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Venous Thromboembolism in Patients Discharged after COVID-19 Hospitalization

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Abstract

Background Venous thromboembolism (VTE) is a frequent complication of COVID-19, so that the importance of adequate in-hospital thromboprophylaxis in patients hospitalized with COVID-19 is well established. However, the incidence of VTE after discharge and whether postdischarge thromboprophylaxis is beneficial and safe are unclear. In this prospective observational single-center study, we report the incidence of VTE 6 weeks after hospitalization and the use of postdischarge thromboprophylaxis.

Methods Patients hospitalized with confirmed COVID-19 were invited to a multidisciplinary follow-up clinic 6 weeks after discharge. D-dimer and C-reactive protein were measured, and all patients were screened for deep vein thrombosis with venous duplex-ultrasound. Additionally, selected high-risk patients received computed tomography pulmonary angiogram or ventilation–perfusion (V/Q) scan to screen for incidental pulmonary embolism.

Keywords
- venous thromboembolism
- deep vein thrombosis
- pulmonary embolism
- COVID-19
- SARS-CoV-2
- anticoagulation
- thromboprophylaxis after discharge
- postdischarge thromboprophylaxis

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Results Of 485 consecutive patients hospitalized from March through June 2020, 146 patients were analyzed, of which 39% had been admitted to the intensive care unit (ICU). Postdischarge thromboprophylaxis was prescribed in 28% of patients, but was used more frequently after ICU stay (61%) and in patients with higher maximal D-dimer and C-reactive protein levels during hospitalization. Six weeks after discharge, elevated D-dimer values were present in 32% of ward and 42% of ICU patients. Only one asymptomatic deep vein thrombosis (0.7%) and one symptomatic pulmonary embolism (0.7%) were diagnosed with systematic screening. No bleedings were reported.
Conclusion In patients who had been hospitalized with COVID-19, systematic screening for VTE 6 weeks after discharge revealed a low incidence of VTE. A strategy of selectively providing postdischarge thromboprophylaxis in high-risk patients seems safe and potentially effective.

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One year after the first outbreak in Wuhan, China, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 100 million people and caused over 2.2 million known deaths worldwide.[1] Clinicians quickly learned that the coronavirus disease 2019 (COVID-19) is associated with high incidence of symptomatic venous thromboembolism (VTE) in hospitalized patients, especially in those admitted to intensive care units (ICUs). Systematic screening for VTE in patients hospitalized with COVID-19 has also revealed a higher incidence of subclinical VTE, even in patients receiving prophylactic doses of low-molecular-weight heparin (LMWH).[2–11] Furthermore, more extensive activation of the coagulation system has been associated with worse clinical outcomes, so that LMWH administration at intermediate or therapeutic doses has been suggested to improve outcome in patients hospitalized with COVID-19.[12–17] Therefore, many studies have focused on identifying the optimal dose of LMWH for in-hospital thromboprophylaxis.[11,17–20]

In contrast, limited data are available on incidence of symptomatic and subclinical VTE after COVID-19 hospitalization, as systematic screening for VTE in the outpatient setting can be cumbersome. Consequently, the optimal thromboprophylactic strategy after discharge remains mostly unknown.

In this study, we performed systematic VTE screening in a well-characterized cohort of patients discharged after COVID-19 hospitalization to investigate the incidence of VTE after COVID-19 hospitalization by postdischarge thromboprophylactic strategy and by disease severity.

Methods

This single tertiary-center study was performed at the University Hospitals Leuven in Belgium. We prospectively followed adult patients (18 years or older) after hospitalization with COVID-19 at a multidisciplinary outpatient follow-up clinic, 6 weeks after discharge. The study was approved by the ethics committee and all patients provided written informed consent.

Hospital Stay and Clinical Decision Making on Postdischarge Thromboprophylaxis

During hospitalization, COVID-19 diagnosis was confirmed with polymerase chain reaction test and/or pulmonary computed tomography (CT). During hospitalization, patients received enoxaparin with a prophylactic (0.5 mg/kg once daily, on the ward) or intermediate (0.5 mg/kg twice daily, in the ICU) dosing regimen, as described in more detail by our group in April 2020[21] and recommended by the Belgian Society of Thrombosis and Hemostasis.[22]

Guidelines and data on postdischarge thromboprophylaxis were lacking. Therefore, when there was no indication for therapeutic anticoagulation after discharge (e.g., atrial fibrillation, VTE, mechanical heart valve, and so forth), low dose enoxaparin (0.5 mg/kg once daily) for 2 to 6 weeks after discharge was considered on individualized basis, and especially in high-risk patients (defined as ICU stay, known thrombophilia, obesity, immobilization, heart failure, respiratory failure, age over 70 years, personal or familial history of VTE, active cancer or major surgery in the last 3 months). The risk and benefits of postdischarge thromboprophylaxis were weighted on individual basis, especially in patients with (recent) history or a high risk of bleeding. The prescription and duration of thromboprophylaxis after discharge were therefore left to the clinician's discretion as the risk of VTE after discharge was unknown and established guidelines on postdischarge thromboprophylaxis were lacking.

