INTERNATIONAL SEVEN JOURNAL
OF HEALTH RESEARCH
ISSN: 2764-9415

Prevention of venous thromboembolism in surgical patients: A proposal for a protocol based on the reality of a university hospital

Prevenção de tromboembolismo venoso em pacientes cirúrgicos: Uma proposta de protocolo baseado na realidade de um hospital universitário

DOI: 10.56238/isevjhv3n1-002
Receipt of originals: 11/12/2023
Publication acceptance: 12/29/2023

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ABSTRACT

Introduction: Venous thromboembolism (VTE) results from the formation of thrombi in the endothelial space, following factors related to endothelial injury, venous stasis and coagulation disorders. Such a scenario can result in deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), which is the third leading cause of cardiovascular death in the world. In view of the possibility of avoiding VTE in most in-hospital cases, it is recommended that every hospital have a formal strategy for the prevention of VTE, including in patients undergoing elective surgeries. To this end, it is possible to use risk stratification scales, both for the development of VTE and the baseline risk of bleeding in postoperative patients. Objective: To provide a systematized and updated institutional protocol according to the main national and international literature on the prevention of venous thromboembolism in elective surgeries at the Júlio Muller University Hospital (HUJM/UFMT). Materials and Methods: A protocol was written based on the systematic analysis of updated scientific evidence on thromboprophylaxis in elective surgeries, adapted to the routine of the Júlio Muller University Hospital (HUJM/UFMT), using the UpToDate, Pubmed and Cochrane Library platforms, as well as the Guidelines of the Brazilian Society of Angiology and Vascular Surgery (SBACV) and the *American College of Chest Physicians* (*ACCP*). Conclusion: The risk of developing VTE is largely due to avoidable or predicted risk factors, depending on the type of surgery, mobilization time, and bleeding risk. The use of the venous thromboembolism prevention protocol through risk stratification will allow greater individualization of the patient in relation to the established prophylaxis, based on scientific evidence. Further studies on the subject are still needed, especially in the setting of elective surgeries.

Keywords: Venous thromboembolism, Elective surgery, Clinical protocols.

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INTRODUCTION

VTE is defined as a dysfunction of hemostasis in the venous network, which leads to the formation of thrombi in the venous space, and can manifest as DVT, defined by the acute formation of thrombi in deep veins of the limbs. Such thrombi can detach from the sites of origin, transiting through the body until they reach the lungs, causing PTE. PTE is a serious complication of VTE and is the third leading cause of cardiovascular death worldwide, behind acute myocardial infarction (AMI) and stroke.

The pathophysiology of VTE is mainly based on three pathophysiological mechanisms that together form what is known as Virchow's triad, composed of endothelial injury, venous stasis, and coagulation disorders. Such a scenario is inherent to surgical procedures, and it is the responsibility of the medical team to develop strategies that prevent or predict complications. According to the 8th edition of the *ACCP* VTE prevention guidelines, it is recommended that every hospital have a formal strategy for the prevention of VTE in patients undergoing surgery.

Surgical patients are very vulnerable to the development of VTE, with the highest risk in the first 12 weeks after the procedure, and may persist for up to a year after surgery. It is necessary to consider the age of the patient, the characteristics of the surgery, and the individual risk factors of each patient. Regarding the surgical procedure, the duration of the surgery, the positioning of the patient, the type of anesthesia and the postoperative recovery of the patient are factors that need to be stratified. Major surgeries (lasting more than 45 minutes), abdominal or thoracic topography, or requiring postoperative immobilization of more than four days tend to increase the patient's risk.

To systematize the classification of patients at higher risk of VTE, and thus the greatest need for prophylaxis, it is possible to use scales to support clinical decisions. The Caprini Modified Risk Assessment Model is currently one of the most widely used scales to predict the risk of surgical patients, even though the decision needs to be individualized for each case.

