Association of Padua prediction score with in-hospital prognosis in COVID-19 patients

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Abstract

**Background:** Nearly 20% novel coronavirus disease 2019 (COVID-19) patients have abnormal coagulation function. Padua prediction score (PPS) is a validated tools for venous thromboembolism (VTE) risk assessment. However, its clinical value in COVID-19 patients evaluation was unclear.

**Methods:** We prospectively evaluated the VTE risk of COVID-19 patients using PPS. Demographic and clinical data were collected. Association of PPS with 28-days mortality was analyzed by multivariate logistic regression and Kaplan-Meier analysis.

**Results:** 274 continuous patients were enrolled, with total mortality of 17.2%. Patients in high PPS group, with significantly abnormal coagulation, have a higher levels of interleukin 6 (25.27 pg/ml vs. 2.55 pg/ml, P<0.001), prophylactic anticoagulation rate (60.7% vs. 6.5%, P<0.001) and mortality (40.5% vs. 5.9%, P<0.001) as compared with that in low PPS group. Critical patients showed higher PPS (6 score vs. 2 score, P<0.001) than that in severe patients. Multivariate logistic regression revealed the independent risk factors of in-hospital mortality included high PPS (OR: 7.35, 95%CI: 3.08 - 16.01), increased interleukin-6 (OR: 11.79, 95%CI: 5.45 - 26.20) and elevated d-dimer (OR: 4.65, 95%CI: 1.15 - 12.15). Kaplan-Meier analysis indicated patients with higher PPS had a significant survival disadvantage. Prophylactic anticoagulation in higher PPS patients show a mild advantage of mortality but without statistical significance (37.1% vs. 45.7%, P=0.42).

**Conclusion:** Higher PPS associated with in-hospital poor prognosis in COVID-19.
patients. Prophylactic anticoagulation showed a mild advantage of mortality in COVID-19 patients with higher PPS, but it remain need further investigation.

**Key words**: COVID-19; venous thromboembolism; Padua prediction score; prognosis

**Background**

The 2019 novel coronavirus disease (COVID-19) has spread to more than 100 countries or regions since the outbreak in December 2019 in Wuhan, China. Recent study revealed that the potential risk factors of older age, high SOFA score, and elevated d-dimer greater could help to identify patients with poor prognosis at an early stage. The inflammatory process, cytokine storm, and lung injury that are associated with COVID-19 can put patients at an increased risk of venous thromboembolism (VTE). Previous reports indicated that nearly 20% COVID-19 patients have abnormal coagulation function, and almost all severe or critical patients have coagulation disorders. In severe or critical COVID-19 patients, symptom of pulmonary thromboembolism (such as dyspnea or shortness of breath) might be covered by the respiratory symptom of COVID-19, which raised the risk of misdiagnosis.
Recent small scale investigations showed that the incidence of VTE for COVID-19 patients in ICU were 25% to 31% \(^4\,5\). But it is uncertain the total incidences of thrombotic events in COVID-19 patients. Update, no report evaluated the VTE risk in COVID-19 patients with different disease severity, especially outside of ICU.

Although VTE appeared to be associated with death \(^6\,8\), the role of prophylactic anticoagulation in COVID-19 patients is unknown. Preliminary data show that in patients with severe COVID-19, anticoagulant therapy appears to be associated with lower mortality in the subpopulation meeting sepsis-induced coagulopathy criteria or with markedly elevated d-dimer \(^3\,9\). However, another study suggested that routine chemical venous thromboembolism prophylaxis may be inadequate in preventing venous thromboembolism in severe COVID-19 patients \(^10\).

In this prospectively study, we assessed VTE risk of COVID-19 patients using PPS and analyzed its relationship with in-hospital mortality. We also evaluated the prophylactic anticoagulation in COVID-19 patients.

**Methods**

**Study design and participants**

This study included 274 adult patients who were lab-confirmed with COVID-19, according to WHO interim guidance in Wuhan Tongji Hospital from February 09 to March 09, 2020. Exclusion criteria were bleeding, hospital stay <7 days, lack of
information of coagulation drugs, age <18 years. Severe and critically ill COVID-19 patients were identified by reviewing and analyzing admission logs and histories of all available electronic medical records and patient care resources by two physicians. All patients were diagnosed with COVID-19 using pharyngeal swabs or throat swab specimens obtained for nucleic acid of SARS-CoV-2 PCR detection. This study was approved by the institutional review boards at Wuhan Tongji Hospital and The First Affiliated Hospital of Soochow University. Due to the rapid emergence of this infectious disease, the requirement for written informed consent was waived by the Ethics Commission.