Patient Selection

Patients hospitalized from March 27 through July 1, 2020 were evaluated at the outpatient clinic 6 weeks after discharge. Eligible patients were aged 75 or younger, unless they had been admitted to ICU. Residents of a medical care facility, patients with cognitive impairment, with geriatric profile (clinical frailty scale >5) were excluded as for this group specific geriatric care was pursued on an individual needs assessment. Patients admitted for nonrespiratory reasons with incidental finding of SARS-CoV-2 infection or patients with a hospital stay <2 days were also excluded from follow-up to exclude patients with limited disease not

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requiring (prolonged) hospitalization. Patients with a preexisting reason for (therapeutic) anticoagulation, such as patients with atrial fibrillation or prior VTE, were also excluded, as these patients do not qualify for prophylactic doses of anticoagulation. The use of therapeutic doses of anticoagulation could affect VTE incidence, and prior VTE could affect diagnosis of the study outcome.

Screening for deep venous thrombosis with venous duplex-ultrasound (CX 50 and EPIQ 5, Philips) was performed in all patients by dedicated vascular technologists. CT pulmonary angiogram (CTPA) or ventilation–perfusion scan (V/Q) was only performed—when logistically possible—in selected high-risk patients as defined by ICU stay (if no CTPA was performed during hospitalization), D-dimer levels above 2,000 ng/mL during admission, or clinical suspicion.

Outcomes

The primary outcome was the incidence of VTE upon systematic screening 6 weeks after discharge; the secondary outcomes comprised the type and duration of outpatient thromboprophylaxis, bleeding rate (major and clinically relevant nonmajor bleeding as defined by the International Society on Thrombosis and Haemostasis[23,24]), and evolution of D-dimer (fibrinogen equivalent units; ACL TOP 700 LAS, Werfen; HemosIL D-dimer HS 500, Werfen) and C-reactive protein (CRP; Cobas 8000, Roche; Cobas CRP4, Roche).

Data Collection and Statistics

In-hospital data were retrospectively obtained and follow-up data were prospectively collected (M.M.E. and E.C.), only after consent was obtained according to the General Data Protection Regulation.

Continuous variables are expressed as median (interquartile range, IQR) and the differences in patient characteristics (►**Table 1**) were tested with the nonparametric Kruskal–Wallis test. Categorical variables are represented as frequencies and proportions (%) and compared by chi-squared or Fisher-exact test. To assess the changes over time from discharge D-dimer and CRP values to follow-up, linear mixed effects models are used with time, postdischarge thromboprophylaxis effect, and an interaction effect between time and postdischarge thromboprophylaxis as fixed effects. The statistical analysis was performed by using R-software (version 4.0.3). ►**Figure 1** was created with Adobe Illustrator (version 25.2.1). ►**Figures 2** and **3** were created using GraphPad Prism (version 9.0.0); statistics include nonparametric testing. All tests were performed using a 0.05 significance level.

Results

Baseline Characteristics

Of the 485 patients who were hospitalized from March 27 until July 1, we screened a total of 176 patients 6 weeks after discharge at the outpatient clinic. Eventually, 146 patients were analyzed (►**Fig. 1**). Patient characteristics are shown in ►**Table 1**. In this cohort, 62% were males with a median age of 58 years (IQR: 51–67). Only four patients had history of VTE prior to the index hospitalization. The median hospital stay was 11 (IQR: 6–19) days, and 39% of these patients had been admitted to the ICU with a median ICU stay of 13 (IQR: 8–22) days. Of those critically ill patients, 63% needed invasive mechanical ventilation, and 9% required extracorporeal membrane oxygenation (ECMO). As far as chronic antithrombotic treatment is concerned, patients with anticoagulation (started during or before index hospitalization) were excluded and 20% of patients were on antiplatelet drugs (►**Table 1**).

Use of Postdischarge Thromboprophylaxis Was Higher in Patients with more Severe COVID-19

Of 146 patients, 41 (28%) received thromboprophylaxis with prophylactic dose of enoxaparin (0.5 mg/kg once daily) for a median of 14 (IQR: 10–23.5) days after hospital discharge (►**Table 2**). Patients who received postdischarge thromboprophylaxis had more frequent ICU admission, longer ICU and hospital stay, a greater need for invasive mechanical ventilation or ECMO, and higher maximal D-dimer and CRP values (►**Table 1**). The use of postdischarge thromboprophylaxis was more frequently prescribed in patients with a complicated disease course, thus increasing significantly from 18% in patients hospitalized on the ward to 44% in ICU patients ($p = 0.001$) and 71% in patients with ICU stay of $\geq$2 weeks ($p = 0.021$). Similarly, postdischarge thromboprophylaxis was related to the type of respiratory support, as it was prescribed significantly more in patients previously requiring ECMO (100%) or invasive mechanical ventilation (56%) than in those requiring only oxygen during hospitalization (30%) ($p = 0.003$ and 0.006).

