

Original Paper

Open Access

## Evaluation of prophylaxis for venous thromboembolism in a university hospital intensive care unit

Nathalia Melo LIMA<sup>1</sup> , Afonso Celso SANTOS<sup>1</sup> , Gysllene de Melo BRITO<sup>1</sup> , Soraya de Sa COELHO<sup>1</sup> , Leandra Marla VIANA<sup>1</sup> ,  
Elton Jonh SANTOS<sup>1</sup> , Iara Antônia NOGUEIRA<sup>1</sup> 

<sup>1</sup>Hospital Universitário da Universidade Federal do Maranhão

Corresponding author: Nogueira IA, iaraantonia@hotmail.com

Submitted: 30-10-21 Resubmitted: 30-03-2021 Accepted: 20-04-2021

Peer review: blind reviewers

### Abstract

**Objectives:** To assess the risk profile and prophylactic measures for venous thromboembolism (VTE) in clinical patients in an intensive care unit and the role of clinical pharmacists in risk assessment and VTE prophylaxis. **Method:** Cross-sectional study in an intensive care unit (ICU) of a University Hospital, where data were collected from 76 patients, clinical and surgical, monitored by clinical pharmacists from September to December 2020. Patients admitted on weekends with a hospital stay of less than 24-48 hours, pediatric patients, pregnant women or those who were already undergoing therapeutic treatment with anticoagulants were not included in the study. Data were captured from the analysis of medical prescription, clinical history and pharmaceutical evolution contained in electronic medical records. An assessment of the risk profile was performed using the Padua Scores for clinical patients and Caprini Score for surgical patients and the adequacy of VTE prophylaxis assessed according to the guidelines of the American College of Chest Physicians. **Results:** 76 patients were included, of which 64.7% were surgical and 35.3% clinical. Of the total number of patients, 67 (88.3%) were classified as high risk, of which 64.2% were surgical patients and 35.8% were clinical. As for pharmacological prophylaxis for VTE, 44.7% of the patients evaluated did not find prescribed chemoprophylaxis. As for the clinical performance of the pharmacist, in 13.1% of the adopted patients, there was a need for intervention to include pharmacological prophylaxis, with 13.4% at high risk of VTE. **Conclusions:** Patients admitted to the ICU have a high risk of developing VTE. Prophylactic measures for VTE are still inadequate in both clinical and clinical patients, evidencing the importance of the role of the clinical pharmacist in the process of evaluating and implementing prophylactic measures for this condition.

**Keywords:** heparin; venous thrombosis; chemoprophylaxis; critical care; pharmacists; clinical pharmacy service.

## Avaliação da profilaxia para tromboembolismo venoso em unidade de terapia intensiva de um hospital universitário

### Resumo

**Objetivos:** Avaliar o perfil de risco e medidas profiláticas para tromboembolismo venoso (TEV) de pacientes clínicos e cirúrgicos em unidade de terapia intensiva e a atuação do farmacêutico clínico na avaliação de risco e profilaxia de TEV. **Método:** Estudo transversal, em unidade de terapia intensiva (UTI) de um Hospital Universitário, onde foram coletados dados de 76 pacientes, clínicos e cirúrgicos, acompanhados por farmacêuticos clínicos durante os meses de setembro a dezembro de 2020. Pacientes admitidos aos finais de semana com internação inferior a 24-48h, pacientes pediátricos, gestantes ou aqueles que já estavam em tratamento terapêutico com anticoagulantes não foram incluídos no estudo. Os dados foram obtidos da análise de prescrição médica, história clínica e evolução farmacêutica contidas em prontuário eletrônico. A avaliação do perfil de risco foi realizada através dos Scores de Pádua, para pacientes clínicos, e Score de Caprini, para pacientes cirúrgicos e a adequação de profilaxia para TEV avaliada segundo diretrizes da nona edição do *American College of Chest Physicians*. **Resultados:** 76 pacientes foram incluídos, dos quais 64,7% eram cirúrgicos e 35,3% clínicos. Do total de pacientes, 67 (88,3%) foram classificados como alto risco, destes 64,2% pacientes cirúrgicos e 35,8% clínicos. Quanto à profilaxia farmacológica para TEV, 44,7% dos pacientes avaliados não tinham quimioprofilaxia prescrita. Quanto à atuação clínica do farmacêutico, em 13,1% dos pacientes avaliados houve a necessidade de intervenção para a inclusão de profilaxia farmacológica, dos quais 13,4% apresentavam alto risco de TEV. **Conclusões:** Pacientes internados em UTI possuem risco elevado de desenvolver TEV. As medidas profiláticas para TEV ainda se mostram inadequadas tanto em pacientes cirúrgicos como em pacientes clínicos, evidenciando a importância da atuação do farmacêutico clínico no processo de avaliação e implementação de medidas profiláticas para esta condição.