Severe form COVID-19 patients should meet any one of the following: 1. Shortness of breath, respiratory rate (RR) ≥ 30 breaths/minute; 2. SaO₂ or SPO₂ ≤ 93% on room air; 3. PaO₂/FiO₂ ≤ 300mmHg. Critical form is defined as one or more of the following: 1. Respiratory failure with the requirement of mechanical ventilation; 2. Shock; 3. Combined other organs failure requiring monitoring and treatment in intensive care unit. The clinical classification of severe form were determined by two trained physicians via analyzing the data of all available electronic medical records and patient care resources.

**Data collection**

The demographic, clinical, laboratory and outcome data were collected from the electronic medical records using a standardized data collection form. The primary outcome was the in-hospital mortality after hospitalization. All data were checked by
two physicians. Routine blood examinations included complete blood count and coagulation profile. Anticoagulant treatment group was defined as receiving unfractionated heparin (UFH, 100-200 IU/kg/day) or low molecular weight heparin (enoxaparin 100IU/kg/day or nadroparin 86 IU/kg/d) for 7 days or longer. PPS was performed by two physician with 24h after admission as previously reported.

**Statistical analysis**

Categorical or continuous variables were presented as n (%) or median respectively. We used the X² test or Mann-Whitney U test to compare differences between survivors and non-survivors where appropriate. Survival curves were plotted using the Kaplan-Meier method using the log-rank test. Multivariate logistic regression models were used to determine the independent risk factors for in-hospital mortality after hospitalization. Data were analyzed using SPSS 25.0. A two-tailed P value < 0.05 was considered statistically significant.

**Results**

**Baseline characteristics of total COVID-19 patients**

In this single retrospective cohort study, 274 consecutive patients were enrolled in this study, including 47 death. For all of patients, the median age was 62·0 years (50-71 years), ranging from 18 years to 87 years (Table 1). The most common comorbidity was hypertension (99/274, 36.1%), followed by diabetes (45/27, 16.4%)
and cardiac disease (44/274, 16.1%). Total mortality was 17.2% (47/274). The median PPS was 2 (IQR: 2, 5) and the total prophylactic anticoagulation rate was 24.1% (66/274).

Clinical features of COVID-19 patients with higher PPS or lower PPS

As shown in Table 1, patients in higher PPS group (PPS ≥4) was older (72.0ys vs. 56.6ys, \( P<0.001 \)), have more comorbidities and a higher WBC count (7.62\( \times 10^9 \)/L vs. 5.80\( \times 10^9 \)/L, \( P<0.001 \)), a lower lymphocytes count (0.75\( \times 10^9 \)/L vs. 1.54\( \times 10^9 \)/L, \( P<0.001 \)) and platelet count (192\( \times 10^9 \)/L vs. 238\( \times 10^9 \)/L, \( P<0.001 \)) than that in lower PPS group (PPS <4). They also have a higher levels of inflammatory markers, including hs-CRP (37.7mg/L vs. 3.2mg/L, \( P<0.001 \)) and IL-6 (25.27pg/ml vs. 2.55pg/ml, \( P<0.001 \)). Patients in higher PPS group have a significantly higher levels of PT (14.5s vs. 13.3s, \( P<0.001 \)), d-dimer (2.49μg/L vs. 0.36μg/L, \( P<0.001 \)) and fibrinogen (5.14g/L vs. 3.74g/L, \( P<0.001 \)), but their APTT levels were similar to that in lower PPS group (38.10s vs. 37.80s, \( P=0.123 \)).

As PPS has been recommended as validated tools for VTE risk assessment, patients with higher PPS in our study received a higher rate of prophylactic anticoagulation (60.7% vs. 6.5%, \( P<0.001 \)). It is not surprised that their mortality was significantly higher than that in VTE low risk group (40.5% vs. 5.9%, \( P<0.001 \)), as higher PPS reflecting a more popular co-morbidity and disease severity index.