Evolution of Markers of Inflammation and Thrombosis during and After Discharge

D-Dimer levels were higher in ICU patients compared with those hospitalized on the ward at any time point during hospitalization (►**Fig. 2**). Even at discharge, the previously critically ill had higher D-dimer levels than those admitted to the ward. At follow-up 6 weeks after discharge, the difference between those groups was no longer significant. Trajectories over time of D-dimer values between discharge and follow-up were not different between patients with or without postdischarge thromboprophylaxis (Coef [standard deviation, SD] of interaction term $= -40.6$ [21.7], $p = 0.07$). However, even then, persistently (very) high D-dimer values were no exception (►**Fig. 2**). Overall, 36% of patients had D-dimer values above the cut-off of 500 ng/mL at outpatient follow-up (32% for ward patients vs. 42% for ICU patients, $p = 0.22$).

Initially, a similar evolution is observed for CRP, with significantly higher values for ICU patients at admission and during hospitalization at maximal values. At discharge however, the median level of this biomarker was still slightly elevated in ward patients, thus reflecting quicker discharge when not critically ill. At follow-up, CRP levels were low and comparable in ICU and ward patients (►**Fig. 3**). When assessing change in CRP values between discharge and follow-up, we do observe a significant difference in trajectories over time (Coef [SD] of interaction term $=0.8$ [0.4] $p = 0.04$).

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Table 1 Patient characteristics

	All patients ($N = 146$)	Prophylaxis after discharge ($N = 41$)	No prophylaxis after discharge ($N = 105$)	*p*-Value
History				
Age, median years (IQR)	58 [51–67]	60 [51–68]	58 [51–66]	0.64
Male sex, no. (%)	91 (62)	26 (63)	65 (62)	1.00
Body weight, median kilogram (IQR)	82.0 [71.4–95.8]	83.5 [71.7–98.0]	82.0 [71.3–95.0]	0.82
Body mass index, median (IQR)	26.6 [24.1–31.7]	27.9 [24–32.5]	26.5 [24.2–31.5]	0.76
Diabetes mellitus, no. (%)	42 (29)	16 (39)	26 (25)	0.13
HbA1c, median (IQR)	6.20 [5.8–6.6]	6.30 [5.9–6.9]	6.20 [5.80–6.5]	0.19
Smoking (ever), no. (%)	62 (44)	21 (55)	41 (39)	0.14
Hypertension, no. (%)	66 (45)	19 (46)	47 (45)	1.00
Chronic kidney disease				
eGFR < 60 mL/min/1.73 m^2, no. (%)	29 (20)	10 (24)	19 (18)	0.53
eGFR < 30 mL/min/1.73 m^2, no. (%)	5 (3)	2 (5)	3 (3)	0.62
eGFR (mL/min/1.73 m^2), median (IQR)	87.5 [64.2–98.8]	85.0 [60–100]	88 [69–98]	0.54
History of VTE, no. (%)	4 (3)	0 (0)	4 (4)	0.58
Active cancer, no. (%)	9 (6)	2 (5)	7 (7)	1.00
Concomitant drugs[a], no. (%)				
Antiplatelet drugs	29 (20)	10 (24)	19 (18)	0.53
Aspirin	26 (18)	9 (22)	17 (16)	0.56
P2Y12 inhibitor	7 (5)	3 (7)	4 (4)	0.40
Statin therapy	42 (29)	17 (42)	25 (24)	0.06
Antihypertensive drugs	59 (40)	19 (46)	40 (38)	0.47
COVID-19 diagnosis				
Confirmed by PCR, no. (%)	130 (89)	40 (98)	90 (86)	0.04
Hospital stay				
ICU, no. (%)	57 (39)	25 (61)	32 (31)	<0.01
ICU stay (days), median (IQR)	13 [8–22]	22 [15–30]	9.00 [6–13.2]	<0.01
Total hospital stay (days), median (IQR)	11 [6–19]	23.0 [11–34]	9 [6–13]	<0.01
Respiratory support during hospitalization, no. (%)				
Oxygen	128 (88)	38 (93)	90 (86)	0.39
Mechanical ventilation	36 (25)	20 (49)	16 (15)	<0.01
ECMO	5 (3)	5 (12)	0 (0)	0.02
Laboratory values, median (IQR)				
Hemoglobin, admission (g/dL)	14.1 [12.7–14.9]	14.2 [11.4–14.9]	14.1 [13.1–15]	0.42
Platelet count, admission (x10^9/L)	206 [162–282]	176 [144–226]	212 [167–305]	0.04
White blood cell count, admission (x10^9/L)	6.26 [4.4–8.1]	7.07 [4.1–9.2]	6.13 [4.4–7.6]	0.53
D-dimer (ng/mL)				
Admission	776 [568–1,308]	964 [582–1520]	763 [564–1,148]	0.19
Maximum	1,593 [844–2,862]	2,158 [1,681–16073]	1,107 [746–2,014]	<0.01
Discharge	922 [676–1,538]	1,236 [816–1,912]	900 [510–1257]	0.07
Follow-up	422 [300–599]	512 [361–829]	378 [291–532]	0.01
C-Reactive protein (mg/L)				
Admission	71.9 [29.7–132]	64.4 [36.1–139]	71.9 [24.3–127]	0.42
Maximum	118 [54.4–259]	213 [84–330]	94.6 [48.1–209]	<0.01
Discharge	14.2 [4.35–31.6]	9.40 [3–25]	17.0 [5.1–33.9]	0.05
Follow-up	1.50 [0.6–3.3]	1.50 [0.8–4.5]	1.50 [0.6–3.2]	0.36

