Author(s): Cruciani F, De Crescenzo F, Vecchi S, Saulle R, Mitrova Z, Amato L, Davoli M. Question: Should Heparin compared to Anticoagulant prophylaxis be used for COVID-19 patients? Setting: Inpatient

Certainty assessment								patients	Effect		Certainty	
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Heparin	Anticoagulant prophylaxis	Relative (95% Cl)	Absolute (95% CI)		
All-caus	All-cause mortality											
5 1,2,3,4,5	randomised trials	serious ^a	not serious	not serious	not serious	none	416/2076 (20.0%)	419/1987 (21.1%)	RR 1.02 (0.91 to 1.14)	4 more per 1.000 (from 19 fewer to 30 more)	⊕⊕⊕⊖ MODERATE	

Number of patients with serious adverse events

2 ^{2,3}	randomised trials	not serious	serious ^b	not serious	not serious	none	34/747 (4.6%)	53/762 (7.0%)	RR 0.87 (0.28 to 2.69)	9 fewer per 1.000 (from 50 fewer to 118 more)	⊕⊕⊕⊖ MODERATE
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Number of patients discharged

1 ³	randomised trials	serious c	not serious	not serious	not serious	none	123/276 (44.6%)	126/286 (44.1%)	RR 1.01 (0.84 to 1.22)	4 more per 1.000 (from 70 fewer to 97 fewer)	⊕⊕⊕⊖ MODERATE
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Duration of hospitalization

1 ⁵	randomised	serious	not serious	not serious	not serious	none	HR: 1.03 (0.94 to 1.13)	$\Theta \Theta \Theta \bigcirc$
	trials	a						MODERATE

Explanations

- a. Downgraded of one level for one study at high risk of selection bias, performance bias at high risk in one study and unclear in 3 studies, 2 studies at unclear risk of detection bias and 2 studies at unclear risk of attrition and reporting bias
- b. Downgraded of one level for heterogeneity: I²=69%
- c. Downgraded of one level for unclear risk of performance, detection, attrition and reporting bias
- d. Downgraded of one level for high risk of performance bias and unclear risk of attrition and reporting bias

References

- 1. Lemos ACB, do Espírito Santo DA, Salvetti MC, Gilio RN, Agra LB, Pazin-Filho A, Miranda CH. Therapeutic versus prophylactic anticoagulation for severe COVID-19: A randomized phase II clinical trial (HESACOVID). Thromb Res. 2020 Dec;196:359-366. doi: 10.1016/j.thromres.2020.09.026. Epub 2020 Sep 21.
- 2. Zarychanski R. Therapeutic Anticoagulation in Critically III Patients with Covid-19 Preliminary Report. medRxiv. 2021:2021.03.10.21252749.
- 3. Bikdeli B, Talasaz AH, Rashidi F, Bakhshandeh H, Rafiee F, Matin S. Intermediate vs Standard-dose Prophylactic Anticoagulation in Patients with COVID-19 Admitted to ICU: Ninety-day Results from the INSPIRATION Trial. Thromb Haemost. 2021 Apr 17. doi: 10.1055/a-1485-2372. Epub ahead of print.

- 4. Perepu U, Chambers I Wahab A Ten Eyck P Wu C Sanjana D et al. Standard Prophylactic Versus Intermediate Dose Enoxaparin in Adults with Severe COVID-19: A Multi-Center, Open-Label, Randomised Controlled Trial. Available at SSRN: https://ssrn.com/abstract=3840099 or http://dx.doi.org/10.2139/ssrn.3840099
- 5. ATTACC, ACTIV-4a, and REMAP-CAP Lawler PR, Goligher EC, Berger JS, Neal MD, McVerry BJ, Nicolau JC, et al. Therapeutic Anticoagulation in Non-Critically III Patients with Covid-19. medRxiv. 2021:2021.05.13.21256846.