Supplementary Table S1 Classification of anticoagulation regimens

Route	Drug	Prophylactic dosing	Therapeutic dosing
Oral	Warfarin	None[a]	Any dose[a]
	Rivaroxaban	10 mg daily[a]	10 mg bid,15 mg daily, 15mg bid, 20 mg bid[a]
	Apixaban (GFR ≥30)	2·5 mg bid	5 mg bid
	Apixaban (GFR < 30)	2·5 mg bid	2·5 mg or 5 mg bid
SC	Enoxaparin (GFR ≥30)	≤0·5 mg/kg bid or ≤1·0 mg/kg daily	≥1 mg/kg bid or ≥1·5 mg/kg daily
	Enoxaparin (GFR < 30)	≤0·35 mg/kg bid or ≤0·7 mg/kg daily	≥ 0·7 mg/kg bid or ≥1 mg/kg daily
	Enoxaparin no weight adjustment	30–60 mg daily	None
	UFH	4,000 IU - 10,000 units bid or tid	None
IV	UFH	None	Any dose
	Bivalirudin	None	Any dose
	Argatroban	None[b]	Any dose[b]
	TPA (tissue plasminogen activator)	None[b]	Any dose[b]
	Desirudin	None[b]	Any dose[b]

Abbreviations: bid, two times a day; GFR, glomerular filtration rate; IV, intravenous; SC, subcutaneous; tid, three times a day; UFH, unfractionated heparin.
[a]Too few patients in each category—all collapsed into therapeutic category with warfarin as "Rivwarf" and excluded from most analyses.
[b]Deleted due to fewer than 5 patients.

Supplementary Table S2 Drug choice and indication

Therapy	No anticoagulation	Prophylaxis standard dose	Prophylaxis high dose	Therapy	Total
Apixaban	0	554	0	474	1,028 (28·4%)
Enoxaparin	0	748	0	84	832 (23·0%)
Heparin standard	0	796	0	0	796 (22·0%)
Heparin high dose	0	0	176	0	176 (4·9%)
IV heparin	0	0	0	79	79 (2·2%)
Other	0	2	0	73	75 (2·1%)
No anticoagulation	639	0	0	0	639 (17·6%)
Total	639 (17·6%)	2,100 (57·9%)	176 (4·9%)	710 (19·6%)	3,625 (100%)

Abbreviation: IV, intravenous.

Supplementary Table S3 Chosen therapy by first D-dimer within 48 hours of admission

	D-dimer level (μg/mL)					
	< 1	1–3	> 3–10	> 10	No D-dimer obtained	Total
No therapy	105 (13·5%)	116 (11·5%)	57 (12·5%)	38 (13·7%)	323 (29·4%)	639 (17·6%)
Apixaban prophylaxis	211 (27·1%)	264 (26·1%)	26 (5·7%)	17 (6·1%)	36 (3·3%)	554 (15·3%)
Apixaban therapy	59 (7·6%)	128 (12·6%)	166 (36·3%)	77 (27·7%)	44 (4·0%)	474 (13·1%)
Enoxaparin prophylaxis	223 (28·6%)	222 (21·9%)	67 (14·7%)	27 (9·7%)	209 (19·0%)	748 (20·6%)
Enoxaparin therapy	6 (0·8%)	17 (1·7%)	32 (7·0%)	25 (9·0%)	4 (0·4%)	84 (2·3%)
UFH prophylaxis	122 (15·7%)	193 (19·1%)	57 (12·5%)	55 (19·8%)	369 (33·6%)	796 (22·0%)
UFH HD prophylaxis	26 (3·3%)	44 (4·3%)	22 (4·8%)	6 (2·2%)	78 (7·1%)	176 (22·0%)
UFH therapy	9 (1·2%)	17 (1·7%)	17 (3·7%)	28 (10·1%)	8 (0·7%)	79 (2·2%)
Other	18 (2·3%)	12 (1·2%)	13 (2·8%)	5 (1·8%)	27 (2·5%)	75 (2·2%)
Total for D-dimer category	779	1,013	457	278	1,098	3,625
% of Total	21·5%	27·9%	12·6%	7·7%	30·3%	100·0%

Abbreviations: HD, high dose; UFH, unfractionated heparin.