Clinical features of critical and severe COVID-19 patients

As shown in table 2, severe patients were older (60ys vs. 40ys, \( P=0.007 \)), have a
higher fibrinogen levels (4.01 g/L vs. 3.27 g/L, \(P=0.031\)) and a higher Padua score (4 score vs. 1 score, \(P<0.001\)) than that in moderate patients. Critical patients were older than severe patients (74ys vs. 60ys, \(P<0.001\)), and have a significantly higher levels of PT (15.35s vs. 13.30s, \(P<0.001\)), d-dimer (5.38 \(\mu\)g/L vs. 0.52 \(\mu\)g/L, \(P<0.001\)) and fibrinogen (5.14 g/L vs. 4.01 g/L, \(P=0.004\)). The PPS in critical patients were both higher than that in severe patients (6 score vs. 2 score, \(P<0.001\)).

**Prophylactic anticoagulation in COVID-19 patients**

The total prophylactic anticoagulation ratio was 24.1% (66/274, Table 1), all of whom were severe or critical form patients. The prophylactic anticoagulation ratio in critical patients were higher than that in severe patients (77.9% vs. 10.5%, \(P<0.001\), Figure 1A). As PPS has been recommended as validated tools for VTE risk assessment, patients with higher PPS in our study received a higher rate of prophylactic anticoagulation (60.7% vs. 6.5%, \(P<0.001\), shown in Table 1). Next, we analyzed the role of prophylactic anticoagulation in VTE high-risk subgroup patients (PPS \(\geq 4\)). After subgroup analysis in patients with higher PPS, we found that prophylactic anticoagulation show a mild advantage of mortality (decreased 18.8%) in patients with VTE high-risk, but without statistical significance (37.1% vs. 45.7%, \(P=0.42\), Figure 1B).

**Association of Padua score with prognosis**

Multivariate logistic regression analysis (Figure 1C) revealed that the independent risk factors of 28-days outcome included age (OR: 1.18, 95%CI: 0.64 - 3.28), higher
PPS (OR: 7.35, 95%CI: 3.08 - 16.01), decreased lymphocytes (OR: 2.97, 95%CI: 0.84 - 9.18), increased interleukin-6 (OR: 11.79, 95%CI: 5.45 - 26.20) and elevated d-dimer (OR: 4.65, 95%CI: 1.15 - 12.15). Kaplan-Meier analysis indicated that patients with VTE low risk (Padua score < 4) had a significant survival advantage (Figure 1D, log-rank $P < 0.01$) as compared to patients with VTE high risk (Padua score $\geq 4$).

**Discussion**

This study firstly evaluated PPS and prophylactic anticoagulation in COVID-19, which suggested that high PPS was associated with poor prognosis and as an independent risk factor of in-hospital mortality. Prophylactic anticoagulation showed a mild advantage of mortality in VTE high-risk COVID-19 patients, but without statistically significant difference. This remain need further evidence.

Infection is an independent risk factors for VTE and should be considered as potential indications for prophylaxis. Observational reports showed that coagulation disorders existed in COVID-19 patients, especially in severe and critical cases. Actually, PPS has been recommended as validated tools for VTE risk assessment. PPS can help discriminate between medical patients at high and low risk of VTE. The adoption of adequate thromboprophylaxis in high-risk patients during hospitalization leads to longstanding protection against thromboembolic events with a low risk of bleeding. Usage of PPS for VTE risk assessment was associated with a
higher rate of appropriate thromboprophylaxis prescription and a reduced VTE incidence\textsuperscript{15-16}. Moreover, PPS-guiding management could reduce unnecessary radiation exposure, such as CT pulmonary angiography, through the implementation of the score. Our study is the first observation about PPS and prognosis in COVID-19 patients. It showed the higher PPS in severe and critical patients and its association with short-term prognosis. It was consistent to previous reports. Some data suggest that a positive PPS, reflecting a more popular co-morbidity and disease severity index, associated with early mortality in internal medicine patients\textsuperscript{17-18}. This revealed that PPS was one of the potential tool for the evaluation of early prognosis in COVID-19.

