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Venous Thromboembolism Prevention Protocol: Experience of 2,000 Cases in Total Knee Arthroplasty*

Protocolo de prevenção do tromboembolismo venoso: Experiência de 2.000 casos em artroplastia total de joelho

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Abstract

Objective The objective of the present study is to evaluate the impact evaluate the impact of an institutional protocol on a tertiary hospital for the prevention of venous thromboembolism in 2005 patients submitted to primary total knee arthroplasty (TKA).

Methods Data from medical records of patients submitted TKA before ($n = 1,115$) and after ($n = 890$) the implementation of the institutional protocol, totaling 2,005 patients, were retrospectively reported. Demographics, comorbidities, and outcomes were analyzed.

Results There was no significant change in the cases of deep venous thrombosis (DVT) (1.6% versus 2.4%; $p = 0.211$). There was an increase in cases of pulmonary embolism (PE) (0.2% versus 0.8% $p = 0.049$).

Conclusion Despite the implementation of the prevention protocol, no reduction in the studied events was observed. The small global incidence makes further studies with larger series necessary to confirm or rule out these findings.

Keywords
- thromboembolism/ complications
- arthroplasty, replacement, knee
- risk factors

Resumo

Objetivo O objetivo do presente estudo é avaliar o impacto de um protocolo institucional em um hospital terciário na prevenção do tromboembolismo venoso em 2.005 pacientes submetidos a artroplastia total primária de joelho.

Métodos Os dados dos prontuários de pacientes submetidos a artroplastia total do joelho antes ($n = 1.115$) e após ($n = 890$) a implantação do protocolo institucional, totalizando 2.005 pacientes, foram relatados retrospectivamente. Dados demográficos, comorbidades e desfechos foram analisados.

Resultados Não houve alteração significativa nos casos de trombose venosa profunda (TVP) (1,6% *versus* 2,4%; $p = 0,211$). Houve um aumento nos casos de embolia pulmonar (EP) (0,2% *versus* 0,8%; $p = 0,049$).

Conclusão Apesar da implementação do protocolo de prevenção, não houve redução nos eventos estudados. A pequena incidência global faz com que novos estudos, com séries maiores, sejam necessários para confirmar ou descartar esses achados.

Palavras-chave
- tromboembolismo/ complicações
- artroplastia do joelho
- joelho
- fatores de risco

* Work conducted at the Hospital Madre Teresa, Belo Horizonte, state of Minas Gerais, Brazil.

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Introduction

Total knee arthroplasty (TKA) is one of the most realized orthopedic procedures worldwide.[1,2] More than 600.000 of these surgeries are performed annually in the USA.[1] Different complications were described, and one of the most feared is venous thromboembolism (VTEs): deep venous thrombosis (DVT) and pulmonary embolism (PE).[2]

Without prophylaxis, DVT, symptomatic or not, could be detected in 41 to 84% of the image exams.[3] Pulmonary embolism is not that common, with incidences varying between 1.5 and 10%, but with mortality rates between 0.1 and 1.7%.[4] Many risk factors were described: age $>$ 60 years old, obesity, use of oral contraceptives, hormonal reposition therapy, bowel inflammatory disease, personal or family history of DVT or PE, and long tourniquet time.[5]

Basically, there are mechanical and pharmacological methods to prevent PE and DVT. Up to 2015, many of them were used for prevention after TKA at our institution. After that, an institutional prevention protocol was initiated to standardize its prevention. We hypothesize that after the implementation of the protocol, smaller numbers of DVTs and PEs may be found. The objective of the present study is to verify if this new standardized protocol interfered in the incidence of VTEs after primary TKA.

Material and Methods

Data from patients submitted to primary TKA between January 2011 and December 2017 were retrospectively collected from our institution database, totalizing 2,005 patients. The present study was approved by the ethical committee of the institution. An informed signed consent was obtained before the study. No financial incentive was offered to any participant. Every primary TKA patient was included. The exclusion criteria were another surgical procedure together with TKA, and associated infectious disease.