**Palavras-chave:** heparina; trombose venosa; quimioprofilaxia; cuidados críticos; farmacêuticos; serviço de farmácia clínica.



## Introduction

Venous thromboembolism (VTE) consists in diseases such as deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE). Such problems are the most common preventable cause of death in hospitalized patients and generate serious public health problems, due to the high costs associated with acute VTE episodes and long-term complications<sup>1,2</sup>.

During hospitalization, half of the patients are at risk of developing VTE, with higher incidence among surgical patients<sup>3</sup>. The patients admitted to Intensive Care Units (ICUs) are classified as at high risk, even if they are receiving prophylaxis, as they present a greater number of risk factors such as sepsis, use of vasopressors, central catheters, mechanical ventilation devices, and respiratory, cardiac or renal failure<sup>4,5</sup>.

Annually, approximately 10 million new cases of venous thromboembolism are identified in the world. VTE incidence can be even higher because many patients present nonspecific or mild PTE or DVT symptoms, not being diagnosed<sup>4,6</sup>. According to the 9<sup>th</sup> Consensus of the *American College of Chest Physicians (ACCP)*<sup>7,8</sup> on VTE prevention, most hospitalized patients have at least one risk factor for VTE development, and nearly 40% have three or more.

Among the European Union countries, there are approximately 465,000 annual cases of VTE, approximately 300,000 cases of pulmonary embolism and 370,000 VTE-related deaths<sup>9</sup>. In Brazil, there is an important variation in VTE incidence across the regions of the country, with 1,648 cases of hospital morbidity caused by arterial embolism and thrombosis recorded in 2016. When it comes to critically-ill patients, incidence becomes even higher, leading to an increase in the ICU hospitalization times<sup>6-10</sup>. Brazil has a mean thromboprophylaxis inadequacy rate of 61%, varying from 52% to 69%, although not very distant from the global mean<sup>11</sup>.

The latest ACCP guidelines for VTE prevention have emphasized the importance of risk stratification before prescribing its prophylaxis<sup>7-8</sup>. The international guidelines describe recommendations with a high level of evidence for pharmacological prophylaxis in moderate or high risk situations. For surgical patients, this risk stratification is generally made through the Caprini Score<sup>12</sup>. In turn, the Padua Score is used for the evaluation of clinical patients<sup>13</sup>.

There are several therapeutic options available in the market for prophylaxis regarding occurrence of these events. Non-pharmacological methods, including graduated compression elastic stockings (GCEs), intermittent pneumatic compression (IPC), and venous foot pumps, have proved to be efficient in reducing DVT in several groups of patients<sup>14</sup>. Regarding the pharmacological method for thromboembolism prophylaxis, unfractionated heparins (UFHs) and low molecular weight heparins (LMWHs) stand out. These drugs have different mechanisms of action and impose a risk of causing adverse reactions when administered improperly<sup>15</sup>.

The frequency of thromboembolic complications in hospitalized patients, the adverse consequences of these events and their economic impact justify the priority of thromboprophylaxis for the safety of these patients, representing a significant factor to reduce short- and long-term morbidity and mortality<sup>2</sup>.

Considering the severity of the problem<sup>1-10</sup> and the high incidence of venous thromboembolism in hospitalized patients<sup>4-6</sup>, with consequences in longer hospitalization times and increased hospital costs<sup>1,2</sup>, this study sought to evaluate the risk profile and prophylactic measures for VTE in clinical and surgical patients admitted to the intensive care unit and the role of the clinical pharmacist in the risk assessment and prophylaxis for VTE.

