Author(s): Holger Schünemann, Robby Nieuwlaat, Wojtek Wiercioch

Question: Prophylactic-intensity DOACs, LMWH, UFH, Fondaparinux, Aspirin, Clopidogrel, Prasugrel, Ticagrelor compared to no anticoagulation/antiplatelets in patients with COVID-19 who are being discharged from the hospital who do not have suspected or confirmed VTE and who do not have another indication for antithrombotic therapy

Setting: Inpatient

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, Aspirin, Clopidogrel, Prasugrel, Ticagrelor	no anticoagulation/antiplatelets	Relative (95% CI)	Absolute (95% CI)		
Mortality - Anticoagulation (follow up: 30 days)												
1 [a,b]	observational studies	serious [c]	not serious	not serious [d]	not serious	none	0/612 (0.0%)	1.1% [e]	OR 0.55 (0.37 to 0.83)	5 fewer per 1,000 (from 7 fewer to 2 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Pulmonary Embolism - Anticoagulation (follow up: 30 days)												
2 [b,f]	observational studies	serious [g]	not serious	not serious	not serious	none	0/802 (0.0%)	0.6% [e]	OR 0.76 (0.46 to 1.25)	1 fewer per 1,000 (from 3 fewer to 1 more)	⨁◯◯◯ VERY LOW	CRITICAL
Deep Venous Thrombosis - Anticoagulation (follow up: 30 days)												
2 [b,f]	observational studies	serious [c]	not serious	not serious	not serious	none	0/802 (0.0%)	0.2% [e]	OR 0.76 (0.46 to 1.25)	0 fewer per 1,000 (from 1 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Venous Thromboembolism - Anticoagulation (follow up: 30 days; assessed with: PE or DVT)												
2 [b,f]	observational studies	serious [g]	not serious	not serious	not serious	none	0/802 (0.0%)	1.7% [e]	OR 0.76 (0.46 to 1.25)	4 fewer per 1,000 (from 9 fewer to 4 more)	⨁◯◯◯ VERY LOW	CRITICAL
Major Bleeding - Anticoagulation (follow up: 30 days)												

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, Aspirin, Clopidogrel, Prasugrel, Ticagrelor	no anticoagulation/antiplatelets	Relative (95% CI)	Absolute (95% CI)		
1 [a]	observational studies	very serious [h]	not serious	not serious	not serious	none	0/612 (0.0%)	0.1% [e]	OR 1.52 (0.86 to 2.67)	1 more per 1,000 (from 0 fewer to 2 more)	⨁◯◯◯ VERY LOW	CRITICAL

NON-COVID acutely ill - Major Bleeding - Anticoagulation

4	randomised trials	not serious	not serious	very serious [i]	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% [j]		13 more per 1,000 (from 4 more to 27 more)		

Ischemic Stroke - Anticoagulation (follow up: 30 days)

2 [f]	observational studies	serious [g]	not serious	not serious	not serious	none	0/802 (0.0%)	0.1% [e]	OR 0.76 (0.46 to 1.25)	0 fewer per 1,000 (from 1 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	CRITICAL

ST-elevation Myocardial Infarction - Anticoagulation (follow up: 30 days; assessed with: Myocardial Infarction)

2 [f]	observational studies	serious [g]	not serious	not serious	not serious	none	0/802 (0.0%)	0.2% [e]	OR 0.76 (0.46 to 1.25)	0 fewer per 1,000 (from 1 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	CRITICAL

Readmission - Anticoagulation (timing of exposure: 30 days)

1 [k]	observational	serious [l]	not serious	not serious	serious [m]	none	61 cases 61 controls		OR 0.92	-	⨁◯◯◯	CRITICAL

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, Aspirin, Clopidogrel, Prasugrel, Ticagrelor	no anticoagulation/antiplatelets	Relative (95% CI)	Absolute (95% CI)		
	studies						-	6.1% [e]	(0.41 to 2.05)	5 fewer per 1,000 (from 35 fewer to 57 more)	VERY LOW	

CI: Confidence interval; OR: Odds ratio; RR: Risk ratio

Explanations

a. Giannis 2021

b. The panel also considered evidence from the ASH 2018 guidelines for management of VTE, from the recommendation regarding extended duration pharmacological prophylaxis after discharge in acutely ill hospitalized medical patients (online table: https://guidelines.gradepro.org/profile/B7E7908E-FFD0-19C4-862E-16561BEC51FE). Although this evidence was judged to be too indirect to officially assess and use for COVID-19 patients, with the exception of the effect on major bleeding, the panel checked whether effect estimates were comparable.

c. Adjusted effect estimate, but 39% of discharged patients without follow-up data. Characteristics of patients lost to follow-up comparable with those included

d. Effect estimate for composite outcome of mortality, venous thrombosis, and arterial thrombosis

e. Median among eligible studies

f. Eswaran 2021 & Giannis 2021

g. Eswaran 2021 only corrected for age and ICU admission, residual confounding likely; Giannis 2021 reported adjusted effect estimate, but 39% of discharged patients without follow-up data. Characteristics of patients lost to follow-up comparable with those included

h. Unadjusted effect estimate, and 39% of discharged patients without follow-up data. Characteristics of patients lost to follow-up comparable with those included

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

j. 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

k. Parra 2020

l. Small case-control study only matched for age, gender and time period

m. There is a clinically important difference between the smallest and largest possible effect of prophylactic intensity antithrombotic therapy, lowering the certainty by one level for imprecision