Every patient was operated on by the same surgical team, with pneumatic tourniquet, through the anterior approach and with medial parapatelar arthrotomy. Every TKA was with sacrifice of the posterior cruciate ligament, and both components were cemented at the same time. A patellar component was not used. Up to December 2014, there was not a standard protocol regarding VTE prophylaxis, either pharmacological or mechanical, inside or outside the institution. The prevention was performed according to the guidance provided by each surgeon to the patient. Starting in January, 2015, the Hospital Madre Teresa standardized a clinical protocol to deal with VET prevention (►**Fig. 1**). In this protocol, every patient received 40 mg of low molecular weight heparin (LMWH) subcutaneously starting 6 hours after the end of the surgery, and continuously every 24 hours up to the hospital discharge. In this occasion, oral anticoagulants (factor Xa inhibitors) were initiated for up to 14 days postoperatively. The same dose of LMWH was used every 12 hours if the body mass index (BMI) of the patient was $>$ 30. Among the mechanical measures, full-weight bearing with a walker was initiated in the first postoperative day after peripheral nerve recovery, or after release from the intensive care unit. The average length of stay in the hospital was 54 hours. Home rehabilitation, as well as ambulatory physiotherapy facilities, were prescribed for every patient.

The patient data analyzed were gender, age, weight, height, classification according to the American Anesthesiology Association (ASA), presence of diabetes, high blood pressure, smoking habits, time to the first walking, anticoagulant use after discharge, EP or DVT history and their occurrence up to 6 months postoperatively. Only VTE symptomatic cases were analyzed, as well as those who needed any form of treatment. Asymptomatic cases were not studied.

Statistical Analysis

Data were analyzed using averages and standard deviation (SD). Categorical data were compared using the chi-squared and the Fisher exact tests. For continuous variables, an evaluation was performed regarding a normal distribution using the Kolmogorov-Smirnov test. The difference between averages was calculated using the parametric Student t-test and, for others, the nonparametric Mann-Whitney test. The significance level was set at 0,05. The statistical analysis was performed with IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 2,005 patients were analyzed. A total of 1,115 patients were part of the group operated before the implementation of the protocol; 275 patients were male (24.7%), and 840 (75.3%) were female. The average age was 72 years old. The average weight was 78.9 kg, and the average height was 1.63 m, with an average BMI of 29.69. A total of 4.8% of the patients were classified as ASA I, 91.4% as ASA II, and 3.8% as ASA III. Diabetes mellitus (DM) was present in 14.9% of the patients, and 60.9% had high blood pressure (HBP). A total of 2.5% of the patients were smokers. Walking training started in up to 24 hours after the surgery in 85.8% of the patients. In this group, 44.1% used anticoagulants up to 2 weeks postoperatively. A history of DVT or of PE was present in 3.8% of the cases. Deep venous thrombosis was detected in 1.6% of the patients, and PE in 0.2%.

A total of 890 patients were part of the group operated after the implementation of the protocol; 233 were male (26.2%), and 657 were female (73.8%). The average age was 72 years old. The average weight was 78.3 kg; the average height was 1.63 m, with an average BMI of 29.47. A total of 9.7% of the patients were classified as ASA I, 83.6% as ASA II, and 6.7% as ASA III. Diabetes mellitus was present in 22.7% of the patients, and 76.9% had HBP. A total of 5.2% of the patients were smokers. Walking training started in up to 24 hours after the surgery in 78% of the patients. In this group, 98% used anticoagulants for up to 2 weeks postoperatively. A history of DVT or of PE was present in 4.8% of the cases. Deep venous thrombosis was detected in 2.4% of the patients, and PE in 0.8%.

