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Original article

Venous thromboprophylaxis in medical patients: an application review[☆]

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ABSTRACT

Objective: Routine thromboprophylaxis, despite its well-known effectiveness and the fact that venous thromboembolism is a potentially avoidable condition, is not fully established in clinical practice. The objectives of the present study were to determine how often thromboprophylaxis is used and the presence of thromboembolism risk factors, and to verify the appropriateness of its use in medical inpatients, assuming a long-standing national guideline as a parameter.

Methods: This was a retrospective cross-sectional study, involving inpatients with medical conditions in the adult general ward of a faculty hospital. The review was based on a defined guideline.

Results: 146 patients were included in the review. At least one risk factor for venous thromboembolism was found in 94.5%. In 130 (89%) patients, prophylactic heparin was indicated, and some kind of heparin was prescribed in 73.3%. Regarding the adequacy of prophylaxis, 53.4% of prescriptions were correct regarding prophylaxis indication and dose; 24% had incorrect dose or frequency of use; 19.2% had no prophylaxis prescription, although it was indicated; and in five cases (3.4%), the drug was prescribed, even though it was not indicated.

Conclusion: Thromboprophylaxis is underused in this population, and an inappropriate dose was prescribed in 50% of cases. Therefore, future studies and interventions should include an educational program started from the emergency department care, an essential step to bring evidence closer to clinical practice.

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Trombopprofilaxia venosa em pacientes clínicos: análise de sua aplicação

R E S U M O

Palavras-chave:

Fatores de risco
Fidelidade a diretrizes
Heparina
Profilaxia
Tromboembolismo venoso

Objetivo: A trombopprofilaxia de rotina, a despeito de sua efetividade estar bem estabelecida e o tromboembolismo venoso ser uma condição potencialmente evitável, não se apresenta completamente consolidada na prática clínica. Os objetivos do presente estudo são: 1. Determinar a frequência da utilização da trombopprofilaxia e presença dos fatores de risco para tromboembolismo; 2. Verificar a adequação de sua utilização em pacientes clínicos internados, assumindo como parâmetro uma diretriz nacional estabelecida.

Métodos: Estudo retrospectivo transversal envolvendo pacientes internados por doenças clínicas em uma enfermaria geral de adultos de um hospital escola. A análise foi baseada em diretriz definida.

Resultados: Foram incluídos 146 pacientes para análise. Destes, 94,5% possuíam pelo menos um fator de risco para tromboembolismo venoso. Em 130 (89%) pacientes havia indicação para uso de heparina profilática, sendo que em 73,3% dos casos estava prescrito algum tipo de heparina. Quanto à adequação da profilaxia, 53,4% das prescrições estavam corretas em relação à indicação e à dose da profilaxia; 24% apresentavam dose ou frequência incorretas; 19,2% não tinham prescrição de profilaxia, apesar de ela ser indicada; e em cinco casos (3,4%) o fármaco foi prescrito, apesar de não haver indicação.

Conclusão: Existe subutilização da trombopprofilaxia nesta população, com inadequada dose prescrita em 50% dos casos. Portanto, estudos e intervenções futuros devem incluir um programa educacional que se inicie desde o atendimento em pronto-socorro, sendo essencial para aproximar a evidência à prática clínica.

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Introduction

Venous thromboembolism (VTE) is a group of diseases including deep venous thrombosis (DVT), central venous catheter-related thrombosis, thrombosis in different sites, and the most severe type, pulmonary thromboembolism (PTE), all of which are potentially avoidable causes of morbidity and mortality.¹⁻⁴

Hospitalization for a nonsurgical acute disease is associated with an eight-fold rise in VTE risk, representing approximately 25% of all events assigned to this condition.⁵ Furthermore, postmortem studies demonstrate that approximately 10% of inpatient death causes result from pulmonary embolism.⁶ Thus, a low degree of clinical suspicion is assumed, considering that in part of PTE cases, symptoms are forme fruste.^{6,7}