## Methods

A cross-sectional study conducted in the *Presidente Dutra* University Hospital, which has 15 ICU hospitalization beds and treats a mean of 361 patients/day. During the study period, the hospital did not have a standardized VTE Prevention Protocol in the ICU where this study was conducted. The Clinical Pharmacy service monitors all hospitalized patients, within 72 hours after admission, in the ICU service of that university hospital regarding the risk factors for VTE and the consequent need for pharmacological and/or mechanical thromboprophylaxis. Of the 85 patients selected, 76 were included in the data collection procedure of the follow-up performed by two clinical pharmacists from September to December 2020. Patients admitted during the weekends with hospitalization times of less than 24-48h were not included in the study. Pediatric patients, pregnant women or individuals who were already undergoing therapeutic treatments with anticoagulants were excluded from the study.

The data were obtained through an analysis of the medical prescriptions, clinical histories and pharmaceutical evolutions included in the medical records. The risk profile was evaluated through the Padua Score in the case of clinical patients and by means of the Caprini Score for the surgical ones<sup>12,13</sup>. VTE prophylaxis adequacy was evaluated according to the guidelines set for in the ninth edition of the ACCP<sup>7,8</sup>.

The chemical prophylaxis provided for by the ACCP guideline and standardized in the hospital were considered adequate, namely: enoxaparin 20 mg/1x/day, enoxaparin 40 mg/1x/day, and unfractionated heparin 5,000 international units (IU) in 8/8-hour or 12/12-hour regimes. The mechanical prophylaxis methods evaluated were those prescribed in the hospital's computerized system, such as guiding/stimulating early walking and motor physiotherapy.

The statistical analysis was performed using *Microsoft Excel*<sup>®</sup> and the *R* Program. The categorical variables were described using absolute and relative frequencies, and the numerical variable was described as mean and standard deviation. The differences of the variables between the groups were assessed using the

Chi-Square and Fisher's Exact tests. The statistical significance level established was p-value<0.05. The study was approved by the Research Ethics Committee of the UFMA University Hospital under opinion No. 4,522,980.

