



Use of anticoagulants in patients with COVID-19: a living systematic review and meta-analysis

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Table S1. Grading of Recommendations Assessment, Development and Evaluation analysis of prophylactic anticoagulation vs. standard of care in non-hospitalized COVID-19 patients: quality of evidence for included randomized controlled trials.

No. of studies	Certainty assessment			Other considerations	No. of patients Thrombo-prophylaxis in post-discharge COVID-19 patients	SOC	Relative CI (95% CI)	Effect Absolute (95% CI)	Certainty	Importance
	Study design	Risk of bias	Inconsistency							
1	Severe ^a	Not severe	Not severe	Very severe ^b	Deep venous thrombosis	3/160 (1.9%)	RR 0.14 (0.01 to 2.74)	16 fewer per 1,000 (from 19 fewer to 33 more)	⊖○○○ Very low	Important
Symptomatic pulmonary embolism										
1	Severe ^a	Not severe	Not severe	Very severe ^b	Symptomatic pulmonary embolism	2/160 (1.3%)	RR 0.50 (0.05 to 5.49)	6 fewer per 1,000 (from 12 fewer to 56 more)	⊖○○○ Very low	Important
Fatal pulmonary embolism										
1	Severe ^a	Not severe	Not severe	Very severe ^b	Fatal pulmonary embolism	3/160 (1.9%)	RR 0.14 (0.01 to 2.74)	16 fewer per 1,000 (from 19 fewer to 33 more)	⊖○○○ Very low	Important
Symptomatic VTE + all-cause mortality										
1	Severe ^a	Not severe	Not severe	Very severe ^b	Symptomatic VTE + all-cause mortality	9/160 (5.7%)	RR 0.44 (0.14 to 1.41)	32 fewer per 1,000 (from 49 fewer to 23 more)	⊖○○○ Very low	Important

SOC: standard of care; RR: risk ratio; and VTE: venous thromboembolism.

Explanations

a. blinding, blinding of outcome assessment, randomization

b. large confidence interval

Table S2. Grading of Recommendations Assessment, Development and Evaluation analysis of therapeutic anticoagulation vs. placebo/standard of care in moderate-to-severe hospitalized COVID-19 patients: quality of evidence for included randomized controlled trials.

No. of studies	Study design	Certainty assessment			Other considerations	No. of patients		Relative (95% CI)	Effect Absolute (95% CI)	Certainty	Importance	
		Risk of bias	Inconsistency	Indirectness		Imprecision	Therapeutic anticoagulation					SOC
Mortality at 30 days												
6	randomized trials	Very severe ^a	Severe ^b	Not severe	Severe ^c	none	359/2,491 (14.4%)	379/2,422 (15.6%)	RR 0.95 (0.71 to 1.28)	8 fewer per 1,000 (from 45 fewer to 44 more)	⊖○○○ Very low	Important
Thrombotic events at 30 days												
5	randomized trials	Severe ^a	Not severe	Not severe	Not severe	none	97/2,449 (4.0%)	162/2,338 (6.9%)	RR 0.59 (0.43 to 0.79)	28 fewer per 1,000 (from 39 fewer to 15 fewer)	⊖⊖⊖○ Moderate	Important
Major bleeding at 30 days												
4	randomized trials	Very severe ^a	Very severe ^b	Not severe	Very severe ^c	none	80/2,449 (3.3%)	44/2,338 (1.9%)	RR 1.62 (0.76 to 3.43)	12 fewer per 1,000 (from 5 fewer to 46 more)	⊖○○○ Very low	Important
Mortality at 30 days, moderate COVID-19												
4	randomized trials	Severe ^a	Very severe ^b	Not severe	Very severe ^c	none	142/1,812 (7.8%)	141/1,637 (8.6%)	RR 0.76 (0.45 to 1.30)	21 fewer per 1,000 (from 47 fewer to 26 more)	⊖○○○ Very low	Important
Thrombotic events at 30 days, moderate COVID-19												
2	randomized trials	Severe ^a	Not severe	Not severe	Severe ^c	none	15/1,418 (1.1%)	29/1,291 (2.2%)	RR 0.47 (0.25 to 0.88)	12 fewer per 1,000 (from 17 fewer to 3 fewer)	⊖⊖⊖○ Low	Important
Major bleeding at 30 days, moderate COVID-19												
3	randomized trials	Severe ^a	Very severe	Not severe	Very severe ^c	none	54/1,728 (3.1%)	29/1,595 (1.8%)	RR 1.60 (0.52 to 4.88)	11 more per 1,000 (from 9 fewer to 71 more)	⊖○○○ Very low	Important
Mortality at 30 days, severe COVID-19												
1	randomized trials	Severe ^{a,d}	Not severe	Not severe	Very severe ^c	none	199/591 (33.7%)	200/616 (32.5%)	RR 1.04 (0.88 to 1.22)	13 more per 1,000 (from 39 fewer to 71 more)	⊖○○○ Very low	Important