Most studies on thromboprophylaxis in clinical populations involve patients at high risk for a thromboembolic event. Recently, studies and guidelines have standardized and promoted thromboprophylaxis in medium- and low-risk patients.^{5,8-11} In this setting, some authors have described interventions markedly reducing the risk of VTE in medical patients.^{11,12} An effort of current guidelines has been to introduce thromboprophylaxis recommendations for several inpatient groups.¹³⁻¹⁶

VTE risk stratification is performed by initially considering the patient's age, mobility level, and comorbidities. Individuals aged 40 years and over, with reduced mobility and at least one additional risk factor (among the following: stroke, cancer, central and Swan-Ganz catheters, bowel inflammatory disease, severe respiratory disease, acute rheumatic disease, pregnancy

and postpartum, previous VTE history, acute myocardial infarction [AMI], class III or IV congestive heart failure [CHF], age over 55 years, infection [except for thoracic conditions], arterial insufficiency, intensive care unit admission, obesity, lower limb weakness/paralysis, chemo/hormonal therapy, hormone replacement therapy, nephrotic syndrome, and thrombophilia) for VTE should be considered at risk. In the absence of contraindications, prophylaxis is indicated. For individuals under 40 years, specific guidelines should be followed.^{4,10}

However, despite the well-proven benefits, routine thromboprophylaxis for medical patients with risk factors is poorly established into daily medical practice.^{17,18} There is non-adherence to consensus and guideline recommendations, for which the main reasons are: 1) lack of a systematic assessment for VTE risk factors and the contraindications for heparin use;^{17,19} 2) unawareness of VTE risk, likely favored by patients' diversity; 3) difficult definition for risk factors and thromboprophylaxis indication, as well as the several available guidelines, resulting in inaccurate and unclear indications for thromboprophylaxis.¹¹ This study hypothesized that VTE prophylaxis is underused.

The objectives of this study were to retrospectively assess medical inpatients at risk of VTE admitted to a general medical ward, to define the ratio of medical patients at risk of VTE receiving prophylaxis, and to evaluate the adequacy of prophylaxis use. The Brazilian Guideline for Venous Thromboembolism: Prophylaxis in Medical Patients¹⁰ a freely available publication for the general public based on the local reality and approved by several medical societies and the Federal

Council of Medicine, aiming to reconcile medical information and standardize behaviors aiding reasoning and the decision-making process.

Methods

This study was conducted in 2009 and included 187 adult patients in a medical ward in the Hospital das Clínicas (HC I), a health care reference hospital at the secondary and tertiary levels located in the city of Marília, São Paulo, Brazil, which provides care for 62 municipalities, with an estimated combined population of 1.2 million inhabitants.

For convenience, the study did not have a probability sampling. The analysis was made by review of medical records; the patients' identity was fully preserved. The search period was 12 months (January, 2009 to December, 2009), selecting all the admissions in the first ten days of four non-consecutive months (January, April, August, and December, 2009). The patients were studied in non-consecutive months in order to achieve greater representativeness of the physicians involved in care (since the institution is a teaching hospital, where physicians in charge of the ward rotate) and a larger range of diseases can be found due to seasonal variations.

Data collection was made based on a specific tool, consisting of an adaptation of the Brazilian Guideline for Venous Thromboembolism: Prophylaxis in Medical Patients.¹⁰ Data was systematically accessed only once, by two independent examiners.

A clinical-demographic analysis (gender, birth date, admission date, and main and secondary diagnosis), a risk assessment, and an indication and use of VTE prophylaxis were performed, as well as an analysis of the thromboprophylaxis used 48 hours after the admission to the medical ward and prescription changes up to the end of the hospitalization period.

The study inclusion criterion consisted of admission to a medical ward, and exclusion criteria were length of stay under 48 hours, having undergone surgery within a week before the admission, use of any type of oral anticoagulant, and VTE diagnosis at admission.

The primary outcome was to evaluate the venous prophylaxis adequacy based on the recommendations of the Brazilian guideline for VTE prophylaxis.