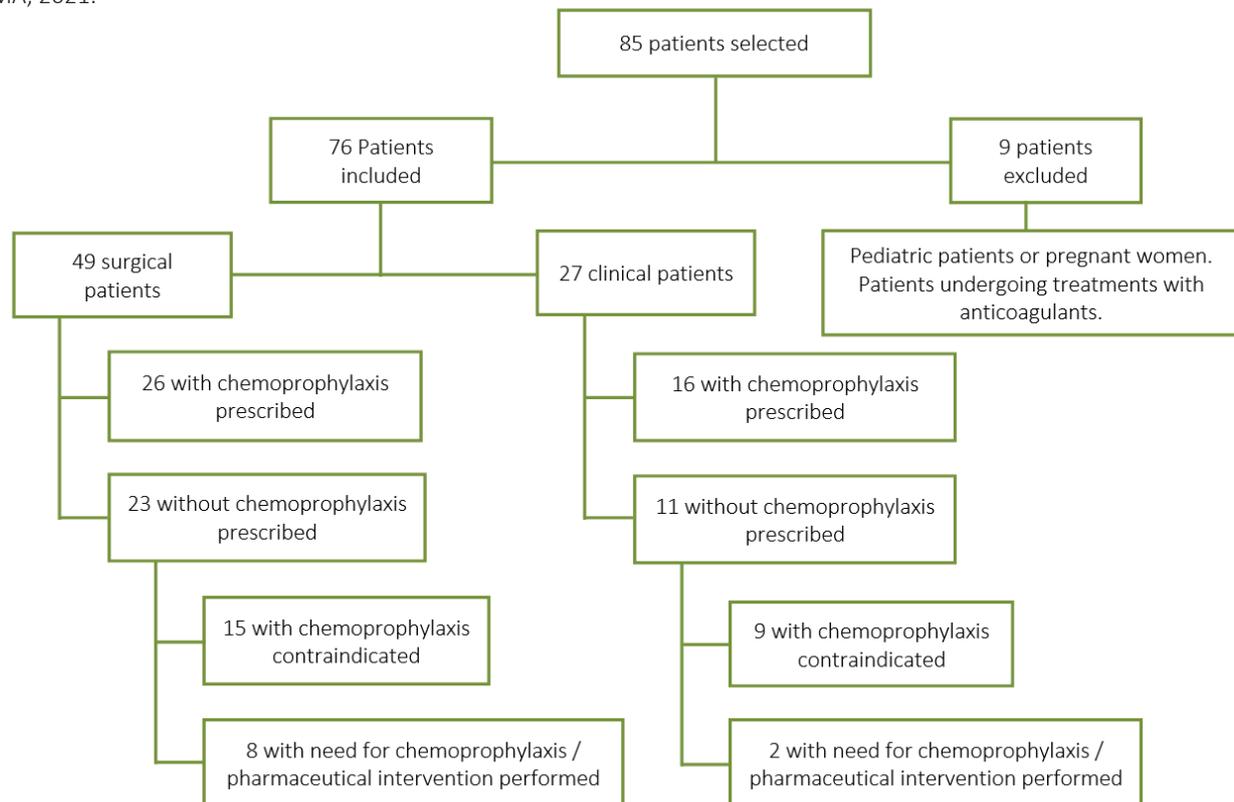
## Results

A total of 85 patients were selected during the study period, with inclusion of 76 participants (49 [64.7%] surgical and 27 [35.3%] clinical patients) aged 53.9±17.7 years old (Figure 1). Of these patients, 39 (51.3%) were female.

The main information related to the sociodemographic data, patient profile, prophylaxis prescribed, contraindication of prophylaxis and pharmaceutical intervention, according to the risk of venous thromboembolism, are detailed in Table 1. Of the total patients evaluated for the risk of thromboembolism, 67 (88.3%) were classified as at high risk; of these, 64.2% and 35.8% were surgical and clinical patients, respectively.



**Figure 1.** Organizational diagram corresponding to the assessment of the prophylaxis in patients admitted to the HUUFMA ICU, São Luis-MA, 2021.



**Table 1.** Sociodemographic and clinical characteristics of the patients admitted to the HUUFMA Intensive Care Unit for adults, São Luis-MA, 2021, according to the risk for venous thromboembolism (n=76).

Information	All n (%)	Risk for VTE n (%)			p-value*
		Low	Moderate	High	
<b>Female gender<sup>1</sup></b>	39 (51.3)	1 (33.3)	5 (83.3)	33 (49.2)	0.350 <sup>3</sup>
<b>Age (years old)</b>					
≤40	17 (22.4)	-	1 (20.0)	16 (25.8)	0.702 <sup>3</sup>
41-60	21 (27.6)	-	2 (40.0)	19 (30.6)	
61-70	17 (22.4)	1 (100.0)	2 (40.0)	14 (22.6)	
≥70	13 (17.2)	-	-	13 (21.0)	
Missing data <sup>2</sup>	8 (10.4)	-	-	-	
<b>Profile of the patient</b>					
Surgical	49 (64.7)	-	6 (100.0)	43 (64.2)	0.013 <sup>3</sup>
Clinical	27 (35.3)	3 (100.0)	-	24 (35.8)	
<b>Prophylaxis prescribed<sup>1</sup></b>	42 (55.3)	1 (33.3)	3 (50.0)	38 (56.7)	0.702 <sup>3</sup>
<b>Prophylaxis contraindication<sup>1</sup></b>	25 (32.9)	1 (33.3)	2 (33.3)	22 (32.8)	1.000 <sup>3</sup>
<b>Pharmaceutical intervention performed<sup>1</sup></b>	11 (14.5)	1 (33.3)	1 (16.7)	9 (13.4)	0.516 <sup>3</sup>

<sup>1</sup>Dichotomous variable for which the results of only one of the categories were presented. <sup>2</sup>The missing data were disregarded when evaluating the associations; <sup>3</sup>Fisher's Exact test, p<0.05.

Regarding pharmacological prophylaxis for VTE, 44.7% of the patients did not have any chemoprophylaxis prescribed and, of these, 43.3% were at a high risk for VTE. In the evaluation of contraindication for chemoprophylaxis, it was verified that 32.9% of the patients presented some contraindication and that most of them were at a high risk for VTE.

Regarding performance of the pharmacist, it was observed that, in 13.1% of the patients evaluated, there was a need for

intervention for the inclusion of pharmacological prophylaxis, and 13.4% were at a high risk for VTE. The interventions performed by the clinical pharmacist occurred during the multidisciplinary rounds and pharmaceutical evolutions in the electronic medical records. All the suggestions regarding inclusion of anticoagulants made by the pharmacist were accepted by the prescribing professional.