Pharmacological thromboprophylaxis can significantly reduce the risk of VTE in the medical patient\textsuperscript{19}. However, the role of prophylactic anticoagulation in COVID-19 patients is unclear. Some studies revealed the potential benefit of anticoagulant treatment in severe COVID-19 patients with higher VTE risk\textsuperscript{3,9,13}. But other report indicated that routine chemical prophylaxis was inadequate in preventing VTE in severe COVID-19 patients\textsuperscript{10}. In our study, prophylactic anticoagulation showed a mild advantage of mortality in patients with VTE high-risk (decreased 18.8%), but without statistical significance. This result was opposite to the previous reports which suggesting the potential benefit of anticoagulant treatment in severe COVID-19 patients with higher VTE risk\textsuperscript{3,9,13}. This might be due to two reasons. First of all, the enrolled patients and the epidemiological characteristics were different. Most of COVID-19 patient in our study were severe or critical form, with more comorbidities and higher mortality. The subjects enrolled in previous report have a proportion of
60.6% with underlying diseases, which was lower than that in our study (69.7%)\textsuperscript{9}.

The mortality of heparin users in previous report was also lower than that in our study (30.3% vs. 37.1%)\textsuperscript{9}. Secondly, the prophylactic anticoagulation rate in our study in VTE high-risk COVID-19 patients was only 60.7%, which was far lower than tumor patients and critically ill\textsuperscript{18,21}. VTE assessment was inadequate due to the insufficient medical resources at the peak period of COVID-19 pandemic in Wuhan. The usage of prophylactic anticoagulation was limited. So, a larger scale trial or randomized controlled trial might provided more convincing evidence for the clinical value of prophylactic anticoagulation in COVID-19.

There were several limitations in this study. First, it is a retrospective and single-center study. More data and large samples were needed to confirm the results and correct the bias. Second, the VTE or pulmonary embolism (PE) incidence in whole patients was uncertain. Despite that, our report evaluated the VTE risk and the benefit of prophylactic anticoagulation in COVID-19 patients. We described the high-risk of VTE and low prophylactic anticoagulation rate in severe and critical COVID-19 patients.

In conclusion, this study revealed that severe and critical COVID-19 patients have a high risk of VTE and higher Padua Score, which was associated with poor prognosis. Prophylactic anticoagulation show a mild decrease of mortality in patients with VTE high risk. However, the prophylactic anticoagulation remain need improvement in COVID-19 patients with VTE high risk.
Acknowledgment

This work was supported by Program of Key Talents of Medical Science in Jiangsu Province [QNRC2016745], Suzhou science and technology development plan [SYS202008].

References:

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395 (10229):1054-1062.

2. Xiong M, Liang X, Wei YD. Changes in Blood Coagulation in Patients with Severe Coronavirus Disease 2019 (COVID-19): a Meta-Analysis. Br J Haematol. 2020 Jun;189(6):1050-1052.

3. Kollias A, Kyriakoulis KG, Dimakakos E, Poulakou G, Stergiou GS, Syrigos K. Thromboembolic risk and anticoagulant therapy in COVID-19 patients: Emerging evidence and call for action. Br J Haematol. 2020 Jun;189(5):846-847.

4. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost 2020 Jun;18(6):1421-1424.
5. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020 Jul;191:145-147.

6. Spiezia L, Boscolo A, Poletto F, Cerruti L, Tiberio I, Campello E, et al. COVID-19-Related Severe Hypercoagulability in Patients Admitted to Intensive Care Unit for Acute Respiratory Failure. Thromb Haemost. 2020 Jun;120(6):998-1000.

7. Middeldorp S, Coppens M, van Haaps TF, Foppen M, Vlaar AP, Müller MCA, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. J Thromb Haemost. 2020 May 5. doi: 10.1111/jth.14888.

8. Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020 Jun;46(6):1089-1098.

9. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020 May;18(5):1094-1099.

10. Maatman TK, Jalali F, Feizpour C, Douglas A 2nd, McGuire SP, Kinnaman G, et al. Routine Venous Thromboembolism Prophylaxis May Be Inadequate in the Hypercoagulable State of Severe Coronavirus Disease 2019. Crit Care Med. 2020 May 27. doi: 10.1097/CCM.0000000000004466. Online ahead of print.