The following were considered venous thromboprophylaxis mandatory indication: 40 years of age and over and reduced mobility, associated with at least one risk factor in the absence of heparin contraindication.

The doses considered correct for thromboprophylaxis were based on the clinical settings in accordance with the Brazilian guideline for VTE prophylaxis, and are briefly shown in Table 1. Any other heparin dose or indication not found in the recommendations was considered as inappropriate, such as: a) cases with no prophylaxis prescription who required it; b) cases where prophylaxis was prescribed, but was unnecessary; c) cases with prescribed prophylaxis, but in an inappropriate dose or frequency (noncompliant with those recommended by the guideline). At the time of the study, the HC I had no formal program encouraging VTE prophylaxis in medical patients. The

Table 1 – Specific evidence and recommendations of venous thromboembolism prophylaxis.

Condition	Method (level of recommendation)	Dose
Previous history of VTE + risk condition	UFH (d)	5,000 IU every 8 h
	LMWH (d)	Dalteparin or enoxaparin (40 mg/day)
Chronic venous insufficiency/varicose veins	Enoxaparin (c)	40 mg/day
	Dalteparin (d)	5,000 IU/day
Obesity + risk condition	Enoxaparin (c)	40 mg/day
	Dalteparin (d)	5,000 IU/day
Thrombophilias + risk condition	UFH (d)	5,000 IU every 8 h
	LMWH (d)	Enoxaparin (40 mg/day)
HRT/HCC + risk condition	Warfarin	INR (2-3)
	UFH (d)	5,000 IU every 8 h
	LMWH (D)	Dalteparin or enoxaparin (40 mg/day)
CHF	UFH (a)	5,000 IU every 8 h
	Enoxaparin (a)	40 mg/day
	Dalteparin (d)	3,800 IU < 70 kg
	Nadroparin (d)	5,700 IU > 70 kg
AMI	UFH (a)	5,000 IU every 12 h or full dose
	Dalteparin (b)	120 IU/kg
	Early walking (b) ICS (b)	
Ischemic stroke	UFH (b)	5,000 IU every 8 or 12 h
	LMWH (a)	Enoxaparin (40 mg/day)
	ICS	
Hemorrhagic stroke	Enoxaparin (b)	Do not use
	Dalteparin (b)	40 mg/day
ARD/BID	UFH (a)	5,000 IU/day
	Enoxaparin (b)	40 mg/day
SRD	Dalteparin (b)	5,000 IU/day
	ICS (b)	Uninterrupted
	UFH (a)	5,000 IU every 8 or 12 h
	Enoxaparin (a)	40 mg/day
Infections	Dalteparin (b)	5,000 IU/day
	Enoxaparin (b)	40 mg/day
Nephrotic syndrome	Enoxaparin (b)	40 mg/day
	Enoxaparin (b)	40 mg/day
Neoplasms	UHF (c)	5,000 IU every 12 h
	Enoxaparin (d)	40 mg/day
	Nadroparin (a)	3,800 or 5,700 IU/day
	ICS/IPC	
ICU admission	UHF (a)	5,000 IU every 6, 12 h or 1 U/mL to 3 U/mL in PN
	UFH (a)	
CVC for PN	Dalteparin (b)	2,500 IU/day
	Nadroparin (d)	2,850 IU to 7,600 IU/day
CVC in cancer patients	Warfarin (a)	1 mg/day

AMI, acute myocardial infarction; ARD, acute rheumatic diseases; CHF, congestive heart failure; CVC, central venous catheters; HCC, hormonal contraception; HRT, hormone replacement therapy; ICS, intermittent compression stockings; ICU, intensive care unit; INR, international normalized ratio; IPC, intermittent pneumatic compression; LMWH, low molecular weight heparin, PN, parenteral nutrition; SRD, severe respiratory diseases; UFH, unfractionated heparin; VTE, venous thromboembolism.