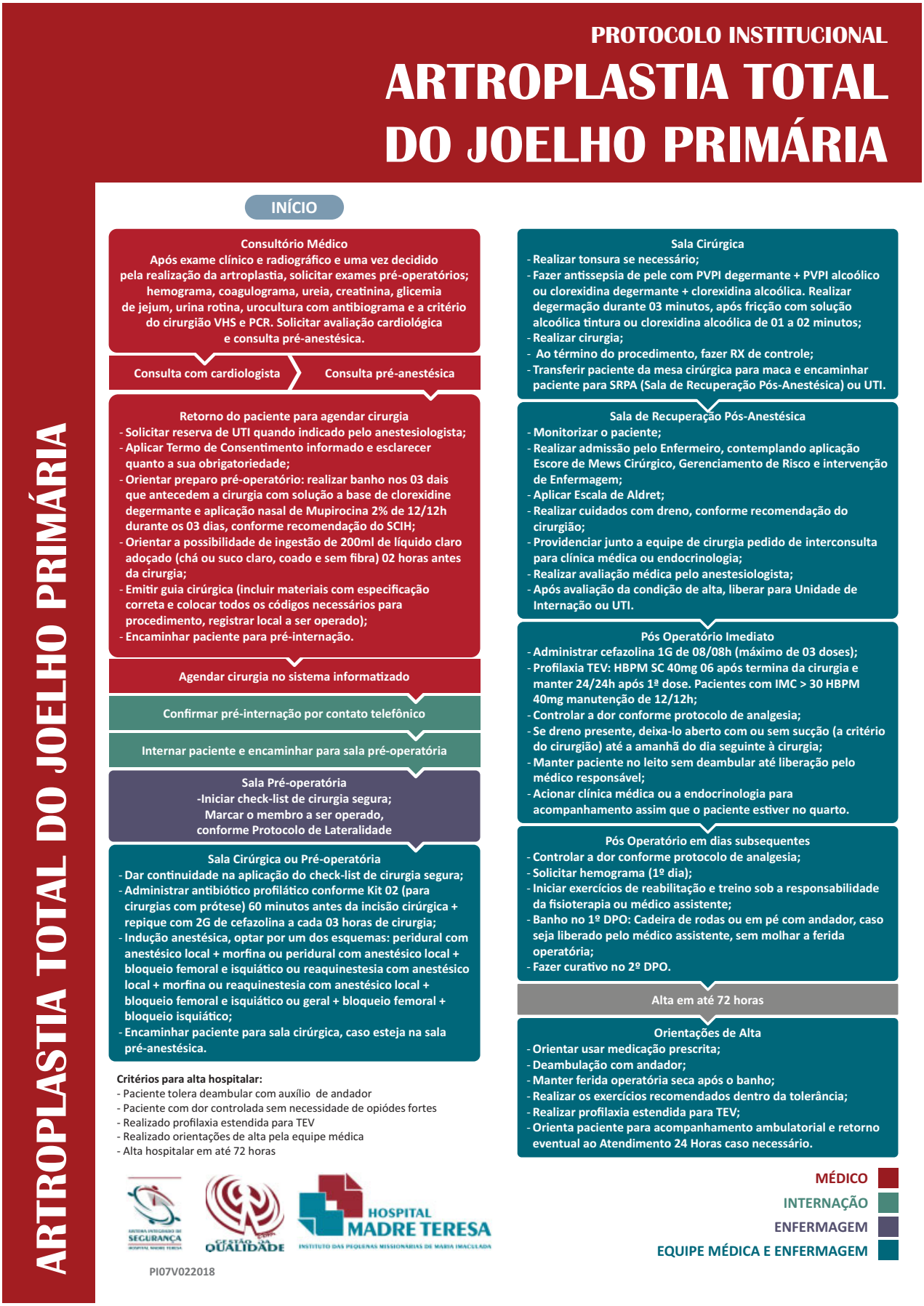

Fig. 1 Institutional protocol for venous thromboembolism prevention - Total knee arthroplasty.

Table 1 Characteristics of the Patients

Condensed Table							
Variable	**Category**	**General ($n = 2.0005$)**		**Before 2014 ($n = 1.115$)**		**After 2015 ($n = 890$)**	
		N	**%**	**N**	**%**	**N**	**%**
Gender	Male	508	25,3	275	24,7	233	26,2
	Female	1,497	74,7	840	75,3	657	73,8
	Total	**2,005**	**100,0**	**1115**	**100,0**	**890**	**100,0**
VTE	Yes	9	0,4	2	0,2	7	0,8
	No	1,980	98,8	1112	99,7	868	97,5
	Not informed	16	0,8	1	0,1	15	1,7
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
DVT	Yes	39	1.9	18	1.6	21	2.4
	No	1,950	97.3	1,096	98.3	854	96.0
	Not informed	16	0.8	1	0.1	15	1.7
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
Anticoagulants use	Yes	1,364	68.0	492	44.1	872	98.0
	No	641	32.0	623	55.9	18	2.0
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
HBP	Yes	1,294	64.5	613	55.0	681	76.5
	No	598	29.8	393	35.2	205	23.0
	Not informed	113	5.6	109	9.8	4	0.4
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
DM	Yes	368	18.4	166	14.9	202	22.7
	No	1,636	81.6	949	85.1	687	77.2
	Not informed	1	0.0	0	0.0	1	0.1
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
Smoking	Yes	74	3.7	28	2.5	46	5.2
	No	1,931	96.3	1,087	97.5	844	94.8
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
VTE history	Yes	85	4.2	42	3.8	43	4.8
	No	1,918	95.7	1,073	96.2	845	94.9
	Not informed	2	0.1	0	0.0	2	0.2
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
Walking training	2 hour	2	0.1	2	0.2	0	0.0
	24 hour	1,648	82.2	954	85.6	694	78.0
	48 hour	316	15.8	141	12.6	175	19.7
	72 hour	32	1.6	14	1.3	18	2.0
	96 hour	4	0.2	1	0.1	3	0.3
	120 hour	3	0.1	3	0.3	0	0.0
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**
ASA	I	100	5.0	14	1.3	86	9.7
	II	1,005	50.1	265	23.8	740	83.1
	III	70	3.5	11	1.0	59	6.6
	Not informed	830	41.4	825	74.0	5	0.6
	Total	**2,005**	**100.0**	**1,115**	**100.0**	**890**	**100.0**

Abbreviations: ASA, American Anesthesiology Association; DM, Diabetes Mellitus; DVT, Deep vein thrombosis; HBP, had high blood pressure; VTE, venous thromboembolism.