In view of the risk stratification between very low, low, moderate, and high risk, it is possible for the surgical team to establish prophylactic strategies to avoid VTE, following high levels of evidence. Such strategies can vary between early ambulation, mechanical prophylaxis, or pharmacological prophylaxis, as well as an association between them, depending on the stratification, always evaluating the risks and benefits of the methods.

MATERIALS AND METHODS

A protocol was written based on the systematic analysis of updated scientific evidence on

thromboprophylaxis in elective surgeries, adapted to the routine of the Júlio Muller University Hospital (HUJM/UFMT), aiming at greater adherence among health professionals.

The UpToDate, Pubmed and Cochrane Library platforms were used as databases, as well as the Guidelines of the Brazilian Society of Angiology and Vascular Surgery (SBACV) and the *American College of Chest Physicians* (*ACCP*).

Literature describing thromboprophylaxis in elective surgeries (defined as scheduled, non-urgent surgeries that enable perioperative care) were included; and approaches to oncological or orthopedic patients, or in urgent and emergency situations were excluded.

The protocol was presented to the Department of Clinical Surgery of the HUJM for evaluation and necessary adaptations.

PATHOPHYSIOLOGICAL MECHANISMS OF VTE

Virchow's triad, characterized by endothelial injury, venous stasis, and coagulation disorders, practically summarizes the risk factors for the development of VTE, even though the vast majority develop without a known triggering factor. Table *1* shows the main risk factors related to each mechanism involved in the triad:

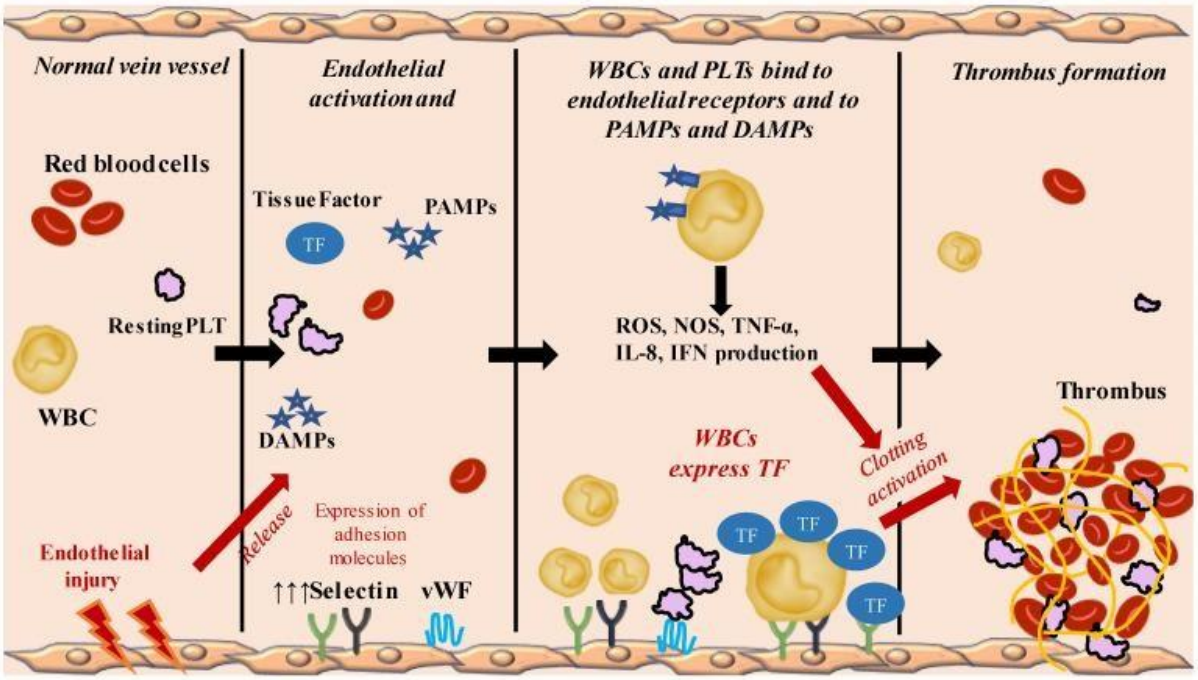
Table 1. Risk factors for the development of VTE