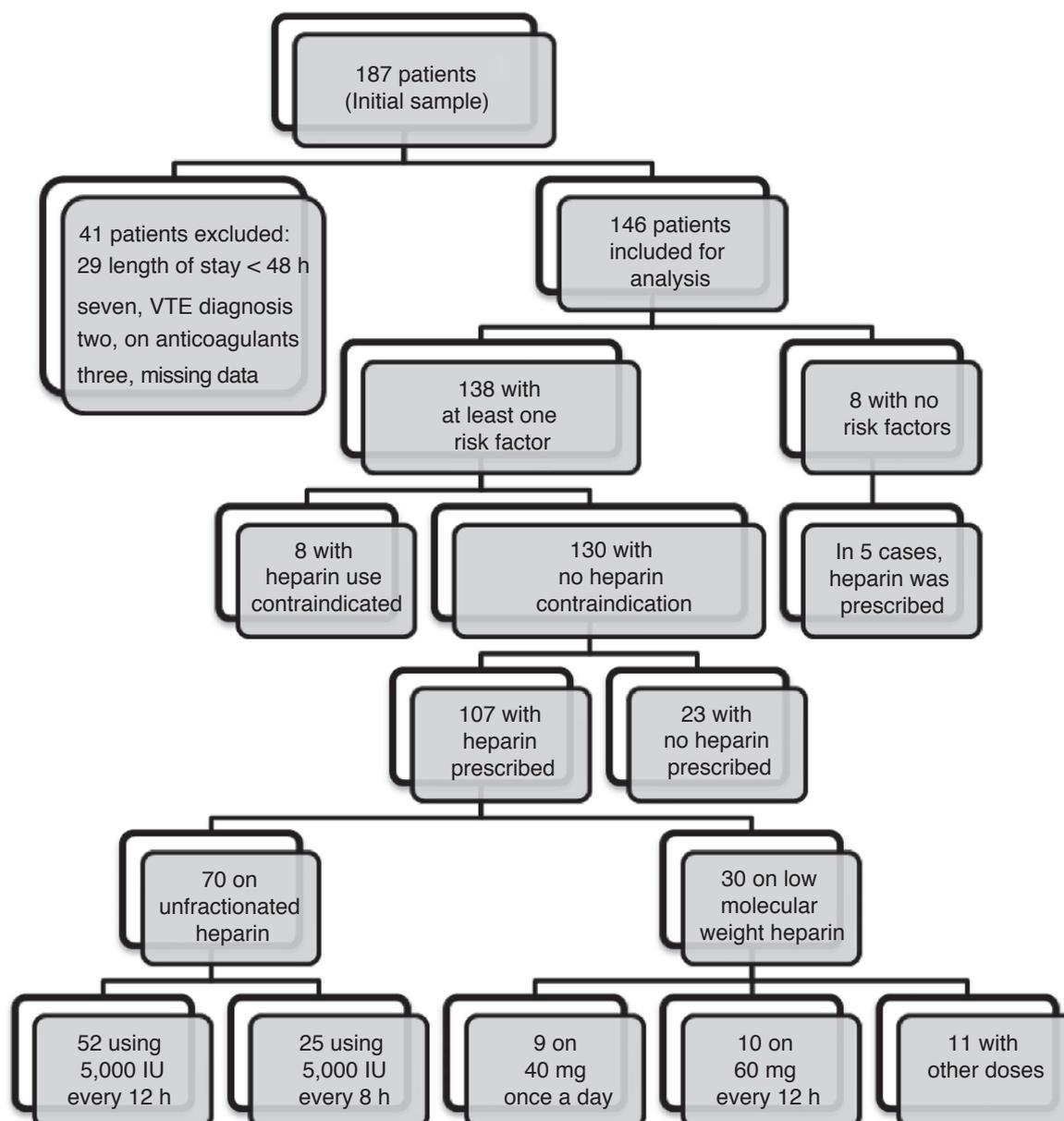


Fig. 1 – Study design. VTE, venous thromboembolism.

present study was approved by the Ethics Committee of the Medical School of Marília (Famema) in February 22, 2010, under protocol No. 050/10

Data were descriptively and inferentially analyzed. Central tendency (mean) and dispersion (standard deviation) measurements were used to summarize numeric variables. Categorical variables (prophylaxis indicated/not indicated; use of prophylaxis/no use of prophylaxis; correct/incorrect prophylactic dose; prophylaxis change/no prophylaxis change during the hospitalization; prophylaxis corrected/not corrected) were compared through the chi-squared test. Confidence intervals were calculated with a 95% probability, and a p-value < 0.05 was established.

