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Question: Prophylactic-intensity DOACs, LMWH, UFH, Fondaparinux compared to no anticoagulation for post-discharge thromboprophylaxis in patients with COVID-19 who are being discharged from the hospital and who do not have suspected or confirmed VTE or another indication for anticoagulation

Setting: Hospital discharge

Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prophylactic-intensity DOACs, LMWH, UFH, Fondaparinux	no anticoagulation	Relative (95% CI)	Absolute (95% CI)		
Mortality (follow-up: range <30 days to 92 days)[a]												
1[1]	randomised trials	not serious	not serious	not serious[b]	extremely serious[c]	none	3/159 (1.9%)	1.4%[d]	**OR 0.75** (0.16 to 3.38)	**3 fewer per 1,000** (from 12 fewer to 32 more)	⨁◯◯◯ Very low	CRITICAL
								2.5%[e]		**6 fewer per 1,000** (from 21 fewer to 55 more)		
								4.4%[f]		**11 fewer per 1,000** (from 37 fewer to 91 more)		
Pulmonary Embolism (follow-up: range <30 days to 92 days)[g]												
1[1]	randomised trials	serious[h]	not serious	not serious	very serious[i]	none	1/159 (0.6%)	0.3%[d]	**OR 0.19** (0.02 to 1.69)	**2 fewer per 1,000** (from 3 fewer to 2 more)	⨁◯◯◯ Very low	CRITICAL
								0.7%[e]		**6 fewer per 1,000** (from 7 fewer to 5 more)		
								2.0%[f]		**16 fewer per 1,000** (from 20 fewer to 13 more)		
Deep Venous Thrombosis of the upper leg (Proximal lower extremity DVT) (follow-up: range <30 days to 92 days)[j]												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prophylactic-intensity DOACs, LMWH, UFH, Fondaparinux	no anticoagulation	Relative (95% CI)	Absolute (95% CI)		
1[1]	randomised trials	serious[k]	not serious	not serious	very serious[i]	none	0/159 (0.0%)	0.1%[d]	**OR 0.14** (0.01 to 2.74)	**1 fewer per 1,000** (from 1 fewer to 2 more)	⨁◯◯◯ Very low	CRITICAL
								0.3%[e]		**3 fewer per 1,000** (from 3 fewer to 5 more)		
								1.2%[f]		**10 fewer per 1,000** (from 12 fewer to 20 more)		

Major Bleeding (follow-up: range 35 days to 92 days)[l]

1[1]	randomised trials	not serious	not serious	not serious	very serious[m]	none	0/159 (0.0%)	0/159 (0.0%)	not estimable	**0 fewer per 1,000** (from -- to --)	⨁⨁◯◯ Low	CRITICAL
								0.0%[n]				
								1.6%[o]				

NON-COVID acutely ill - Major Bleeding[l]

4[2,3,4,5]	randomised trials	not serious	not serious	very serious[p]	not serious	none	0/13872 (0.0%)	0.4%	**RR 2.09** (1.33 to 3.27)	**4 more per 1,000** (from 1 more to 9 more)	⨁⨁◯◯ Low	CRITICAL
								1.2%[q]		**13 more per 1,000** (from 4 more to 27 more)		

Ischemic Stroke (follow-up: range 35 days to 92 days)[r]

1[1]	randomised trials	serious[s]	not serious	not serious	very serious[m]	none	0/159 (0.0%)	0/159 (0.0%)	not estimable	**0 fewer per 1,000** (from -- to --)	⨁◯◯◯ Very low	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	prophylactic-intensity DOACs, LMWH, UFH, Fondaparinux	no anticoagulation	Relative (95% CI)	Absolute (95% CI)		
								0.4%[t]				

ST-elevation Myocardial Infarction (follow-up: range 35 days to 92 days; assessed with: Myocardial Infarction)[u]

1[l]	randomised trials	serious[s]	not serious	not serious	very serious[m]	none	0/159 (0.0%)	0/159 (0.0%) 0.5%[v]	not estimable	**0 fewer per 1,000** (from -- to --)	⨁◯◯◯ Very low	IMPORTANT

Readmission (follow-up: range 35 days to 92 days)

1[l]	randomised trials	not serious	not serious	not serious	very serious[w]	none	0/159 (0.0%)	2/159 (1.3%) 15.5%[x]	**OR 0.20** (0.01 to 4.15)	**10 fewer per 1,000** (from 12 fewer to 38 more) **120 fewer per 1,000** (from 153 fewer to 277 more)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. The decision thresholds for All-Cause Mortality were: 16 per 1,000 for Trivial/Small; 31 per 1,000 for Small/Moderate; 60 per 1,000 for Moderate/Large

b. The MICHELLE trial included patients at high risk of VTE and low risk of bleeding. It is unclear what proportion of all discharged COVID-19 patients this represents.

c. The 95% CI of the absolute effect estimate crosses multiple decision thresholds and includes small benefit and moderate harm; rated down 3 levels for extremely serious imprecision

d. Lower boundary of 95% CI of pooled baseline risk analysis

e. Mean of pooled baseline risk analysis

f. Higher boundary of 95% CI of pooled baseline risk analysis

g. The decision thresholds for Pulmonary Embolism (Moderate severity) were: 27 per 1,000 for Trivial/Small; 53 per 1,000 for Small/Moderate; 103 per 1,000 for Moderate/Large

h. Patients and providers were not blinded to group allocation and it is unclear if test ordering was balanced during the trial. The CTPA that was planned in all patients at 35 days, but performed in <80%, was assumed to primarily capture asymptomatic events

i. The effect estimate is based on few events; rated down 2 levels for very serious imprecision

j. The decision thresholds for Proximal Deep Venous Thrombosis (Moderate severity) were: 37 per 1,000 for Trivial/Small; 73 per 1,000 for Small/Moderate; 142 per 1,000 for Moderate/Large

k. Patients and providers were not blinded to group allocation and it is unclear if test ordering was balanced during the trial. The US that was planned in all patients at 35 days, but performed in <80%, was assumed to primarily capture asymptomatic events

l. The decision thresholds for Major Bleeding were: 23 per 1,000 for Trivial/Small; 46 per 1,000 for Small/Moderate; 89 per 1,000 for Moderate/Large

m. No events observed in the trial; rated down 2 levels for very serious imprecision

n. Three of four baseline risk studies reported 0% Major bleeding

o. One baseline risk study reported 1.6% major bleeding during 92 days follow-up

p. Very serious indirectness. Evidence from non-COVID-19 patients; Indirect comparison of interventions although no different effects observed in sensitivity analysis

q. Decousus (2011) reports on incidence of in hospital bleeding in patients who were not bleeding at admission and had data regarding bleeding during the 3 months prior to admission (n=10,866) based on data from the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) from July 2002 and September 2006

r. The decision thresholds for Ischemic Stroke (severe) were: 18 per 1,000 for Trivial/Small; 36 per 1,000 for Small/Moderate; 69 per 1,000 for Moderate/Large

s. Patients and providers were not blinded to group allocation and it is unclear if test ordering was balanced during the trial

t. One observational study reporting 0.4% ischemic stroke during 92 days follow-up.

u. The decision thresholds for ST-elevation Myocardial Infarction were: 23 per 1,000 for Trivial/Small; 44 per 1,000 for Small/Moderate; 86 per 1,000 for Moderate/Large

v. One observational study reporting 0.5% myocardial infarction during 92 days follow-up.

w. The 95% CI of the absolute effect estimate includes important benefit and important harm; rated down 3 levels for very serious imprecision

x. One baseline risk study reported 15.5% readmission during 92 days follow-up

References

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