Estase venosa
Trauma*
Cirurgia *
Tempo prolongado de repouso*
Viagens prolongadas
Lesão endotelial
Idade avançada
Inserção de cateter venoso*
Diabetes
Infeccção pelo SARS-CoV2
Sepse
Distúrbios na coagulação
Terapia hormonal/ contraceptivos orais
Obesidade
Tabagismo
Trombofilia hereditária ou adquirida
Mecanismos imunomediados*

**Mecanismos relacionados ao procedimento cirúrgico*

When undergoing surgery, the surgical team must be prepared for the cellular and humoral response to the trauma involved, and the simple surgical incision already leads to endothelial injury and the release of an inflammatory cascade in the body. From the systemic inflammatory response and hypoxemia, thrombus formation can occur from platelet aggregation. Figure 1 illustrates how the process occurs:

Figure 1. Mechanism of VTE formation



Fonte: Pastori, D.; Cormaci, V.M.; Marucci, S.; Franchino, G.; Del Sole, F.; Capozza, A.; Fallarino, A.; Corso, C.; Valeriani, E.; Menichelli, D.; et al. A Comprehensive Review of Risk Factors for Venous Thromboembolism: From Epidemiology to Pathophysiology.*Int. J. Mol. Sci.*2023,*24*, 3169. https://doi.org/10.3390/ijms24043169

EVALUATION OF THE RISK OF VTE IN PATIENTS UNDERGOING ELECTIVE SURGERY

The risk of VTE in the postoperative period of elective surgeries should be assessed before the procedure, with a view to performing appropriate prophylaxis depending on the patient's stratification. To this end, the most commonly used scale in routine surgery is the Caprini Modified Risk Assessment Model (*Table 2*). With it, it is possible to classify the patient's baseline risk of thrombosis as very low (<0.5%), low (1.5%), moderate (3%) or high (>6%) and, thus, establish the recommended method for VTE prevention.

Table 2. Modified Caprini Risk Assessment Model for Venous Thromboembolism6.

1 ponto	2 pontos	5 pontos
Idade 41-60 anos	Idade 61-74 anos	AVC (<1 mês)
Cirurgia maior prévia < 1 mês	Artroscopia	Artroplastia
Cirurgia menor	Câncer	Fratura de quadril/ pelve
DII	Cateter venoso central	Politraumatismo
Doença pulmonar grave	Cirurgia maior (>45 minutos)	TRM
DPOC	Imobilização gessada	
Edema de MMII	Laparoscopia (>45 minutis)	
Gravidez e pós-parto (<1 mês)	Restrição ao leito <72h	
Hormônio	**3 pontos**	**Total de pontos**
IAM	Idade >75 anos	
ICC	Anticoagulante lúpico	
Obesidade	Anticorpos anticardiolipina	
Perda fetal/ aborto	Fator V de Leiden	
Restrição ao leito	História familiar de TEV	
Sepse (<1 mês)	História prévia de TEV	
Varizes	Homocisteína elevada	
Outros	Protrombina 20210ª	
	TIH	
	Outros	

DII: doença intestinal infamatória; DPOC: doença pulmonar obstrutiva crônica; MMII: membros inferiores; IAM: infarto agudo do miocárdio; ICC: insuficiência cardíaca congestiva; TEV: tromboembolismo venoso; TIH: trombocitopenia induzida por heparina; AVC: acidente vascular cerebral; TRM: traumatismo raquimedular.