Results

In this study, 146 patients were assessed (Fig. 1). The patients' and the study's general characteristics are shown in Table 2.

In 130 (89%) patients, prophylactic heparin use was indicated; of these, in 107 (73.3%), some kind of heparin was prescribed, with 77 (71.9%) using unfractionated heparin and 30 (28.1%), low molecular weight heparin. Among those using unfractionated heparin, 52 (67.5%) received a dose of 5,000 IU every 12 hours, and 25 (32.4%), every 8 hours. Among those using low molecular weight heparin, 40 mg were prescribed once a day for nine patients (30%); a dose of 60 mg every 12 hours was prescribed for ten (33.3%), and

Table 2 – General characteristics of medical inpatients.

Variables	Patients (n = 146)
Mean age, years (range: 2 SD) (min-max)	61.68 (45.76-77.6) (18/92)
Age ≥ 40 years	133 (91.1%)
Male gender	94 (64.4%)
Length of stay in hospital: mean, days (range: 2 SD) (min-max)	25.95 (1-65.45) (3/289)
Admission diagnosis	
Infection	43 (29.5%)
Acute coronary syndrome	21 (14.4%)
Heart failure	14 (9.6%)
Stroke	19 (13%)
Cancer	7 (4.8%)
Decompensated diabetes	7 (4.8%)
COPD	4 (2.7%)
Others	31 (21.2%)
Main diagnosis and RF for VTE	
RF for VTE (≥ 1)	137 (93.8%)
Heparins contraindicated	10 (6.9%)

COPD, chronic obstructive pulmonary disease; RF, risk factor; SD, standard deviation; VTE, venous thromboembolism.

other doses were prescribed for 11 patients (36.6%). No patient used VTE mechanical prophylaxis. For patients on heparin (unfractionated or low molecular weight heparin) a dosing change was observed in 27 (25.2%), with adequacy occurring in only five (4.6%) patients with any kind of heparin prescription (n = 107).

Regarding prophylaxis adequacy, 78/146 (53.4%) prescriptions were found to be correct concerning indication and dose, 35 (24%) had incorrect doses or frequency, 28 (19.2%) had no prophylaxis prescription, although it was indicated, and in five cases (3.4%), the drug was prescribed, but it was not indicated.

Regarding the studied variables, the frequency of thromboprophylaxis prescription was higher in patients with a formal use indication than in those for whom it was not indicated or was even contraindicated (78.5% versus 31.3%, respectively, $\chi^2 = 16.22$; $p < 0,001$). Among patients who had a prophylaxis regimen change, a higher frequency for adequacy of the corrected prophylaxis regimen over non-adequacy (80% versus 20%, respectively, $\chi^2 = 15.9$; $p < 0.001$) was found.

Regarding the prescription of a correct dose for thromboprophylaxis, no significant statistical difference was observed between frequencies for whether prophylaxis was indicated or not (36.3% versus 40%, respectively, $\chi^2 = 1.14$; $p = 0.284$). The same finding was observed when a prophylactic regimen change during the clinical course (dose or drug) was compared with cases where prophylaxis either was or was not indicated (19.8% versus 12.5%, respectively, $\chi^2 = 0.49$; $p = 0.481$).

Discussion

The current study evaluated the status of VTE prophylaxis after the Brazilian guideline was published.¹⁰

Risk factors for VTE are very frequent (94.5% in the present study), as observed by studies such as IMPROVE, a multicenter study involving 15,156 patients,²⁰ and by the observational study ENDORSE, which included 68,183 patients and demonstrated that over half of those patients, admitted with either surgical or nonsurgical causes, were at risk for VTE,²¹ which warns medical professionals to the attention that should be given to this topic. In the present study, the high frequency is credited to the fact this study was conducted in a tertiary center with a large number of high complexity clinical cases.