In the analysis by the participants' profile (surgical or clinical), it was noticed that most of the patients were aged between 41 and 60 years old. Of the surgical patients, 46.9% had no chemoprophylaxis prescribed, 30.6% had contraindications for anticoagulant use, and 16.3% required the pharmaceutical intervention to institute VTE prophylaxis. In turn, among the clinical patients, 40.7% did not present prophylaxis for VTE, 37% had factors that contraindicated the use of pharmacological thromboprophylaxis and, in 11.1%, there was a need for intervention by the pharmacist to prescribe the anticoagulant. However, there was no significant difference between the groups (Table 2).

**Table 2.** Sociodemographic and clinical characteristics of the patients admitted to the HUUFMA Intensive Care Unit for adults, São Luis-MA, 2021, according to their profile (n=76).

Information	Profile of the patient n (%)		p-value
	Surgical	Clinical	
<b>Age (years old)<sup>2</sup></b>			
≤40	12 (26.1)	5 (22.7)	
41-60	15 (32.6)	6 (27.3)	0.705 <sup>3</sup>
61-70	12 (26.1)	5 (22.7)	
≥70	7 (15.2)	6 (27.3)	
<b>Prophylaxis prescribed<sup>1</sup></b>	23 (53.1)	16 (59.3)	0.702 <sup>3</sup>
<b>Prophylaxis contraindication<sup>1</sup></b>	15 (30.6)	10 (37.0)	1.000 <sup>3</sup>
<b>Pharmaceutical intervention performed<sup>1</sup></b>	8 (16.3)	3 (11.1)	0.516 <sup>4</sup>

<sup>1</sup>Dichotomous variable for which only information of one of the categories was presented. <sup>2</sup>The missing data were disregarded when evaluating the associations; <sup>3</sup>Chi-square test; <sup>4</sup>Fisher's Exact test.

In the clinical patients, the main factors in the VTE risk classification were reduced mobility, respiratory/heart failure and infections. In the surgical patients, the most frequent risk factors were use of a central venous catheter, major surgeries and being bedridden for >72h.

Of the patients who had contraindications for the use of pharmacological prophylaxis, nine (37.5%) presented active bleeding, six (25%) had thrombocytopenia, five (20.8%) were in the neurosurgery immediate postoperative period, three (12.5%) had INR > 1.5 and one (4.2%) had concomitant thrombocytopenia and INR > 1.5.

None of the patients evaluated as at risk for VTE who had contraindications to pharmacological prophylaxis used prophylactic measures with IPC, although most underwent motor physiotherapy when indicated.

## Discussion

Patients admitted to intensive care units are considered to be at high risk due to daily variations regarding the criteria of risk for bleeding and thrombotic threshold, with the possibility of reaching twice the risk when compared to those admitted to the ward, even if in use of prophylaxis methods for VTE<sup>9-16</sup>. These data corroborate the findings of this study, which showed criteria of risk for thrombosis in a significant percentage of the subjects evaluated.

Establishing the risk criteria of patients in categories is considered the most appropriate way to make decisions regarding the prophylactic measure to be adopted. The ACCP guidelines

emphasize the importance of a thoughtful analysis of the risks and early initiation of the recommended prophylaxis<sup>7,8</sup>. Therefore, the Caprini and Padua scores are validated and easy-to-apply tools that have been used to assess the risk of developing venous thromboembolism in surgical and clinical patients, respectively<sup>12,13</sup>.

A number of studies have sought to evaluate the use of chemoprophylaxis for VTE in clinical and surgical patients, evidencing considerable inadequacy in the global rate of pharmacological prophylaxis for VTE<sup>1,17-19</sup>. Surgical patients present higher inadequacy rates when compared to clinical patients<sup>17-19</sup>. These findings corroborate the results of the current study, which, although not showing statistically significant results, it suggests a higher inadequacy rate in surgical patients when compared to clinical ones.

The ACCP recommends chemoprophylaxis with UFHs or LMWHs for high-risk clinical patients and moderate- to high-risk surgical patients. Early use of heparin (24-48 hours) was associated with a reduction of more than 40% in DVT development in the lower limbs, with no increase in the incidence of bleeding<sup>20</sup>. Several studies provide diverse evidence that there are no differences in the action of UFH and LMWH in VTE prevention; however, there is evidence indicating a lower chance of heparin-induced thrombocytopenia when prophylaxis is performed with low molecular weight heparin<sup>21-23</sup>. All the patients who had chemoprophylaxis prescribed were under the prevention measures recommended by the guidelines.