BLEEDING RISK ASSESSMENT

In addition to identifying the risk of VTE, the choice of thromboprophylaxis in surgical patients should consider the patient's baseline risk of bleeding. This estimate is rarely present in studies related to postoperative VTE, but it is of paramount importance when considering the use of drug prophylaxis. In patients at high risk of bleeding, even with indication for drug prophylaxis, it is recommended to use only mechanical prophylaxis in order to prevent complications.

Severe bleeding includes fatal bleeding and/or symptomatic bleeding in a critical area or organ and/or bleeding that causes a drop in hemoglobin ≥2 g/dL or leads to transfusion of two or more units of whole blood or red blood cells. On the other hand, light bleeding includes epistaxis, gingival bleeding lasting more than 5 minutes, hematuria for more than 24 hours, or subcutaneous hematoma at the injection site.

However, there is still no protocolized model for assessing the risk of bleeding in surgical patients, and it is possible to use the IMPROVE Score (*Table 3*) to stratify patients whose drug prophylaxis should be reconsidered.

Table 3. IMPROVE score for bleeding risk9.

Active gastroduodenal ulcer	4,5
Hemorrhage three months prior to admission	4
Platelets <50 mil/mm	4
Age ≥ 85 years	3,5
Hepatic insufficiency with INR ≥ 1.5	2,5
CICr <30ml/min/m	2,5
Intensive care admission	2,5
Central venous catheter	2
Rheumatologic disease	2
Age 40-84 years	1.5
Male	1
Estimated ICC 30-59ml/min/m	1

A score lower than 7 is considered low risk, with an indication for drug prophylaxis, and above 7 an indication for mechanical prophylaxis. It is also important to emphasize that current studies do not correlate drug prophylaxis with a higher risk of bleeding, and further studies are needed.

MECHANISMS OF THROMBOPROPHYLAXIS

Primary prophylaxis is defined as the use of effective mechanical and/or pharmacological mechanisms for the prevention of VTE. When primary prophylaxis is contraindicated or ineffective, the surgical team should be attentive to secondary prophylaxis, through early detection and effective treatment of VTE as soon as possible. It is worth noting that secondary prophylaxis and the use of inferior vena cava filters are not recommended in patients undergoing primary thromboprophylaxis. After stratifying the risk of postoperative VTE using the Caprini scale and listing the patient's bleeding risks, it is up to the team to define the appropriate thromboprophylaxis method.

Prophylaxis should be initiated in the perioperative period and extended during the postoperative recovery period on an individualized basis. Extended pharmacological prophylaxis may have some benefit in patients at high risk for VTE, with the intention of early discharge, and may be extended for up to four weeks in patients undergoing major abdominal surgery.

EARLY AMBULATION

In patients at very low risk of VTE (Caprini score 0), early ambulation is recommended

compared with drug prophylaxis (recommendation with level of evidence 1B). Ultra-early mobilization is possible in this group of patients, in view of the surgeries of low complexity and duration included. Mechanical methods may be employed in case of complications or prolonged hospitalization.

MECHANICAL PROPHYLAXIS

For low-risk patients (Caprini score 1 and 2), mechanical prophylaxis is recommended compared with pharmacological prophylaxis or no prophylaxis (recommendation 2C). In these patients, the risk of VTE is high enough to warrant thromboprophylaxis, but does not justify the risk of bleeding associated with pharmacological methods. It is also recommended for patients at high risk of bleeding where pharmacological prophylaxis is contraindicated.

Among the methods are intermittent pneumatic compression (IPC), graduated compression stockings (MCG) and venous foot pump (BPV). Among them, IPC has the best results, especially when placed immediately before the beginning of surgery and removed at hospital discharge, with no effect on mortality. There is a lack of randomized studies evaluating the impact of the other methods cited.

IPC is contraindicated in patients with peripheral arterial disease or other signs of ischemia, especially in frail older adults.