Regarding venous thromboprophylaxis, a higher rate than that found in other studies was observed,²²⁻²⁷ but it was still underused. It can be assumed that the higher thromboprophylaxis use was a due to the fact that the study was conducted after the disclosure of the Brazilian guideline,¹⁰ and also because it was conducted in a teaching hospital with a formal internal medicine residency program. However, studies conducted so far are controversial on a higher use of thromboprophylaxis in teaching hospitals. Chopard et al.²⁸ found no difference in hospitals with or without medical residency, and Anderson et al.²⁹ showed prophylaxis is most often used in teaching hospitals.

However, despite the fact that VTE prophylaxis was more often used in the present study, only 53.4% of prescriptions were correct regarding prophylaxis indication and dose; conversely, 24% had incorrect dose or frequency. This low rate of correct prescriptions according to the proposition in the Brazilian guideline may be due to the complexity to establish the dosing or frequency for the clinical condition, which makes the indications particularly individualized. This data draws attention to the need for establishing protocols with brief and general guidelines regarding correct thromboprophylaxis use, as inappropriate doses are often ineffective.

Moreover, in the present study VTE mechanical prophylaxis, which has been strengthened as an independent protection to prevent bleeding and death in medical patients at risk, was not used.³⁰ A higher frequency of unfractionated heparin use was also observed, which may represent a local hospital policy or the ease of use for the professionals involved.

In this context, Rocha et al.³¹ has already described that, in addition to prophylaxis underuse for medical patients, it does not adhere to consensus and guideline recommendations, and suboptimal heparin doses are used.

The present findings also suggest that prophylaxis dosing regimen changes lead to higher dose adequacy, which could be related to the wide range of research material and the information exchange between those involved in medical patients' care.

The fact that the HC I does not have a formal program or an established guideline for thromboprophylaxis could have contributed to prophylaxis underutilization and prescription shortcomings. An increased prophylaxis use from 29% to 52% after the introduction of educational strategies was reported by Anderson et al.³² Conterno et al.³³ showed that preparing and implementing a guideline for community-acquired pneumonia promoted therapeutic choice optimization.

The main factors for venous prophylaxis underutilization were: 1) lack of systematic assessment of VTE risk factors

and contraindications for heparin use;^{17,19} 2) lack of awareness about VTE risk, likely favored by the diversity among patients; 3) difficulty in defining risk factors and thromboprophylaxis indication, as well as the various available guidelines, resulting in inaccurate and unclear indications for thromboprophylaxis.¹¹ Thus, incentive policies and inpatients assessment systematization are evidently needed.

The preparation of an educational and care program with a systematic assessment of patients admitted to the medical ward is extremely needed. The definition of cases with indication for prophylaxis should start at the emergency room through a predetermined flow chart containing clinical and epidemiological data, active assessment for risk factors, and frequent reassessments.

The need for professional education should be emphasized by encouraging journal reading and educational lectures where VTE risks, complications, and fatal events are explored. Preparation, implementation, and dissemination of venous thromboprophylaxis guidelines should be encouraged, considering local characteristics.

For this purpose, the authors suggest that every medical patient should undergo an initial screening with models similar to that proposed by the Brazilian guideline in the emergency room or in the medical ward, followed by the utilization of predetermined regimens of venous thromboprophylaxis according to clinical recommendations (Table 1), thus reducing inadequacy risk.

It should also be noted that, as the current study had a retrospective and cross-sectional design, it has methodological limitations. Therefore, prospective complementary studies are suggested for future development.