A number of studies indicate the benefit of IPC in helping reduce VTE in hospitalized patients and in those admitted to Intensive Care Units<sup>24,25</sup>. Mechanical prophylaxis, especially IPC, is fundamental for critically-ill patients with contraindications for the use of chemoprophylaxis, not presenting the hemorrhagic side effects of pharmacological prophylaxis<sup>24,26</sup>. In this study, taking into account clinical and surgical patients, one third of those evaluated presented risk factors for VTE development and contraindication for pharmacological prophylaxis.

A number of studies have evidenced the importance of motor physiotherapy in patients at risk of developing VTE, recommended for all patients with different risks for VTE, and may act in cases with contraindications for the use of anticoagulants or as adjuvant to the pharmacological therapy<sup>21,27</sup>. Motor physiotherapy was found in most of the patients evaluated.

Due to the high incidence of VTE in critically-ill patients, a number of studies have shown the importance of VTE prevention programs and the consequent reduction in the incidence of DVT in patients admitted to intensive care units<sup>4,6,16</sup>. The recommended strategies to increase adherence by the multidisciplinary team to the use of VTE prophylaxis include several tools, such as clinical alerts during the medical visits<sup>8,28</sup>. This study evidenced that the pharmaceutical interventions to include pharmacological prophylaxis for VTE were performed through alerts during the multidisciplinary rounds and pharmaceutical evolutions in the electronic medical records.

Various studies indicate the importance of clinical pharmacists in ICU teams and the positive impact that pharmacological interventions contribute to the patients<sup>29-32</sup>. Rocha *et al.* pointed to barriers that limit optimized implementation of a VTE prophylaxis protocol and emphasizes the crucial role of the multidisciplinary team in this process, indicating clinical pharmacists as the second non-medical professional category involved in risk assessment and adequacy of VTE prophylaxis in most Brazilian hospitals<sup>33</sup>.



A number of studies mention performance of the clinical pharmacist in several clinical recommendations, one of the main interventions being the inclusion of a medication necessary for the care to be provided to the patient<sup>32,34</sup>. Lima *et al.* showed that the clinical pharmacist was responsible for guiding the inclusion of prophylaxis for VTE in most of the interventions related to the prevention of venous thromboembolism<sup>32</sup>. Such findings corroborate the results of the current study, in which the clinical pharmacist requested the inclusion of chemoprophylaxis in all patients without contraindications and without any prophylactic measure for venous thromboembolism prescribed at the time of the analysis.

This study has limitations, such as its small sample size and the single-center and cross-sectional nature of the research. In addition, the activities of the Clinical Pharmacy service are not performed throughout the operation of the ICU, which precludes monitoring patients admitted during holidays, weekends and/or night periods.

## Conclusion

Most of the clinical and surgical patients admitted to the intensive care unit presented a high risk profile for the development of venous thromboembolism, and the prophylactic measures adopted for VTE proved to be inadequate. It was evidenced that effective implementation of pharmaceutical care and its appropriate interventions contributed to the evaluation and implementation of prophylactic measures for VTE.

## Funding sources

The research did not receive funding for its conduction.

## Collaborators

NML, ACJ, SSC and LMV: conception and design, data analysis and interpretation. NML, IAN, GMB and EJS: writing of the article or relevant critical review of the intellectual content.

## Acknowledgments

To the teams of the Clinical Pharmacy Unit and of the Intensive Care Unit for Adults, as well as to the UFMA University Hospital, for enabling conduction of this research.

## Conflict of interest statement

The authors declare that there are no conflicts of interest in relation to this article.

