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*Original Article*

# Prophylaxis for Deep Vein Thrombosis and Pulmonary Embolism Failed or was Insufficient COVID-19

**Maria Regina Pereira de Godoy [1], Aline Giovana Dizero [2], Marcia Valeria Caldeira Angelucci Lopes [2], Henrique José Pereira de Godoy [3], José Maria Pereira de Godoy [4, 5, *]**

[1] Department General Medicine, Medicine School, São José do Rio Preto - FAMERP, São José do Rio Preto, São Paulo, Brazil.
[2] Epidemiology Service, Medicine School, São José do Rio Preto - FAMERP, São José do Rio Preto, São Paulo, Brazil.
[3] Discipline Vascular Surgery, Medicine School, São José do Rio Preto - FAMERP, São José do Rio Preto, São Paulo, Brazil.
[4] Cardiovascular Surgery Department, Medicine School, São José do Rio Preto - FAMERP, São José do Rio Preto, São Paulo, Brazil.
[5] Vascular Surgery Discipline, Medicine School, São José do Rio Preto - FAMERP, São José do Rio Preto, São Paulo, Brazil.

* Correspondence: godoyjmp@gmail.com.

**Abstract:** Patients with COVID-19 exhibit distinct laboratory findings that are compatible with a pro-thrombotic state, in which the key associated underlying episode to thrombotic complications is an excessive inflammatory response of the host to infection. The aim of the present study was to evaluate routine prophylaxis for pulmonary thromboembolism (PTE) at a teaching school and the effect of COVID-19 on the prevalence of deep vein thrombosis (DVT) and PTE in the year 2020. The study was conducted analyzing records the patients, monthly prevalence of adequate prophylaxis and the monthly incidence of DVT and PTE in patients with moderate to high risk based on the Wells score in the year 2020, with an investigation of the effect of COVID-19 on this incidence at São José do Rio Preto Hospital. An analysis was performed of hospital data on the prevalence of adequate prophylaxis for deep vein thrombosis and pulmonary embolism in patients with moderate to high risk for PTE based on the Wells score in the year 2020. For prophylaxis, conventional and low molecular weight heparin, rivaroxaban, warfarin, antithrombotic elastic stockings and pneumatic boots were used, depending on the needs of each patient. Our results show that June and July were the peaks of the COVID-19 pandemic, with a significant increase in the incidence, going from an annual level of 0.29% to 0.88%. The monthly mean incidence went from 0.13% through June to 0.46% from July to December; this difference was statistically significant ($p = 0.002$, Mann-Whitney U test). The coronavirus has increased the incidence of deep vein thrombosis and pulmonary embolism, suggesting a failure in mechanisms of prophylaxis for PTE implanted prior to COVID-19.

**Keywords:** Prophylaxis; Deep Vein Thrombosis; Pulmonary; Embolism; COVID-19.

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## 1. Introduction

Patients with COVID-19 exhibit distinct laboratory findings that are compatible with a pro-thrombotic state, in which the key associated underlying episode to thrombotic complications is an excessive inflammatory response of the host to infection, generating multiple inflammatory mediators, especially cytokines and complement activation products [1, 2]. A review study reports that the overall prevalence of pulmonary embo-

lism and deep vein thrombosis (DVT) in all hospitalized patients is 8.5% and 8.2%, respectively [3].

One study detected no differences in venous thromboembolism between COVID-19 and non-COVID-19 cohorts; except for the subgroup of patients in intensive care [4]. COVID-19 is associated with a significantly greater risk of pulmonary thrombosis, even in patients receiving prophylactic anticoagulation therapy. This may be due to a hypercoagulable state responsible for large vessel thrombosis and thromboembolism as well as direct vascular and endothelial injury responsible for in situ microvascular thrombosis [5, 6]. Current guidelines recommend the management of patients hospitalized with COVID-19 in the same way as any other acute disease [7]. A histopathological evaluation of the lungs revealed pulmonary microthrombi in 242 of 326 patients, DVT in 41% and pulmonary embolism in 15% [8]. Clinicians should be warned of the need for ward patients with a high initial D-dimer level or an accentuated increase from the baseline level to undergo Doppler ultrasound of the lower limbs. In the intensive care unit (ICU), however, Doppler ultrasound should be a routine screening method, given the high prevalence of thrombosis despite standard anticoagulant prophylaxis [9].