Conclusion

VTE prophylaxis underutilization was found in the study population. The prescription adequacy (dose and frequency) needs to be improved. Venous thromboprophylaxis occurrence does not indicate that it is correctly used. It is important to disseminate among physicians the guidelines regarding the correct manner to indicate and prescribe VTE prophylaxis. For this purpose, an educational program starting from the emergency room care is essential so that the evidence comes closer to clinical practice.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- Pitta GBB, Leite TL, Silva MDC, Melo CFL, Calheiros GA. Avaliação da utilização de profilaxia da trombose venosa profunda em um hospital escola. *J Vasc Bras.* 2007;6(4):344-51.
- Geerts WH, Heit JA, Claggett GP, Pineo GF, Colwell CW, Anderson FA, et al. Prevention of venous thromboembolism. *Chest* 2001;119(1 Suppl):132S-75S.
- Carneiro JLA, Targueta GP, Marino LO. Avaliação da profilaxia do tromboembolismo venoso em hospital de grande porte. *Rev Col Bras Cir.* 2010;37(3):204-10.
- Nacif SAP, Gazoni FM, Lopes RD. Profilaxia de tromboembolismo venoso em pacientes clínicos: como e quando? *Rev Soc Bras Clin Med.* 2009;7(5):331-8.
- Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest.* 2008;133(6 Suppl):381S-453S.
- Yoo, HHB, Mendes FG, Alem CER, Fabro AT, Corrente JE, Queluz TT. Achados clinicopatológicos na tromboembolia pulmonar: estudo de 24 anos de autópsias. *J Bras Pneumol.* 2004;30(5):426-32.
- Rocha AT, Paiva EF, Lichtenstein A, Milani R Jr, Cavalheiro CF, Maffei FH, et al. Risk-assessment algorithm and recommendations for venous thromboembolism prophylaxis in medical patients. *Vasc Health Risk Manag.* 2007;3(4):533-53.
- Cohen AT, Alikhan R, Arcelus JI, Bergmann JF, Haas S, Merli GJ, et al. Assessment of venous thromboembolism risk and the benefits of thromboprophylaxis in medical patients. *Thromb Haemost.* 2005;94(4):750-9.
- Arnold DM, Kahn SR, Shrier I. Missed opportunities for prevention of venous thromboembolism: an evaluation of the use of thromboprophylaxis guidelines. *Chest.* 2001;120(6): 1964-71.
- Rocha AT, Paiva EF, Lichtenstein A, Milani-Jr R, Cavalheiro-Filho C, Maffei FH, et al. Tromboembolismo venoso: profilaxia em pacientes clínicos parte I-III. In: Associação Médica Brasileira, Conselho Federal de Medicina. Projeto diretrizes. São Paulo: Associação Médica Brasileira; 2006. v.4, p. 363-407
- Alikhan R, Cohen AT, Combe S, Samama MM, Desjardins L, Eldor A, et al. Risk factors for venous thromboembolism in hospitalized patients with acute medical illness: analysis of the MEDENOX Study. *Arch Intern Med.* 2004;164(9):963-8.
- Prandoni P. Prevention and treatment of venous thromboembolism with low-molecular-weight heparins: clinical implications of the recent European guidelines. *Thromb J.* 2008; 6(9):13 [cited 2011 Feb 22]. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2546366/pdf/1477-9560-6-13.pdf>
- Spyropoulos AC. Emerging strategies in the prevention of venous thromboembolism in hospitalized medical patients. *Chest.* 2005;128(2):958-69.
- Kearon C, Kahn SR, Agnelli G, Goldhaber S, Raskob GE, Comerota AJ, et al. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest.* 2008;133(6 Suppl):454S-545S.
- Vallano A, Arnau JM, Miralda GP, Bartolí-Pérez J. Use of venous thromboprophylaxis and adherence to guideline recommendations: a cross-sectional study. *Thromb J.* 2004; 2(1):3 [cited 2011 Feb 22]. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC416491/pdf/1477-9560-2-3.pdf>
- Mismetti P, Laporte-Simitsidis S, Tardy B, Cucherat M, Buchmuller A, Juillard-Delsart D, et al. Prevention of venous thromboembolism in internal medicine with unfractionated or low-molecular-weight heparins: a meta-analysis of randomized clinical trials. *Thromb Haemost.* 2000;83(1):14-9.
- Elis A, Ellis MH. Preventing venous thromboembolism in acute medical patients. *QJM.* 2004;97(12):797-801.
- Deheinzelin D, Braga AL, Martins LC, Martins MA, Hernandez A, Yoshida WB, et al. Incorrect use of thromboprophylaxis for venous thromboembolism in medical and surgical patients: results of a multicentric, observational and cross-sectional study in Brazil. *J Thromb Haemost.* 2006;4(6):1266-70.
- Agno W, Squizzato A, Ambrosini F, Dentali F, Marchesi C, Mera V, et al. Thrombosis prophylaxis in medical patients: a