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Table S2. Grading of Recommendations Assessment, Development and Evaluation analysis of therapeutic anticoagulation vs. placebo/standard of care in moderate-to-severe hospitalized COVID-19 patients: quality of evidence for included randomized controlled trials. (Continued...)

No. of studies	Certainty assessment			No. of patients	SOC	Effect	Certainty	Importance											
	Study design	Risk of bias	Inconsistency						Indirectness	Imprecision	Other considerations	Therapeutic anticoagulation	Relative (95% CI)	Absolute (95% CI)					
1	randomized trials	Severe ^{a,d}	Not severe	Not severe	Severe ^c	Thrombotic events at 30 days, severe COVID-19													
1	randomized trials	Severe ^{a,d}	Not severe	Not severe	Very severe ^c	Major bleeding at 30 days, severe COVID-19													

SOC: standard of care; and RR: risk ratio.

Explanations

- a. blinding, blinding of outcome assessment, randomization
- b. high heterogeneity
- c. large confidence interval
- d. no sample size calculation

Table S3. Grading of Recommendations Assessment, Development and Evaluation analysis of intermediate prophylactic anticoagulation vs. standard of care/placebo in moderate-to-severe hospitalized COVID-19 patients: quality of evidence for included randomized controlled trials.

No. of studies	Study design	Certainty assessment			Imprecision	Other considerations	No. of patients		SOC	Relative (95% CI)	Effect Absolute (95% CI)	Certainty	Importance
		Risk of bias	Inconsistency	Indirectness			Intermediate prophylactic anti-coagulation	Intermediary prophylactic anti-coagulation					
Mortality at 30 days, severe COVID-19													
2	randomized trials	Severe ^a	Not severe	Not severe	Very severe ^b	none	132/386 (34.2%)	135/385 (35.1%)		RR 0.98 (0.81 to 1.18)	7 fewer per 1,000 (from 67 fewer to 63 more)	⊖○○○ Very low	Important
Venous thromboembolism at 30 days, severe COVID-19													
2	randomized trials	Severe ^a	Not severe	Not severe	Severe ^b	none	16/386 (4.1%)	16/385 (4.2%)		RR 1.00 (0.51 to 1.96)	0 fewer per 1,000 (from 20 fewer to 40 more)	⊖○○○ Low	Important
Arterial thrombosis at 30 days, severe COVID-19													
2	randomized trials	Severe ^a	Severe ^c	Not severe	Very severe ^b	none	5/386 (1.3%)	3/385 (0.8%)		RR 1.65 (0.41 to 6.68)	5 more per 1,000 (from 5 fewer to 44 more)	⊖○○○ Very low	Important
Major bleeding at 30 days, severe COVID-19													
2	randomized trials	Severe ^a	Not severe	Not severe	Very severe ^b	none	9/386 (2.3%)	6/385 (1.6%)		RR 1.50 (0.54 to 4.16)	8 more per 1,000 (from 7 fewer to 49 more)	⊖○○○ Very low	Important

SOC: standard of care; and RR: risk ratio.

Explanations

a. blinding, blinding of outcome assessment

b. large confidence interval

c. high heterogeneity