Supplementary Table S4 Logistic regression analysis of variables: adjusted odds ratios for mortality outcome ($n = 2,450$)
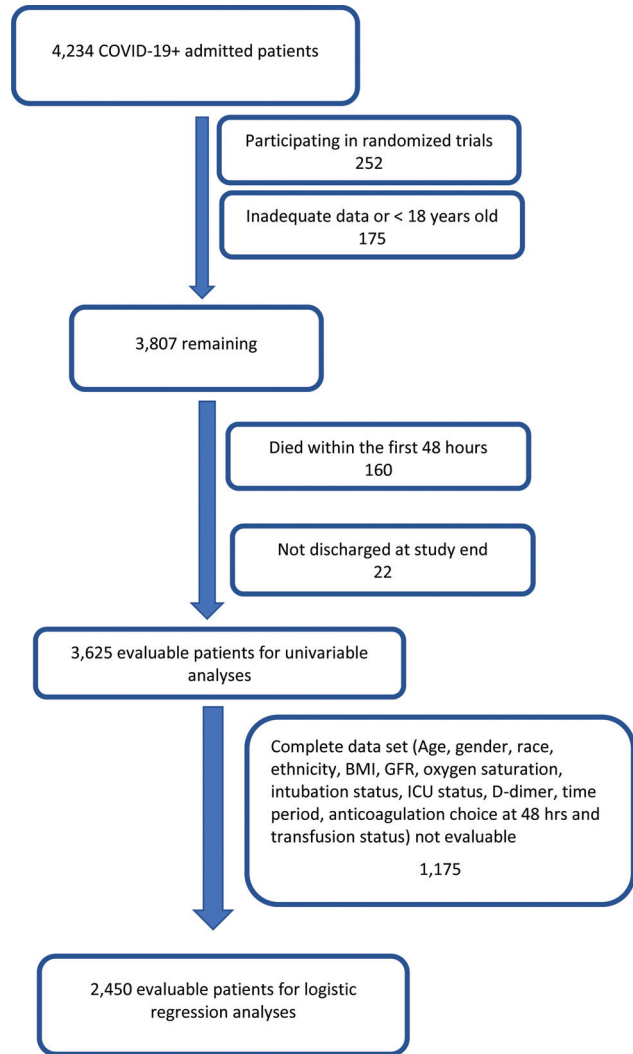
Variable	Odds ratio	95% Confidence interval	p-Value
Age, y			
< 50	1.00		
50–60	2.55	1.44–4.52	0.001
60–70	3.87	2.53–6.66	< 0.001
70–80	5.71	3.32–9.84	< 0.001
≥ 80	8.77	5.04–15.28	< 0.001
Oxygen saturation, %			
> 95%	1.00		
90–95%	1.62	1.22–2.15	0.001
< 90%	2.83	2.12–3.79	< 0.001
eGFR mL/min			
> 60	1.00		
≥ 30–60	1.77	1.32–2.38	< 0.001
15–30	2.68	1.87–3.85	< 0.001
0–15	1.92	1.31–2.81	< 0.001
D-dimer, μg/mL			
< 1	1.00		
1–3	1.61	1.15–2.26	0.005
3–10	1.99	1.35–2.92	< 0.001
≥ 10	2.65	1.74–4.04	< 0.001
Time period			
First time period	1.00		
Wave	0.59	0.45–0.76	< 0.001
Ventilator needed first 48 h			
No ventilator needed	1.00		
Ventilator needed	10.34	6.86–15.61	< 0.001
Medication and regimen, intent type			
No anticoagulation	1.00		
Apixaban prophylaxis	0.52	0.33–0.82	0.005
Apixaban full therapy	0.63	0.42–0.94	0.025
Enoxaparin prophylaxis	0.50	0.33–0.77	0.002
Enoxaparin full therapy	0.96	0.50–1.82	0.90
UFH prophylaxis bid	0.82	0.55 - 1.23	0.34
UFH prophylaxis tid	0.84	0.44–1.61	0.60
UFH full therapy	0.66	0.33–1.34	0.25

Abbreviations: bid, two times a day; eGFR, estimated glomerular filtration rate; tid, three times a day; UFH, unfractionated heparin.
Note: Adjusted for age, oxygen saturation, eGFR, D-dimer, time period, and ventilator requirement.