- retrospective review of clinical practice patterns. *Haematologica*. 2002;87(7):746-50.
20. Tapson VF, Decousus H, Pini M, Chong BH, Froehlich JB, Monreal M, et al. Venous thromboembolism prophylaxis in acutely ill hospitalized medical patients: findings from the International Medical Prevention Registry on Venous Thromboembolism. *Chest*. 2007;132(3):936-45.
 21. Cohen AT, Tapson VF, Bergmann JF, Goldhaber SZ, Kakkar AK, Deslandes B, et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. *Lancet*. 2008;371(9610):387-94.
 22. Andrade EO, Bindá FA, Silva AMM, Costa TODA, Fernandes MC. Fatores de risco e profilaxia para tromboembolismo venoso em hospitais da cidade de Manaus. *J Bras Pneumol*. 2009;35(2):114-21.
 23. Engelhorn ALV, Garcia ACF, Cassou MF, Birckholz L, Engelhorn CA. Profilaxia da trombose venosa profunda: estudo epidemiológico em um hospital escola. *J Vasc Bras*. 2002;1(2): 97-102.
 24. Garcia ACF, Sousa BV, Volpato DE, Deboni LM, Souza MV, Martinelli R, et al. Realidade do uso da profilaxia para trombose venosa profunda: da teoria à prática. *J Vasc Bras*. 2005;4(1):35-41.
 25. Caiafa JS, Bastos M. Programa de profilaxia do tromboembolismo venoso do Hospital Naval Marcílio Dias: um modelo de educação continuada. *J Vasc Bras*. 2002;1(2):103-12.
 26. Marchi C, Schlup IB, Lima CA, Schlup HA. Avaliação da profilaxia da trombose venosa profunda em um hospital geral. *J Vasc Brás*. 2005;4(2):171-5.
 27. Franco RM, Simezo V, Bortoleti RR, Braga EL, Abrão AR, Linardi F, et al. Profilaxia para tromboembolismo em um hospital de ensino. *J Vasc Brás*. 2006;5(2):131-8
 28. Chopard P, Dorffler-Melly J, Hess U, Wuillenmin WA, Hayoz D, Gallino A, et al. Venous thromboembolism prophylaxis in acutely ill medical patients: definite need for improvement. *J Intern Med*. 2005;257(4):352-7.
 29. Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Patwardhan NA, Jovanovic B, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism: the Worcester DVT Study. *Arch Intern Med*. 1991;151(5):933-8.
 30. Kakkar AK, Cimminiello C, Goldhaber SZ, Parakh R, Wang C, Bergmann JF. Low-molecular-weight heparin and mortality in acutely ill medical patients. *N Engl J Med*. 2011;365: 2463-72.
 31. Rocha ATC, Braga P, Ritt G, Lopes AA. Inadequação de tromboprofilaxia venosa em pacientes clínicos hospitalizados. *Rev Assoc Med Bras*. 2006;52(6):441-6.
 32. Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Forcier A, Patwardhan NA. Changing clinical practice: prospective study of the impact of continuing medical education and quality assurance programs on use of prophylaxis for venous thromboembolism. *Arch Intern Med*. 1994;154(6):669-77.
 33. Conterno LO, Moraes FY, Silva Filho, CR. Implementação de uma diretriz para pneumonia adquirida na comunidade em um hospital público no Brasil. *J Bras Pneumol*. 2011;37(2): 152-9.