## References

1. Baer C, Bobato C, Carvalho M, *et al.* Avaliação da profilaxia medicamentosa do tromboembolismo venoso. Rev Bras Clin Med. 2012;10(5):372-376.
2. Raymundo SRO, Lobo SMA, Hussain KMK, *et al.* O que mudou nas últimas décadas na profilaxia do tromboembolismo venoso em pacientes internados: artigo de revisão. J Vasc Bras. 2019;18: 1-11. Doi.org/10.1590/1677-5449.002118
3. Heit JA, Spencer FA, White RH. The epidemiology of venous thromboembolism. J Thromb Thrombolysis. 2016;41(1):3-14. DOI: 10.1007/s11239-015-1311-6
4. Zhang C, Zhang Z, Mi J, *et al.* The cumulative venous thromboembolism incidence and risk factors in intensive care patients receiving the guideline-recommended thromboprophylaxis. Medicine (Baltimore). 2019;98(23): e15833. DOI: 10.1097/MD.00000000000015833.
5. Minet C, Potton L, Bonadona A, *et al.* Tromboembolismo venoso em UTI: principais características, diagnóstico e tromboprolifaxia. Crit Care. 2015; 19 (1): 287. DOI: 10.1186/s13054-015-1003-9.
6. Malato A, Dentali F, Siragusa S, *et al.* The impact of deep vein thrombosis in critically ill patients: a meta-analysis of major clinical outcomes. Blood Transfus. 2015;13(4):559-568. DOI: 10.2450/2015.0277-14
7. Kahn SR, Lim W, Dunn AS, *et al.* Prevention of VTE in non-surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2Suppl): e195S-e226S. DOI: 10.3171/2017.2.JNS162040.
8. Gould MK, Garcia DA, Wren SM, *et al.* Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2Suppl): e227S-e277S. DOI: 10.1378/chest.11-2297.
9. Cohen AT, Agnelli G, Anderson FA. *et al.* Venous thromboembolism (VTE) in Europe. Thromb. Haemost., 2007;98(1):756-764.
10. Lewis TC, Cortes J, Altshuler D, *et al.* Venous thromboembolism prophylaxis: a narrative review with a focus on the high-risk critically ill patient. J Intensive Care Med. 2019;34(11-12):877-888. DOI: 10.1177/0885066618796486
11. Carandina RF. Revisão sistemática e metanálise do perfil de risco e profilaxia de tromboembolismo venoso no Brasil e no mundo. J Vasc Bras. 2016;15: 339-340. https://doi.org/10.1590/1677-5449.004916
12. Lobastov K, Barinov V, Schastlivtsev I, *et al.* Validation of the Caprini risk assessment model for venous thromboembolism in high-risk surgical patients in the background of standard prophylaxis. J Vasc Surg Venous Lymphat Disord. 2016;4(2):153-160. DOI: 10.1016/j.jvs.2015.09.004
13. Barbar S, Noventa F, Rossetto V, *et al.* A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. J Thromb Haemost. 2010;8(11):2450-2457. DOI: 10.1111/j.1538-7836.2010.04044.x
14. Afshari A, Fenger-Eriksen C, Monreal M, *et al.* European guidelines on perioperative venous thromboembolism prophylaxis: Mechanical prophylaxis. Eur J Anaesthesiol. 2018; 35(2):112-115. DOI: 10.1097/EJA.0000000000000726.
15. Leme LEG, Sguizzatto GT. Profilaxia do Tromboembolismo Venoso em Cirurgia Ortopédica. Rev Bras Ortop. 2012; 47(6): 685-693. Doi.org/10.1590/S0102-36162012000600002