The Wells score is a tool that assists in predicting the probability of a patient developing pulmonary thromboembolism (PTE), classifying probability as low, moderate or high [9] The aim of the present study was to evaluate routine prophylaxis for PTE at a teaching school and the effect of COVID-19 on the prevalence of DVT and PTE in the year 2020.

## 2. Methods

### 2.1 Patients

All records patients in the hospital affiliated with the São Jose do Rio Preto School of Medicine (state of São Paulo, Brazil) with moderate to high risk of pulmonary thromboembolism (Wells score) in the year 2020 were evaluated.

### 2.2 Design

The study was conducted analyzing records the patient's monthly prevalence of adequate prophylaxis and the monthly incidence of DVT and PTE in patients with moderate to high risk based on the Wells score in the year 2020, with an investigation of the effect of COVID-19 on this incidence at São Jose do Rio Preto Hospital.

### 2.3 Inclusion and Exclusion Criteria

All records of the patients with moderate to high risk for PTE based on the Wells score in the year 2020 were included. Records of patients hospitalized with low risk of thrombosis in the year 2020 were excluded from the study.

### 2.4 Statistical analysis

Descriptive statistics of the incidence data and use of Mann-Whitney U considering a 5% alpha error.

### 2.5 Development

An analysis was performed of hospital data on the prevalence of adequate prophylaxis for deep vein thrombosis and pulmonary embolism in patients with moderate to high risk for PTE based on the Wells score in the year 2020. The incidence of DVT and PTE in the period and the effect of COVID-19 on this incidence in the peak months of the pandemic in 2020 were also evaluated. For prophylaxis, conventional and low molecular weight heparin, rivaroxaban, warfarin, antithrombotic elastic stockings and pneumatic boots were used, depending on the needs of each patient. Prophylaxis was considered adequate when the established prevention criteria were met in each patient. The data

were entered into an Excel table and the Stats Direct3 program was used for the statistical analysis.

## 3. Results

Figure 1 shows the monthly variation in hospitalizations of patients with moderate and high risk for PTE based on the Wells score. The mean was 2653 patients per month. A total of 1134 patients were hospitalized in July, which corresponds to 42.7% below the monthly mean. Figure 2 shows the monthly variation in the prevalence of adequate prophylaxis in patients with moderate to high risk based on the Wells score. Figure 3 shows the monthly variation in the prevalence of DVT and PTE. June and July were the peaks of the COVID-19 pandemic, with a significant increase in the incidence, going from an annual mean of 0.29% to 0.88%. The monthly mean incidence went from 0.13% through June to 0.46% from July to December; this difference was statistically significant ($p = 0.002$, Mann-Whitney U test).

**Figure 1.** Total number of patients hospitalized monthly in 2020 with intermediate or high risk for PTE according to the wells score.