Abbreviations: ECMO, extracorporeal membrane oxygenation; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; IQR, interquartile range; PCR, polymerase chain reaction; VTE, venous thromboembolism.
[a]Recorded at follow-up.

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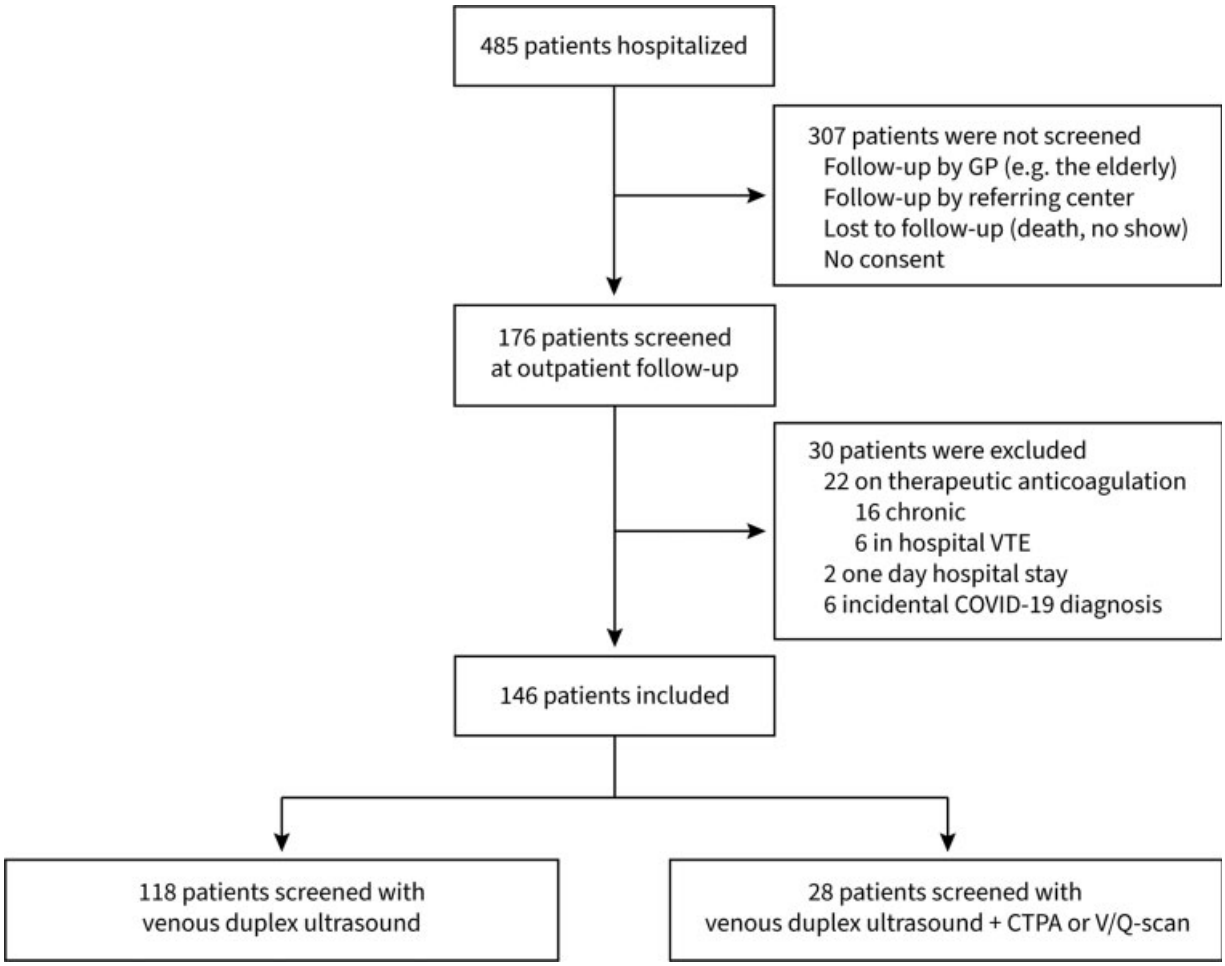

Fig. 1 VTE screening at the outpatient follow-up clinic. This diagram represents all patients hospitalized with COVID-19 between March 7, 2020 and July 1, 2020 and consecutive screening for VTE at the outpatient follow-up clinic 6 weeks after discharge. CTPA, computed tomography pulmonary angiogram; GP, general practitioner; V/Q-scan, ventilation–perfusion scan; VTE, venous thromboembolism.