16. Boddi M, Barbani F, Abbate R, *et al.* Reduction in deep vein thrombosis incidence in intensive care after a clinician education program. *J Thromb Haemost.* 2010;8(1):121-128. DOI: 10.1111/j.1538-7836.2009.03664.x
17. Farhat FCLG, Gregório HCT, Carvalho RDP. Avaliação da profilaxia da trombose venosa profunda em um hospital geral. *J. Vasc. Bras.* 2018;17(3): 184-192. Doi.org/10.1590/1677-5449.007017
18. Curtarelli A, Silva LPC, Camargo PAB, *et al.* Profilaxia de tromboembolismo venoso, podemos fazer melhor? Perfil de risco e profilaxia de tromboembolismo venoso em Hospital Universitário do interior do Estado de São Paulo. *J. Vasc. Bras.* 2019; 18: e20180040. DOI: 10.1590/1677-5449.004018
19. Martínez R, Carrizo C, Cuadro, R *et al.* Adhesión insuficiente a la prevención de la enfermedad tromboembólica venosa en Hospitales Uruguayos. Un grave problema en salud. *Rev. Urug. med. Interna* ;2020; 5(3): 4-13. DOI:10.26445/05.03.
20. Khaldi A, Helo N, Schneck MJ, *et al.* Venous thromboembolism: deep venous thrombosis and pulmonary embolism in a neurosurgical population. *J Neurosurg.* 2011; 114(1): 40-46. Doi.org/10.3171/2010.8.JNS10332
21. Robertson L, Strachan J. Subcutaneous unfractionated heparin for the initial treatment of venous thromboembolism. *Cochrane Database Syst Rev.* 2017; 2(2): CD006771. DOI: 10.1002/14651858.CD006771.pub3.
22. Junqueira DR, Zorzela LM, Perini E. Unfractionated heparin versus low molecular weight heparins for avoiding heparin-induced thrombocytopenia in postoperative patients. *Cochrane Database Syst Rev.* 2017; 4(4): CD007557. DOI: 10.1002/14651858.CD007557.pub3.
23. Van Matre ET, Reynolds PM, MacLaren R, *et al.* Evaluation of unfractionated heparin versus low-molecular-weight heparin and fondaparinux for pharmacologic venous thromboembolic prophylaxis in critically ill patients with cancer. *J Thromb Haemost.* 2018; 16(12): 2492-2500. DOI: 10.1111/jth.14317
24. Kakkos SK, Nicolaidis AN, Caprini JA. Interpretation of the PREVENT study findings on the adjunctive role of intermittent pneumatic compression to prevent venous thromboembolism. *Ann Transl Med.* 2020;8(11):725. DOI: 10.21037/atm.2020.01.68
25. Haykal T, Zayed Y, Dhillon H, *et al.* Meta-analysis of the role of intermittent pneumatic compression of the lower limbs to prevent venous thromboembolism in critically ill patients. *Int J Low Extrem Wounds.* 2020; 11:1534734620925391. DOI: 10.1177/1534734620925391.
26. Arabi YM, Alsolamy SJ, Al-Dawood A. The journey to zero deep-vein thrombosis in critically ill patients. *Ann Thorac Med.* 2019; 14(4): 223-225. DOI: 10.4103/atm.ATM\_179\_19
27. LiXB, Peng KW, JiZH, *et al.* Prevention of venous thromboembolism after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: development of a physiotherapy program. *Clin Appl Thromb Hemost.* 2019;25:1076029619890415. DOI: 10.1177/1076029619890415.
28. Leal LF, Falavigna M, Gazzana MB, *et al.* Protocol implementation for venous thromboembolism prophylaxis: a before-and-after study in medical and surgical patients. *J Bras Pneumol.* 2020;46(4): e20180325. DOI: 10.36416/1806-3756/e20180325.
29. Araujo EO, Viapiana M, Domingues EAM, *et al.* Intervenções Farmacêuticas em uma Unidade de Terapia Intensiva de um Hospital Universitário. *Rev. Bras. Farm. Hosp. Serv. Saúde,* 2017; 8(3): 25-30. DOI: 10.30968/rbfhss.2017.083.005
30. Dias D, Wiese LPL, Pereira EM, *et al.* Evaluation of pharmaceutical clinical interventions in the icu of a public hospital of Santa Catarina. *Rev Bras Farm Hosp Serv Saude,* 2019; 9(3): 1-5. DOI: 10.30968/rbfhss.2018.093.005
31. Barros ME, Araújo IG. Evaluation of pharmaceutical interventions in an intensive care unit of a teaching hospital. *Rev Bras Farm Hosp Serv Saude.* 2021;12(3):0561. DOI: 10.30968/rbfhss.2021.123.0561.
32. Lima IM, Vidigal SB, Lima NM, *et al.* Application of FAST-HUG-MAIDENS mnemonic and evaluation of its impact in pharmaceutical intervention in an adult intensive care unit. *Rev Bras Farm Hosp Serv Saude.* 2021;12(1):0566. DOI: 10.30968/rbfhss.2021.121.0566
33. Rocha ATC, Pinheiro TB, Souza PRSP, *et al.* Protocolos de profilaxia de tromboembolismo venoso (TEV) em hospitais brasileiros - PROTEV Brasil. *J. Vasc. Bras.* 2020; 19: e20190119. DOI: 10.1590/1677-5449.190119.
34. Haga CS, Mancio CM, Pioner MC, *et al.* Implementation of vertical clinical pharmacist service on venous thromboembolism prophylaxis in hospitalized medical patients. 2014; 12(1): 27-30. DOI: 10.1590/s1679-45082014ao2526.