Comparing the results between the 2 groups, a statistical difference was found between the ASA classification ($p < 0.05$). Critical cases (ASA III) were much more frequent after the implementation of the protocol ($p < 0.05$). Statistically significant differences were found between patients with DM ($p < 0.05$), HBP ($p < 0.05$) and smoking ($p < 0.05$). After the protocol, these characteristics were more frequent. After the protocol, the time for walking training was significantly delayed ($p < 0.05$). The use of anticoagulants was also higher ($p < 0.05$). No difference was found in the DVT numbers ($p > 0.05$), and the incidence of PE was considered statistically significant ($p = 0.049$). The results are summarized in ►**Table 1**.

Discussion

The main result of the present study was that, despite the implementation of this protocol, there was no reduction in DVT cases, with an increase in the incidence of PE. We should be aware of the increase in the incidence of comorbidities and of a significant increase in intensive care utilization postoperatively. The delay in walking training could explain the increase in the number of patients with VTE, since the patients are not able to walk during their time in the intensive care unit (ICU). Walking is a proven way to reduce VTE. Chandrasekaran et al.[4] reported a 0% incidence in a population that initiated walking training in the first 8 hours postoperatively. Kjaersgaard-Andersen et al.[6] described a 25% reduction in VTE when first walking was initiated in up to 24 hours postoperatively.

Several studies observed the important relationship between VTE and TKA. Khokhar et al.[3] reported 13% of DVT and 3% of PE. O'Reilly et al.[7], using only symptomatic cases, found 0.6 to 5.7% of VTE, with 0.33 to 2.1% of, DVT, and PE between 0 and 1%. Song et al.[8] used bilateral phlebography in 109 patients and found symptomatic DVT in 4.6% of the patients, and asymptomatic DVT in 18.3%. Without prevention, DVT could reach 60% in the first 90 postoperative days[9], and the incidence of fatal PE could be 1.5%.[10] In the present study, the general incidence was 2.3% of VTE, with 1.6% and 2.4% of DVT and 0.2% and 0.8% of PE pre- and postimplementation of the protocol, respectively.

Several risk factors were related to VTE. Zhang et al.[11] performed a metanalysis and evaluated 1,150,000 patients after total knee and hip replacements. They found as risk factors age > 70 years old, female gender, BMI > 30, black ethnicity, and ASA $\geq$ 3.[11] Besides several studies that show that the prevention protocol decreases the incidence of VTE, we found an increase in VTE complications after TKA. An explanation would be the increase in the complexity and comorbidities of the patients. In the present study, we found an increase in DM, HBP and smoking, although these are not related to the higher prevalence of VTE. The small number of patients with a previous or family history of VTE could explain the lack of relationship observed in cases with DVT and PE.

Azboy et al.[12], in a retrospective study with 26.415 primary and revision TKAs, recommended VTE prevention in the first 2 weeks postoperatively, as they found 81% of the documented or symptomatic cases of PE in the first 3 days after surgery, 89% in the first week, and 94% in the first 2 weeks PO. We did not find a prophylaxis protocol similar to the one used in this series. The association between LMWH and Xa inhibitors is not described. Every analyzed study used the same drug during the entire prophylaxis period.[4,7,9,13] Different factor Xa inhibitors were not considered a confounding factor because, in spite of the different drugs used (rivaroxaban, apixaban and dabigatran), all of them have the same site of function and were used in prophylactic doses, according to the recommendation of the manufacturers.[1]

The limitation of the present study lies on its retrospective nature, based on the database of the hospital. The search strategy using procedure codes and a careful reading of each record tried to minimize this fact. Because VTE is a low-prevalence event, a longer follow-up would be necessary to check the real number of this event. Another point is that the protocol has been changing over the years with the publication of new international consensus for the prevention of PE and VTE.

Conclusion

Despite the implementation of the prevention protocol, a reduction in the studied events was not observed. The small global incidence of these diseases demands more studies with a longer follow-up in order to confirm or deny these findings.

Conflicts of Interests
The authors have no conflicts of interests to declare.

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