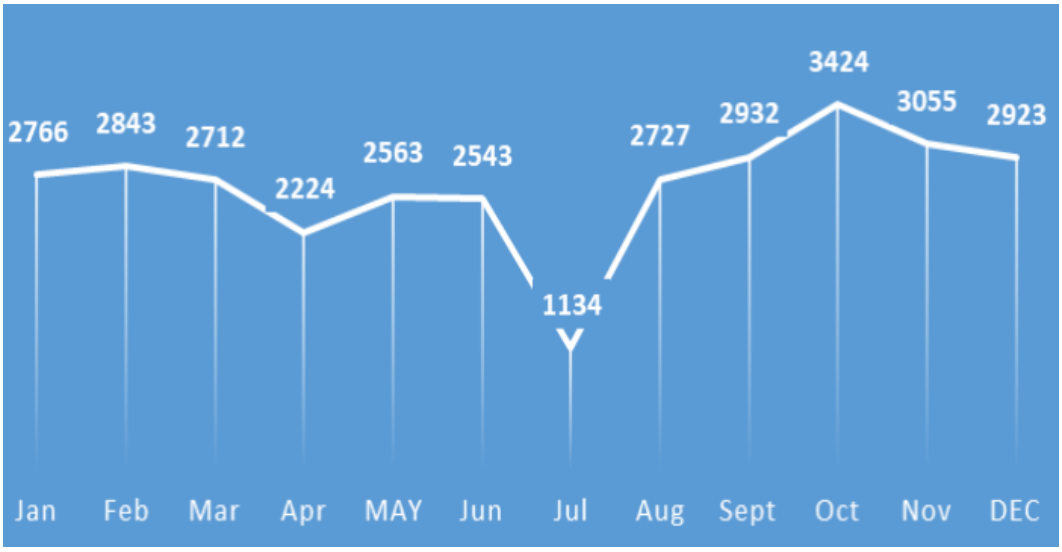



**Figure 2.** Prevalence of adequate DVT prophylaxis in 2020.

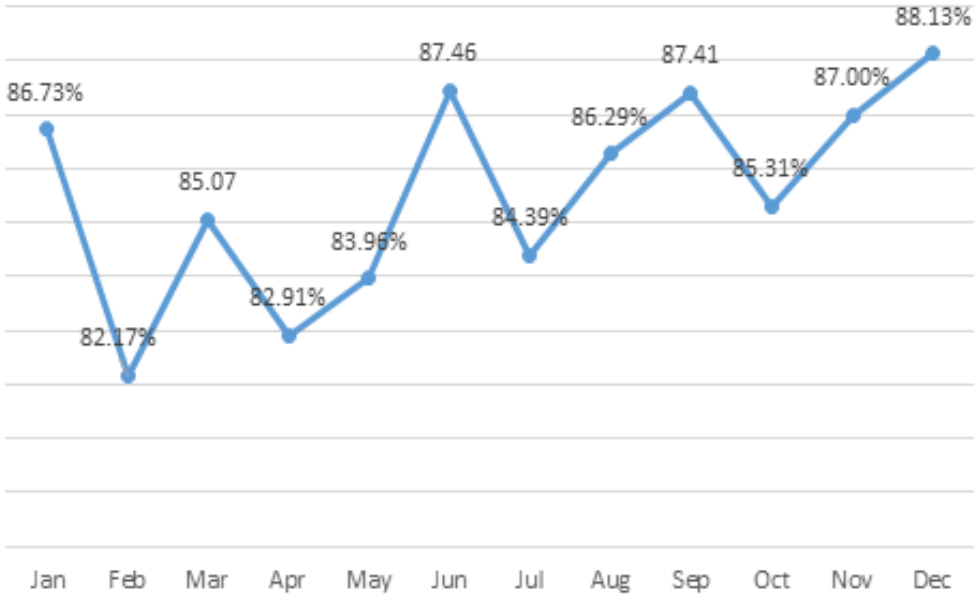
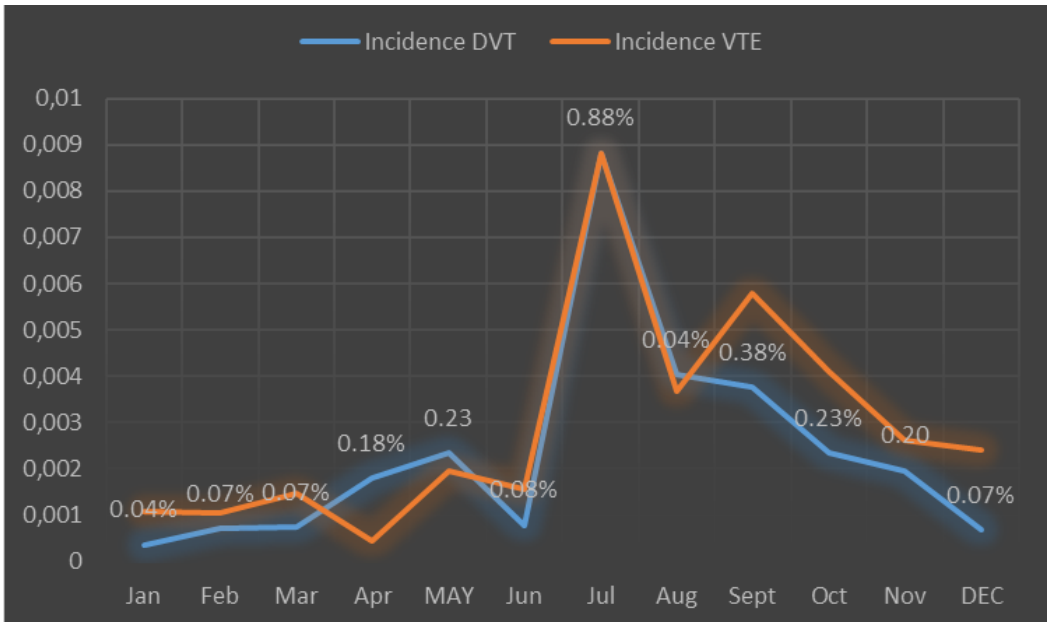