11. Zhai Z, Li C, Chen Y, Gerotziafas G, Zhang Z, Wan J, et al. Prevention and
Treatment of Venous Thromboembolism Associated with Coronavirus Disease 2019 Infection: A Consensus Statement before Guidelines. Thromb Haemost. 2020 Jun;120(6):937-948.

12.Barbar S, Noventa F, Rossetto V, Ferrari A, Brandolin B, Perlati M, 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.

13.Escher R, Breakey N, Lämmle B. Severe COVID-19 infection associated with endothelial activation. Thromb Res. 2020 Apr 15;190:62.

14.Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020;18(5):1023-1026.

15.Germini F, Agnelli G, Fedele M, Galli MG, Giustozzi M, Marcucci M, et al. Padua prediction score or clinical judgment for decision making on antithrombotic prophylaxis: a quasi-randomized controlled trial. J Thromb Thrombolysis. 2016;42(3):336-339.

16.Kandagatla P, Goranta S, Antoine H, Marashi SM, Schmoekel N, Gupta AH. PADUA score as a predictor for pulmonary embolism: a potential strategy for reducing unnecessary imaging. J Thromb Thrombolysis. 2019;47(4):566-571.

17. Arpaia GG, Caleffi A, Marano G, Laregina M, Erba G, Orlandini F, et al. Padua
prediction score and IMPROVE score do predict in-hospital mortality in Internal Medicine patients. Intern Emerg Med. 2020 Jan 2. doi: 10.1007/s11739-019-02264-4.

18. Zhou H, Hu Y, Li X, Wang L, Wang M, Xiao J, et al. Assessment of the Risk of Venous Thromboembolism in Medical Inpatients using the Padua Prediction Score and Caprini Risk Assessment Model. J Atheroscler Thromb. 2018;25(11):1091-1104.

19. Stuck AK, Spirk D, Schaudt J, Kucher N. Risk assessment models for venous thromboembolism in acutely ill medical patients. A systematic review. Thromb Haemost. 2017;117(4):801-808.

20. Lilly CM, Liu X, Badawi O, Franey CS, Zuckerman IH. Thrombosis prophylaxis and mortality risk among critically ill adults. Chest. 2014;146(1):51-57.

21. Lodigiani C, Iapichino G, Carenzo L, Cecconi M, Ferrazzi P, Sebastian T, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thromb Res. 2020 Apr 23;191:9-14.
Tables:

Table 1. Baseline features of COVID-19 patients with different VTE risk.

| Characteristics | All patients (n=274) | High PPS (≥4 score) | Low PPS(<4 score) | P |
|----------------|----------------------|---------------------|------------------|---|
| Age, y         | 62 (50,71)           | 72.0 (63.5-80.0)    | 56.5 (43.0,66.0) | <0.001 |
| Male sex       | 145 (52.9%)          | 56 (62.9%)          | 89 (48.1%)       | 0.007  |
| Comorbidity    |                      |                     |                  |     |
| Hypertension   | 99 (36.1%)           | 46 (51.7%)          | 53 (28.6%)       | <0.001 |
| Diabetes       | 45 (16.4%)           | 18 (20.2%)          | 27 (14.6%)       | 0.223  |
| Cardiac disease | 44 (16.1%)           | 25 (28.1%)          | 19 (10.3%)       | <0.001 |
| COPD           | 8 (2.9%)             | 6 (6.7%)            | 2 (1.1%)         | 0.026  |
| Lab findings on admission |          |                     |                  |     |
| WBC count, ×10⁹/L | 6.17 (4.86,7.90) | 7.62 (5.86,9.67)    | 5.80 (4.51,7.16) | <0.001 |
| Lymphocyte count, ×10⁹/L | 1.30 (0.86,1.81) | 0.75 (0.48,1.17)    | 1.54 (1.16,1.92) | <0.001 |
| Platelet count, ×10⁹/L | 232 (167.00,303.75)| 192 (121,303)       | 238 (194,0,305.5) | 0.001  |
| Creatinine level, μmol/L | 68.00 (57.00,80.00)| 74 (62,101)         | 65.0 (55.5,76.0) | <0.001 |
| ALT level, U/L | 23.00 (15.00,40.50)  | 26.0 (16.5,45.0)    | 22.00 (14.25,39.00) | 0.186 |
| hs-CRP, mg/L   | 8.70 (1.60,61.00)    | 37.7 (33.40,119.28) | 3.2 (1.1,11.6)   | <0.001 |
| IL-6, pg/ml    | 4.60 (1.67,22.73)    | 25.27 (10.99,63.54) | 2.55 (1.50,5.04) | <0.001 |
| Coagulation parameters |          |                     |                  |     |
| PT, s          | 13.50 (12.95,14.30)  | 14.5 (13.9,16.1)    | 13.3 (12.8,13.7) | <0.001 |
| APTT, s        | 37.90 (35.00,41.25)  | 38.10 (34.63,43.60) | 37.80 (35.30,39.95) | 0.123 |
| D-dimer, μg/L  | 0.68 (0.26,1.94)     | 2.49 (1.27,17.02)   | 0.36 (0.22,0.80)  | <0.001 |
| Fibrinogen, g/L| 4.13 (3.16,5.41)     | 5.14 (3.98,6.21)    | 3.74 (3.02,4.94)  | <0.001 |
| PPS at admission | 2 (2,5)              | 5 (5,6)             | 2 (2,2)          | <0.001 |
Continuous variables are expressed as median values (interquartile ranges), and categorical variables are presented as number of patients (percentages).