Incidence of VTE and Bleeding after Discharge

The incidence of postdischarge VTE was low. In this cohort, we diagnosed one (0.7%) asymptomatic distal deep vein thrombosis in a patient without thromboprophylaxis, and one (0.7%) symptomatic pulmonary embolism in a patient while receiving thromboprophylaxis. The patient diagnosed with asymptomatic deep vein thrombosis was 65 years old and had a history of a nonactive malignancy. She was hospitalized only shortly for 5 days at the ward and was screened 36 days after discharge at the follow-up clinic. The patient diagnosed with symptomatic, bilateral, pulmonary embolism was 68 years old and recovering from critical illness myopathy after being hospitalized for 54 days, of which 47 days at the ICU for mechanical ventilation. He was diagnosed 28 days after ICU discharge and 21 days after transfer to a revalidation clinic while receiving a prophylactic dose of enoxaparin. There were no major or clinically relevant nonmajor bleeding events in patients who received thromboprophylaxis (►**Table 2**).

Discussion

We report here the use of postdischarge thromboprophylaxis and 6-week outcomes after hospitalization for COVID-19. In this tertiary single-center prospective study, consecutive patients were treated with weight-adjusted prophylactic to intermediate dosed enoxaparin during hospitalization as outlined in an institutional guidance document.[21] Postdischarge thromboprophylaxis was considered for at-risk patients and weighted against bleeding risk. The postdischarge management was left at the risk–benefit assessment of the treating physician, as well-supported guidelines are lacking. Overall, 28% of all patients, mostly the critically ill, received postdischarge thromboprophylaxis for a median duration of 14 (IQR: 10–23.5) days. Indeed, patients who received postdischarge thromboprophylaxis had more frequent ICU admission, a longer ICU- and hospital stay, a greater need for invasive mechanical ventilation or ECMO, and higher maximal D-dimer and CRP levels. Of note, 20% of patients received antiplatelet therapy, mainly with low-dose aspirin. Use of antiplatelet therapy was not different between patients with or without postdischarge thromboprophylaxis. After systematic screening of 176 consecutive patients 6 weeks after discharge, we included 146 patients and diagnosed only one asymptomatic deep vein thrombosis (0.7%) and one symptomatic pulmonary embolism (0.7%). No major or clinically relevant nonmajor bleedings were observed. It therefore seems that selectively providing

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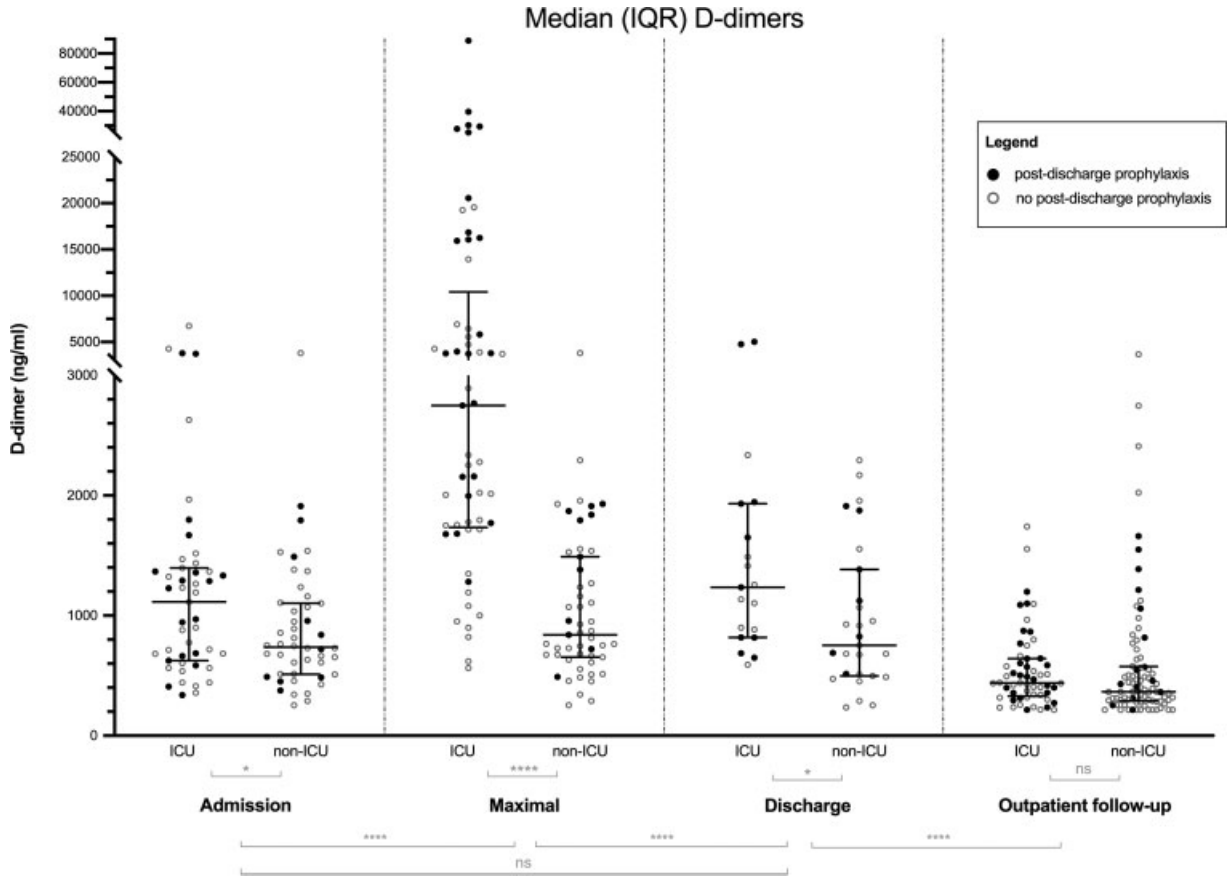