PHARMACOLOGICAL PROPHYLAXIS

In patients at moderate risk (Caprini score 3 and 4), but at low risk of bleeding, drug prophylaxis is recommended (level of evidence 2B)4,7. Among the available drugs, the current highest recommendation for patients undergoing elective surgeries is the use of unfractionated heparin (UFH), 5,000 IU subcutaneously (SC), starting 2 hours before the procedure and remaining 12/12 hours after; or with the administration of LMWH (enoxaparin). Meta-analyses on the subject have shown similar results among heparins.

On the other hand, in patients at high risk of VTE (Caprini score ≥ 5) and low risk of bleeding, drug prophylaxis is recommended (level of evidence 1B), and mechanical prophylaxis can be associated (level of evidence 2C). Enoxaparin 40 mg is recommended 12 hours before surgery and 24 hours after; or fondaparinux 2.5 mg in the same sequence or UFH 5,000 IU, starting 2 hours before the procedure and continuing for 8/8 hours, 12 hours after.

It is also known that despite the relatively low side effect profile, it is necessary to monitor platelet counts regularly in order to detect heparin-induced thrombocytopenia (HIT).

The use of fondaparinux sodium is indicated mainly for patients with a history of HIT or other contraindications, although its actual efficacy is not a consensus among studies.

There are still no major studies on the impact of the use of the new oral anticoagulants in patients undergoing elective non-orthopedic surgery.

RISKS AND BENEFITS OF THE PROCEDURE

BENEFITS

For patients: The benefits of the implication of the venous thromboembolism prevention protocol for elective surgeries are based on current evidence and *Guidelines* from societies that specialize in the subject, decreasing the rates of PTE and DVT in the postoperative period of elective surgeries.

For the surgical team: The application of the protocol aims to standardize primary VTE prophylaxis in surgeries performed at the Júlio Muller University Hospital, enabling consolidated statistical data, in order to promote the improvement of the service and the identification of failures in the care network.

RISKS/COMPLICATIONS

The risks of applying the protocol include the risks inherent in the surgical procedure to which patients will be subjected.

SPECIFICS OF THE VTE PREVENTION PROTOCOL

The method of thromboprophylaxis should be established based on the patient's classification of VTE risk and baseline risk of bleeding, also taking into account cost-effectiveness, patient safety, and availability of necessary resources.

Thus, the first step suggested is to classify the risk of VTE and bleeding according to the Caprini and IMPROVE scores, respectively, and to indicate the best prophylaxis, as shown in Table 4:

Table 4. Indications for VTE prophylaxis in patients undergoing elective surgeries

	Low risk of bleeding (IMPROVE escore <7)	**High risk of bleeding (IMPROVE escore ≥ 7)**
Very low risk for VTE (Caprini escore 0)	Early ambulation	
Low risk for VTE (Goats escore 1 and 2)	Consider mechanical prophylaxis	

Moderate risk for VTE (Goats escore 3 and 4)	HFN 5,000 IU SC starting 2 hours before the procedure and keeping 12/12 hours after	**Mechanical prophylaxis** (preferably CPI)
High risk for VTE (Goats escore ≥ 5)	Enoxaparin 40 mg 12 hours before surgery and 24/24 hours after Considering combination with CPI	

FINAL THOUGHTS

The number of patients undergoing elective surgery at the Júlio Muller University Hospital is quite heterogeneous, as are the surgical procedures performed. The risk of the patient developing VTE is largely due to avoidable or predicted risk factors, depending on the type of surgery, mobilization time, and risk of bleeding.

The use of the venous thromboembolism prevention protocol, through risk stratification following the Caprini and IMPROVE scales, will allow greater individualization of the patient in relation to the established prophylaxis. The main objective is to reduce as much as possible cases of postoperative VTE that would be avoidable with the use of mechanical and/or pharmacological methods.

The establishment of thromboprophylaxis follows the classification of very low, low, moderate, and high risk. Even with the scores established, it is up to the medical team to always individualize the cases, establishing the best treatment based on scientific evidence.

