines can be criticized, but they were adopted as the best established and most widely referenced standard, and have been used in other studies of VTE prophylaxis (10 -12). The data show that a large proportion of hospitalized Tunisians patients as in other countries are at risk of VTE, and that recommended VTE prophylaxis is underused. VTE in Tunisia, is probably a public health problem with potential risk of mortality and morbidity (14) like in other countries (20, 21), other studies are needed to confirm it. Hospital strategies to assess patients VTE risk should be implemented, with measures that ensure that at risk patients receive appropriate VTE prophylaxis.

Références

1. Cohen A T, Topson V F, Bergman J F, et al for the Endorse Investigators. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (Endorse study): a multinational cross-sectional study. Lancet 2008; 371: 387-94
2. Geerts W H, Pineo G F, Heit J A, et al. Prevention of venous thromboembolism: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004; 126 (3 suppl): 338S-400S.
3. Linblad B, Sternbay NH, Bergqvist D. Incidence of venous thromboembolism verified by necropsy over 30 years. BMJ 1991; 302: 709-11.
4. Sandler DA, Martin JF. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? J R Soc Med 1989; 82:203-05.
5. Alikhan R, Peters F, Wilnott R, Choen AT. Fatal pulmonary embolism in hospitalised patients: a necropsy review. J Clin Pathol 2004; 57:1254-57.
6. Prandoni P, Villalta S, Bagatella P, et al. The clinical course of deep-vein thrombosis. Prospective long-term follow-up of 528 symptomatic patients. Haematologica 1997; 82:423-28.
7. Pengo V, Lensing AW, Prins MH, et al. Thromboembolic Pulmonary Hypertension Study Group. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. N Engl J Med 2004; 350:2257-64.
8. Clagett GP, Anderson Jr FA, Levine MN, Salzman EW, Wheeler HB. Prevention of venous thromboembolism. Chest 1992; 102 (4 suppl): 391S-407S.
9. Otero R, Uresandi F, Cayuela A, et al. Use of venous

thromboembolism prophylaxis for surgical patients: a multicentre analysis of practice in Spain. Eur J Surg 2001;167:163-67.
10. Yu HT, Dylan ML, Lin J, Dubois RW. Hospitals'compliance with prophylaxis guidelines for venous thromboembolism. Am J Health Syst Pharm. 2007; 64:69-76.
11. Eikelboom JW, Mazzarol A, Quinlan DJ, et al: The American College of Chest Physicians. Thromboprophylaxis practice patterns in two Western Australian teaching hospitals. Haematologica 2004; 89:586-93.
12. Amin A, Stemkowski S, Lin J, Yang G. Thromboprophylaxis rates in US medical centers: success or failure? J Thromb Haemost 2007; 5:1610-16.
13. Tapson VF, Decousus H, Pini M, et al. Venous thromboembolism prophylaxis in acutely ill hospitalized medical patients: findings from the international medical prevention registery on venous thromboembolism. Chest 2007; 132:936-45.
14. Kakkar VV, Corrigan TP, Fossard DP, Sutherland I, Shelton MG, Thirlwall J. Prevention of fatal postoperative pulmonary embolism by low doses of heparin: an international multicentre trial. Lancet 1975:306; 45-51.
15. Baglin T, Barrowcliffe TW, Cohen A, Greaves M; British Committee for Standards in Haematology. Guidelines on the use and monitoring of heparin. Br J Haematol 2006; 133:19-34.
16. Cohen AT, Alikhan R, Arcelus JI, et al. Assessment of venous thromboembolism risk and the benefits of thromboprophylaxis in medical patients. Thromb Haemost 2005; 94:750-59.
17. Kahn SR, Panju A, Geerts W. et al. Multicenter evaluation of the use of venous thromboembolism in acutely ill medical patients in Canda. Throm Res 2007; 119:145-55.
18. Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. N Engl J Med 199; 341:793-800.
19. Cohen AT, Davidson BL, Gallus AS, et al: ARTEMIS Investigators; Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomized placebo controlled trial. BMJ 2006; 332:325-29.
20. Anderson FA Jr, Zayaruzny M, Heit JA, Fidan D. Cohen AT. Estimated annual numbers of US acute-care hospital patients at risk for venous thromboembolism. Am J Hematol 2007; 82:777-82.
21. Cohen AT, Agnelli G, Anderson FA Jr, et al. Venous thromboembolism in Europe: the number of VTE events and associated