Fig. 2 Evolution of D-dimer values. This figure represents D-dimer values at admission, maximal values during hospitalization, and values at discharge and 6 weeks after discharge at the outpatient follow-up clinic. D-dimer levels are shown for ICU and non-ICU (ward) patients with error bars for the median (IQR) D-dimer values. ICU, intensive care unit; IQR, interquartile range; ns, nonsignificant difference; *-****, level of significance.

postdischarge thromboprophylaxis in high-risk patients is safe and potentially effective.

In general, extension of thromboprophylaxis after discharge in medically ill patients reduces the risk of VTE but increases that of bleeding. Therefore, it is not routinely recommended.[25] However, because of the high incidence of thrombotic complications in hospitalized patients with COVID-19 and the potential benefits of heparin on outcome in such patients,[12,15,16,19] it is unclear whether thromboprophylaxis should be routinely provided after COVID-19 hospitalization. With the ongoing pandemic, data to evaluate the risk and benefit of thromboprophylaxis in this particular COVID-19 population are urgently needed.

Despite the high in-hospital VTE incidence, our results indicate that VTE after discharge may be infrequent, and are in keeping with other observational studies without systematic VTE screening.[10,26,27] In our study, patients discharged after hospitalization for COVID-19 without home thromboprophylaxis had low incidence of VTE. This confirms that thromboprophylaxis can be safely withheld after discharge in a majority of patients, especially if they do not have risk factors for thrombosis. On the other hand, the use of postdischarge thromboprophylaxis in a minority of more severely ill patients was also associated with low incidence of VTE. Furthermore, this approach seems to be safe with regards to the risk of bleeding, as no bleedings were reported in patients with or without postdischarge thromboprophylaxis. This is in contrast to the findings of Patell et al, who reported a cumulative bleeding rate of 3.6% in patients discharged after COVID-19 hospitalization even without postdischarge anticoagulation.[26]

Therefore, routinely treating all patients with postdischarge thromboprophylaxis may not be needed, while targeting high-risk patients could be sufficient. Whether the use of a more restrictive approach is equally effective should be investigated in a controlled study with systematic screening for VTE.

Interestingly, D-dimer levels remained high in 36% of patients, even 6 weeks after discharge. However, the incidence of (a)symptomatic VTE remains low, even with persistent high D-dimer values. Therefore, persistently elevated D-dimers following hospitalization for COVID-19 do not appear to be associated with VTE. This has important implications for outpatient VTE screening. Whether elevated D-dimers are a marker of pulmonary sequalae post-COVID-19 remains to be investigated.

Strengths of this study include the prospective follow-up of a well-characterized ill COVID-19 patient population with extensive venous duplex screening in all patients at a predefined time point after discharge. More advanced imaging (CTPA or V/Q) was performed in a subset of approximately 20% of patients. The study population was thoroughly