Further studies on the prevention of VTE in patients undergoing elective surgeries are still needed, as well as standardization of the methods used, in order to produce solid meta-analyses on the subject. Further studies are needed on the possible complications resulting from primary prophylaxis.

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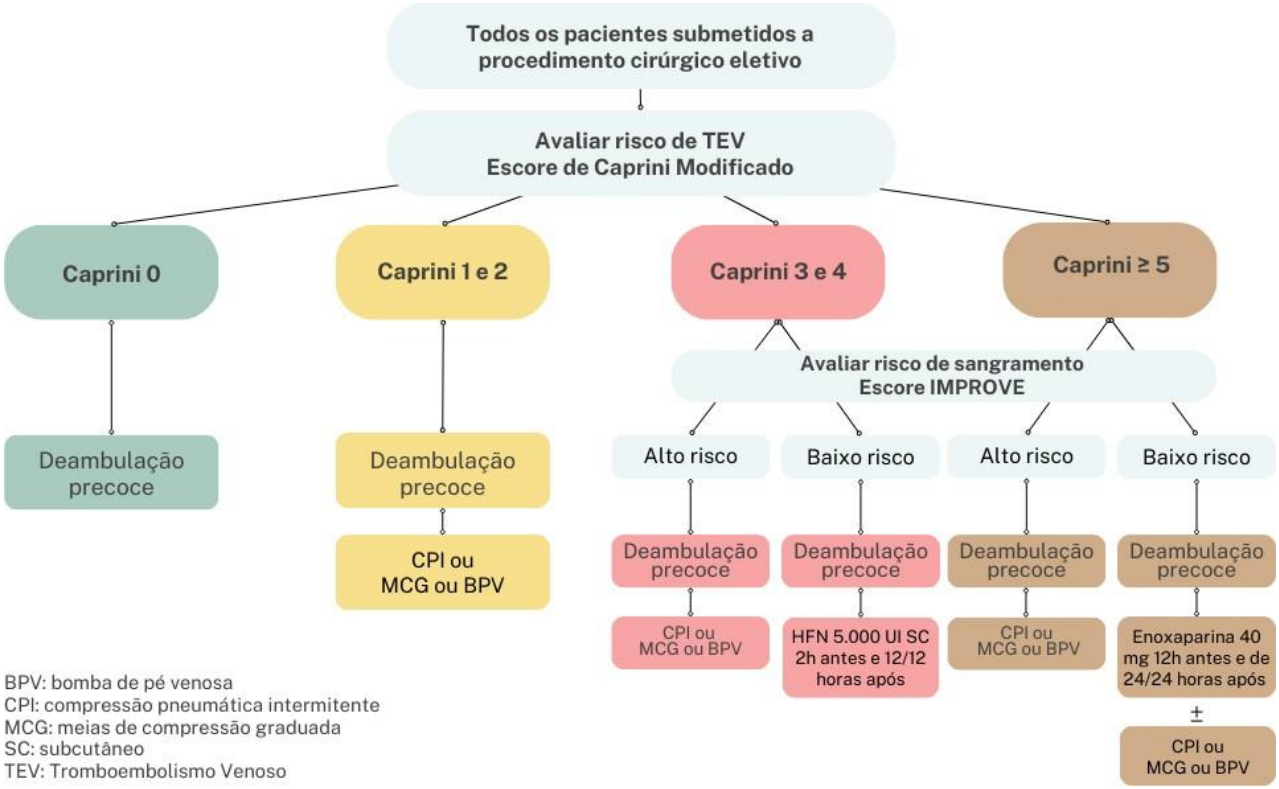
INTERNATIONAL SEVEN JOURNAL
OF HEALTH RESEARCH
ISSN: 2764-9415

ATTACHMENTS

Flow chart



BPV: bomba de pé venosa
CPI: compressão pneumática intermitente
MCG: meias de compressão graduada
SC: subcutâneo
TEV: Tromboembolismo Venoso