**Figure 3.** Monthly incidence of pulmonary embolism and DVT in 2020.




## 4. Discussion

The present study reports the monthly prevalence of adequate prophylaxis for PTE as a quaternary hospital, the incidence of deep vein thrombosis and pulmonary embolism and the effect of COVID-19 in the peak months of the disease. Although hospital control is vigorous, adequate prophylaxis did not reach 95% in any month. However, the rate was higher than 80% throughout the study period. The peaks of the COVID-19 waves were associated with a significant increase in the incidence of both PTE and DVT without a significant increase in the number of patients hospitalized.

The incidence of PTE ranged from 0.04 to 0.20, with a mean of 0.13, suggesting adequate prevention. However, there was no routine Doppler ultrasound screening or evaluation of D-dimer levels. Therefore, these values may be underestimated. One study reports a diagnostic rate of 0.06% for DVT and 0.03% for pulmonary embolism, which is within the range found in the present study [10]. The increase in the incidence of both DVT and PTE with the emergence of COVID-19 suggests a failure in habitual prevention mechanisms. Therefore, novel prophylactic approaches should be evaluated. The overall increase was greater than 300% in the hospital, but the aggravating factor was COVID-19. Moreover, the change in the viral pattern at the hospital with the Gamma variant led to a twofold increase in the prevalence of deep vein thrombosis. A study shows that the mortality rate among COVID-19 patients was more than 60% among those with DVT compared to around 31% among those without thrombosis with Gamma variant [11]. Therefore, deep vein thrombosis is one of the major markers associated with mortality in this population.

The physiopathology of thrombosis in COVID-19 differs from habitual patterns, with the characteristics of immunothrombosis found [12]. Two novel hemostatic mechanisms are suggested, the "two-path unifying theory" and the "two-activation theory of the endothelium", which is different from the macrothrombosis and the coagulopathy that occurs as the result of the combined activation of ultra-large von Willebrand factor (ULVWF) and tissue factor (TF) [13, 14]. Study reports that thrombosis and inflammation may contribute to the risk of death and complications among patients with coronavirus disease 2019 (COVID-19). We hypothesized that therapeutic-dose anticoagulation may improve outcomes in noncritically ill patients who are hospitalized with Covid-19 [5, 15,16].

One of the most widely known mechanisms of immunothrombosis is related to antiphospholipid antibodies, for which the combination of low doses of aspirin and

prophylactic heparan reduces the occurrence of repeated miscarriages and thrombosis [17].

## 5. Conclusion

The coronavirus has increased the incidence of deep vein thrombosis and pulmonary embolism, suggesting a failure or insufficiency in the prophylaxis mechanisms for PTE implanted prior to COVID-19.

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**Research Ethics Committee Approval:** None.

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**Conflicts of Interest:** The authors declare no conflict of interest.

**Supplementary Materials:** None.

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