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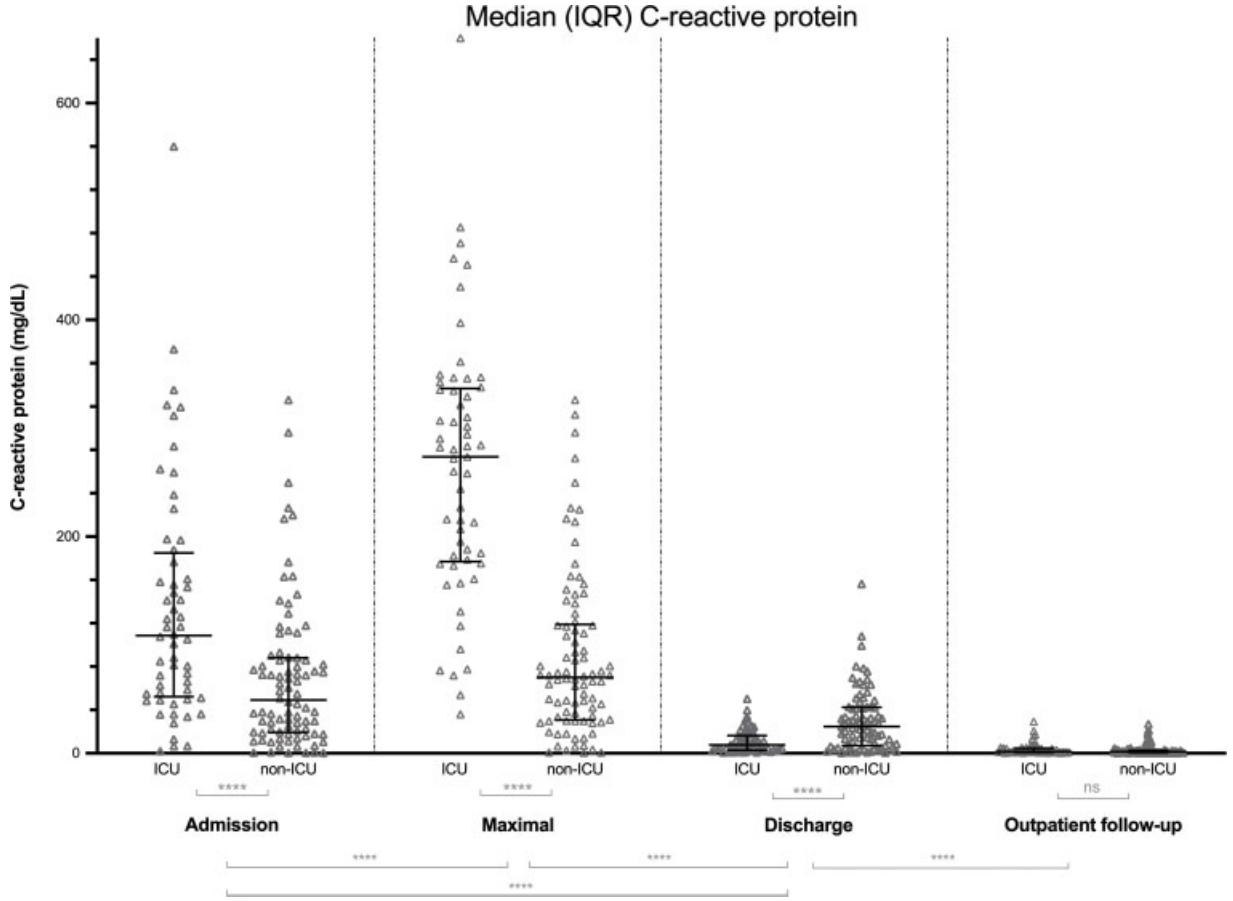

Fig. 3 Evolution of C-reactive protein values. This figure represents C-reactive protein values at admission, maximal values during hospitalization, and values at discharge and 6 weeks after discharge at the outpatient follow-up clinic. C-reactive protein levels are shown for ICU and non-ICU (ward) patients with error bars for median (IQR) C-reactive protein. ICU, intensive care unit; IQR, interquartile range; ns, nonsignificant difference; *****, level of significance.

assessed during follow-up, allowing for detailed clinical information such as bleeding events.

There are several limitations to this study. Importantly, although clinicians were provided with guidance to consider thromboprophylaxis for patients with predefined risk factors for VTE, the selection of patients for postdischarge thromboprophylaxis was ultimately based on the individualized risk–befit assessment of the treating physician. Although this has the benefit of providing information on real-world practice, it is also not clear which criteria exactly were taken into consideration. Such assessments are likely to be influenced by the physician's expertise. Given the low incidence of events, we currently have insufficient data to assess clinical or biochemical markers for VTE postdischarge, so that we are unable to predict which categories of patients should definitely receive postdischarge prophylaxis. However, analysis of the patient group with postdischarge prophylaxis reveals that it included patients with classic risk factors such as immobilization and prior history of VTE, but also those with more severe disease or with higher evidence of inflammation and thrombotic activation. Indeed, postdischarge thromboprophylaxis was more frequently used in patients with more severe disease course and higher inflammatory and thrombotic laboratory markers. This strategy of selective, rather than systematic use of postdischarge thromboprophylaxis, seems safe and potentially effective. In the absence of a control group, however, it remains unknown whether a similarly low risk of postdischarge VTE can be achieved with an even more restrictive use of postdischarge thromboprophylaxis. On the other hand, given the absence of bleeding complications in this cohort, extending this treatment to intermediate or even low-risk patients seems—based on this cohort—not to be harmful either.