Supplementary Table S5 Adjusted mortality per therapeutic modality, stratified by D-dimer (DD): odds ratios and confidence intervals ($n = 2{,}450$)
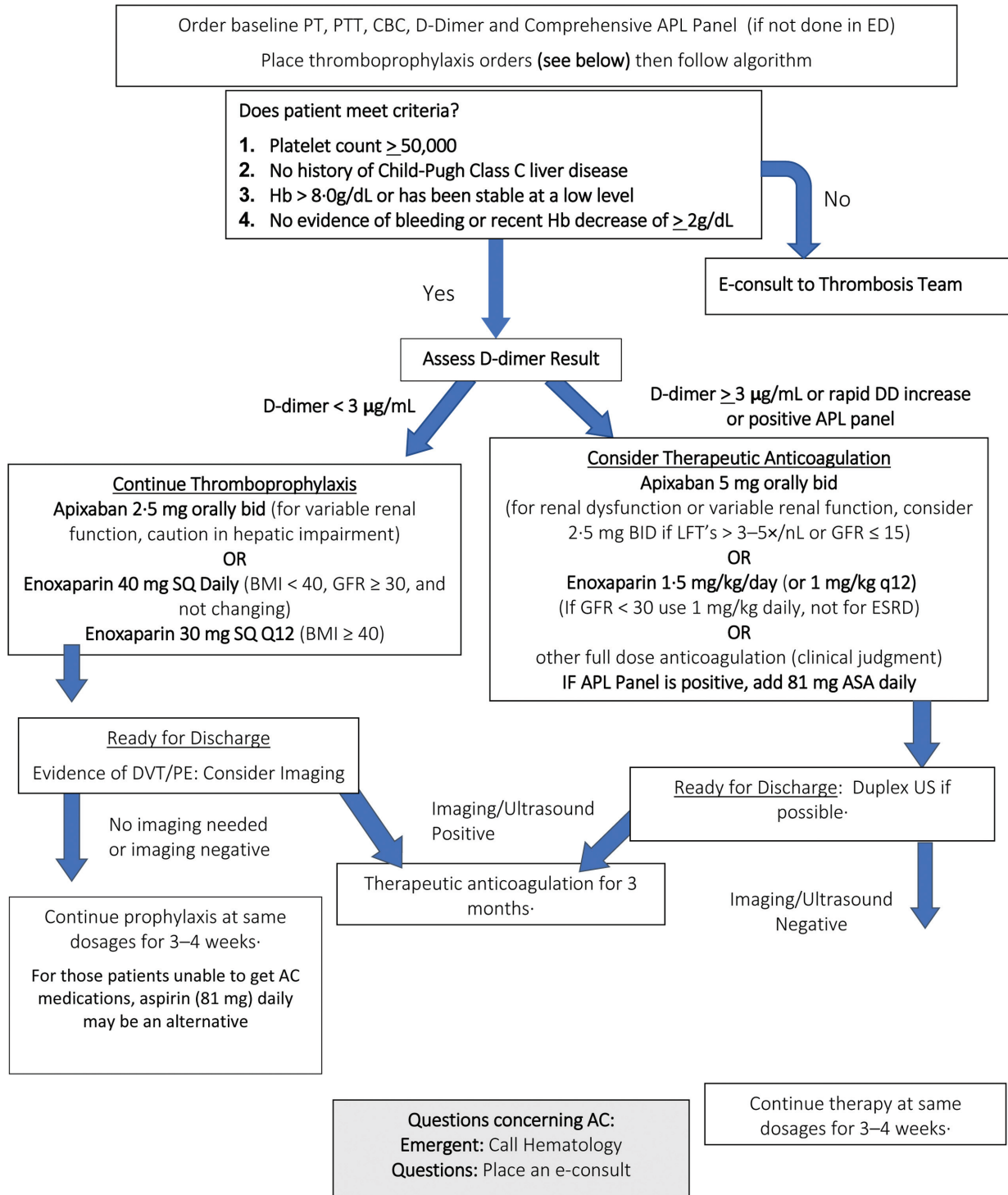
$n = 2{,}450$	Apixaban Prophylaxis	Apixaban Therapy	Enoxaparin Prophylaxis	Enoxaparin Therapy	UFH Prophylaxis	UFH high dose Prophylaxis	UFH Therapy
DD < 1 ($n = 751$)	0.87	1.72	0.93	5.78	2.20	1.71	2.50
	95% CI: 0.26–2.88	95% CI: 0.51–5.79	95% CI: 0.31–2.81	95% CI: 0.49–68.2	95% CI: 0.76–6.38	95% CI: 0.27–10.86	95% CI: 0.32–19.73
	$p = 0.82$	$p = 0.38$	$p = 0.89$	$p = 0.16$	$p = 0.15$	$p = 0.57$	$p = 0.38$
DD 1–< 3 ($n = 991$)	**0.49**	**0.48**	**0.5**	0.95	0.66	0.76	**0.22**
	95% CI: 0.25–0.94	**95% CI: 0.23–0.97**	**95% CI: 0.26–0.96**	95% CI: 0.27–3.30	95% CI: 0.35–1.23	95% CI: 0.28–2.03	**95% CI: 0.05–0.90**
	$p = 0.033$	**$p = 0.041$**	**$p = 0.036$**	$p = 0.93$	$p = 0.19$	$p = 0.59$	**$p = 0.035$**
DD 3–< 10 ($n = 439$)	0.44	0.78	0.45	0.88	0.81	1.02	0.36
	95% CI: 0.11–1.68	95% CI: 0.36–1.72	95% CI: 0.17–1.21	95% CI: 0.26–3.02	95% CI: 0.32–2.07	95% CI: 0.28–3.76	95% CI: 0.73–1.72
	$p = 0.23$	$p = 0.54$	$p = 0.11$	$p = 0.84$	$p = 0.66$	$p = 0.97$	$p = 0.20$
DD ≥ 10 ($n = 269$)	0.25	**0.26**	**0.15**	0.74	0.59	0.36	0.89
	95% CI: 0.06–1.07	**95% CI: 0.09–0.70**	**95% CI: 0.04–0.62**	95% CI: 0.22–2.45	95% CI: 0.21–1.70	95% CI: 0.29–4.44	95% CI: 0.25–3.08
	$p = 0.061$	**$p = 0.0080$**	**$p = 0.0080$**	$p = 0.62$	$p = 0.33$	$p = 0.43$	$p = 0.85$