**Abbreviations:** PPS, Padua prediction score; WBC, white blood cell; hs-CRP, high-sensitive C-reactive protein; AST, aspartate aminotransferase; COPD, chronic obstructive pulmonary disease; IL-6, interleukin-6.

* Includes congestive heart disease and coronary atherosclerotic heart disease.

| Prophylactic anticoagulan | 66 (24.1%) | 54 (60.7%) | 12 (6.5%) | <0.001 |
|---------------------------|-----------|------------|-----------|--------|
| In-hospital mortality     | 47 (17.2%)| 36 (40.5%) | 11 (5.9%) | <0.001 |
Table 2. Comparison of COVID-19 patients with different severity.

| Characteristics                  | Moderate (n=24) | Severe (n=191) | Critical (n=59) | P (moderate vs. Severe) | P (Severe vs. Critical) |
|----------------------------------|----------------|----------------|----------------|-------------------------|-------------------------|
| Age, y                           | 46.00 (37.00,56.75) | 60.00 (47.75,69.00) | 74.00 (64,80) | 0.007                   | <0.001                  |
| Male sex                         | 14 (58.3%)      | 93 (48.7%)      | 38 (64.4%)     | 0.374                   | 0.008                   |

Coagulation parameters at admission

| Parameter               | Moderate (n=24) | Severe (n=191) | Critical (n=59) | P                      | P                      |
|-------------------------|----------------|----------------|----------------|------------------------|------------------------|
| PT, s                   | 13.35 (12.70,13.90) | 13.30 (12.8,13.8) | 15.35(14.08,16.45) | 1.000                  | <0.001                 |
| APTT,s                  | 37.10 (31.55,39.53) | 37.8 (35.1,40.5) | 39.10(36.05,43.70) | 0.588                  | 0.138                  |
| D-dimer, μg/L           | 0.28 (0.22,0.68) | 0.52 (0.22,1.21) | 5.38 (1.57,21.00) | 0.177                  | <0.001                 |
| Fibrinogen, g/L         | 3.27 (2.30,4.08) | 4.01 (3.18,5.28) | 5.14 (3.94,6.45) | 0.031                  | 0.004                  |
| PPS at admission        | 1.00 (1.00,1.75) | 2.00(2,3)       | 6.00 (5,6)      | <0.001                 | <0.001                 |
| Prophylactic anticoagulation | 0 (0%)         | 20 (10.5%)      | 46 (77.9%)     | 0.097                  | <0.001                 |

Continuous variables are expressed as median values (interquartile ranges), and categorical variables are presented as number of patients (percentages).

Figure captions:

Figure 1: Relationship of PPS and prophylactic anticoagulation with in-hospital mortality in COVID-19. A: PPS and prophylactic anticoagulation in COVID-19 with different disease severity. B: Prophylactic anticoagulation show a mild decrease of mortality in VTE high-risk patients (PPS≥4). C: Multivariate logistic regression
analysis of risk factors for 28-days mortality. D: Kaplan-Meier analysis of Overall survival in COVID-19 patients by Padua score.
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