Not all hospitalized patients could be screened 6 weeks after discharge (►**Fig. 1**), making the cohort potentially susceptible to selection bias. Patients with a poor functional outcome or fully recovered patients often declined follow-up evaluation. Additionally, the follow-up of the elderly was organized by the general practitioner rather than at our center, as reflected by this cohort's median age. Hence, it is unclear if our results also apply to more elderly patients who often suffer more comorbidities and are less mobile. Due to incomplete follow-up, we cannot completely exclude potential cases of fatal pulmonary embolism prior to the follow-up outpatient visit. However, we did not have a signal of mortality in patients immediately after discharge in general. Additionally, it is unlikely that the undetected fatal

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Table 2 Outcome six weeks after discharge for COVID-19 hospitalization according to discharge management

	All patients ($N = 146$)			Postdischarge prophylaxis ($N = 41$)			No postdischarge prophylaxis ($N = 105$)		
	All	ICU ($N = 57$)	Ward ($N = 89$)	All	ICU ($N = 25$)	Ward ($N = 16$)	All	ICU ($N = 32$)	Ward ($N = 73$)
Venous thromboembolism (VTE), no. (%)									
Symptomatic VTE	1 (0.7)	1 (1.8)	0	1 (2.4)	1 (4)	0	0	0	0
Deep vein thrombosis	0	0	0	0	0	0	0	0	0
Pulmonary embolism	1 (0.7)	1 (1.8)	0	1 (2.4)	1 (4)	0	0	0	0
Asymptomatic VTE	1 (0.7)	0	1 (1.1)	0	0	0	1 (1)	0	1 (1.4)
Deep vein thrombosis	1 (0.7)	0	1 (1.1)	0	0	0	1 (1)	0	1 (1.4)
Pulmonary embolism	0	0	0	0	0	0	0	0	0
Patients screened, no. (%)									
Venous ultrasound	146 (100)	57 (100)	89 (100)	41 (100)	25 (100)	16 (100)	105 (100)	32 (100)	73 (100)
CTPA or V/Q	28 (19)	28 (49)	0	15 (37)	15 (60)	0	13 (12)	13 (41)	0
Bleeding, no. (%)									
Major bleeding	0	0	0	0	0	0	0	0	0
Nonmajor clinically relevant bleeding	0	0	0	0	0	0	0	0	0
Extended thromboprophylaxis									
Duration, median (IQR)	N/A	N/A	N/A	14 (10–23.5)	20 (10–30.5)	10 (8.5–14)	N/A	N/A	N/A

Abbreviations: CTPA, computed tomography pulmonary angiogram; IQR, interquartile range; V/Q, ventilation–perfusion scan.

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pulmonary embolism rate would be high with the low rate of VTE, including subclinical VTE, in our follow-up patients. Despite missing these patients, a relatively high percentage of critically ill patients (39% with ICU stay) were included in this cohort, who presented with markedly elevated thromboinflammatory parameters, as can be appreciated in ►**Table 1**.

As discussed before, the question remains if an even more restrictive use of postdischarge thromboprophylaxis is similarly effective in preventing VTE. On the other hand, the current study cannot answer the question to which extent thromboprophylaxis may influence potential post-COVID-19 microvascular thrombosis, which is not detected by ultrasound and/or CTPA. As we measure residual elevated D-dimers in 36% of patients 6 weeks after discharge, there is a potential role for ongoing activation of coagulation and fibrinolytic system. Indeed, pulmonary microvascular thrombi post-COVID-19 (i.e., long COVID-19) have been suggested to play a role in the prolonged reduced lung diffusing capacity reported up to 6 months after discharge.[28–30] The role of low dosed thromboprophylaxis in reducing potential microthrombi and thereby the functional short- and long-term outcome after COVID-19 has yet to be investigated.

Conclusion

In conclusion, systematic screening for VTE 6 weeks after COVID-19 hospitalization revealed very low incidence of VTE. Postdischarge thromboprophylaxis (28%) was more frequent in patients with more severe disease course and higher thromboinflammatory burden. No bleedings were reported during follow-up. With adequate in-hospital thromboprophylaxis, a strategy of selectively providing postdischarge thromboprophylaxis in high-risk patients seems safe and potentially effective.

Conflict of Interest

J.W. reports grants and personal fees from Pfizer, MSD, Gilead, outside the submitted work. C.V. reports grants from Belgian Fund for Cardiothoracic Surgery, grants from Abiomed, outside the submitted work. T.V. reports personal fees from Bayer AG, personal fees from Boehringer Ingelheim, personal fees from Daiichi Sankyo, personal fees from BMS/Pfizer, personal fees from Leo Pharma, personal fees from Sanofi Aventis, outside the submitted work. R.V. reports grants from Research Foundation-Flanders (FWO), outside the submitted work. P.V. reports grants and personal fees from Bayer, grants and personal fees from Boehringer Ingelheim, grants and personal fees from BMS, grants and personal fees from Pfizer, grants from Nordic Pharma, grants and personal fees from Daiichi-Sankyo, outside the submitted work. M.J. reports grants from Bayer, grants from Takeda, grants from Instrumentation Laboratory, grants from Thrombogenics, outside the submitted work.

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