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; UFH, unfractionated heparin.
Note: Adjusted for age, oxygen saturation, eGFR, D-dimer, time period, and ventilator requirement.
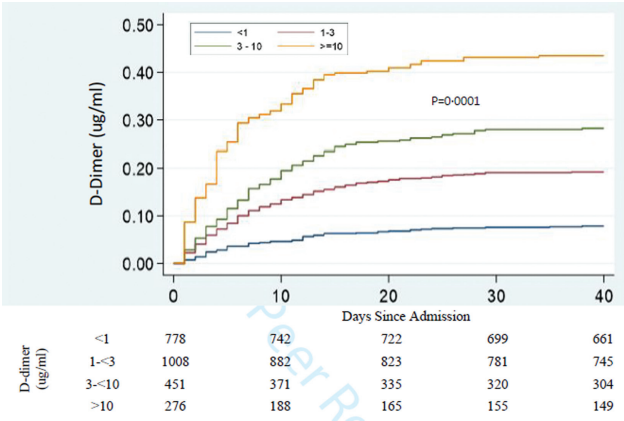
Supplementary Fig. S1 Consort diagram for study.

MONTEFIORE ANTICOAGULATION PROTOCOL
FOR ADULT COVID-19+ INPATIENTS (Not Critical Care)

Order baseline PT, PTT, CBC, D-Dimer and Comprehensive APL Panel (if not done in ED)

Place thromboprophylaxis orders **(see below)** then follow algorithm

Does patient meet criteria?

1. Platelet count ≥ 50,000
2. No history of Child-Pugh Class C liver disease
3. Hb > 8·0g/dL or has been stable at a low level
4. No evidence of bleeding or recent Hb decrease of ≥ 2g/dL

No → E-consult to Thrombosis Team

Yes → Assess D-dimer Result

D-dimer < 3 μg/mL

D-dimer ≥ 3 μg/mL or rapid DD increase or positive APL panel

Continue Thromboprophylaxis
Apixaban 2·5 mg orally bid (for variable renal function, caution in hepatic impairment)
OR
Enoxaparin 40 mg SQ Daily (BMI < 40, GFR ≥ 30, and not changing)
Enoxaparin 30 mg SQ Q12 (BMI ≥ 40)

Consider Therapeutic Anticoagulation
Apixaban 5 mg orally bid
(for renal dysfunction or variable renal function, consider 2·5 mg BID if LFT's > 3–5×/nL or GFR ≤ 15)
OR
Enoxaparin 1·5 mg/kg/day (or 1 mg/kg q12)
(If GFR < 30 use 1 mg/kg daily, not for ESRD)
OR
other full dose anticoagulation (clinical judgment)
IF APL Panel is positive, add 81 mg ASA daily

Ready for Discharge
Evidence of DVT/PE: Consider Imaging

No imaging needed or imaging negative

Imaging/Ultrasound Positive

Ready for Discharge: Duplex US if possible·

Continue prophylaxis at same dosages for 3–4 weeks·

For those patients unable to get AC medications, aspirin (81 mg) daily may be an alternative

Therapeutic anticoagulation for 3 months·

Imaging/Ultrasound Negative

Continue therapy at same dosages for 3–4 weeks·

Questions concerning AC:
Emergent: Call Hematology
Questions: Place an e-consult

Supplementary Fig. S2 Anticoagulation protocol.

Supplementary Fig. S3 Cumulative mortality according to initial D-dimer value.