

Supplement - Baseline Risk studies – PICO 1a (Critically ill – Intermediate Intensity)

Study ID	Study design	Country, City Study Period	Setting	Population	COVID-19 diagnosis	Age	Male (%)	Prior VTE (%)	Anticoagulation prior to study entry (%)	D-dimer	Still in ICU at end of study (%)	Still in hospital at end of study (%). May include ICU, if not specified	Number of patients on prophylactic intensity (N)	Prophylactic intensity description (drug, dose, duration)	Risk of bias
Ferguson 2020	Retrospective cohort	USA, Colorado, March 15 to May 8, 2020	ICU only	Patients with PCR confirmed SARS-CoV-2 respiratory failure necessitating invasive mechanical ventilation were included in the study.	Confirmed SARS-CoV-2 by nasal/oral PCR	Mean (SD):63.7 (3.67)	55.31	NR	NR	Mean (SD):1600 (440.00)	NR	NR	95	Enoxaparin 40 mg subcutaneously daily, enoxaparin 30 mg twice daily, enoxaparin 0.5 mg/kg twice daily, or heparin 5,000 units subcutaneously two or three times daily.	Low
Klok 2020	Prospective cohort	Netherlands, NR, March 7 to April 22, 2020	ICU only	Critically ill patients with proven COVID-19 pneumonia	NR	Mean (SD):64 (12.00)	75.54	NR	NR	NR	75.54	NA	184	Leiden University Medical Center nadroparin 2850 IU sc per day or 5700 IU per day if body weight > 100 kg, Erasmus University Medical Center Nadroparin 5700 IU per day; nadroparin 5700 IU sc twice daily from April 4th 2020 and onwards, Amphia Hospital Breda Nadroparin 2850 IU sc per day or 5700 IU per day if body weight > 100 kg; nadroparin 5700 IU sc per day from March 30th 2020 and onwards	Low
Llitjos 2020	Retrospective cohort	France, NR, March 19 to April 11, 2020	ICU only	Critically ill patients with COVID-19 and respiratory failure	Positive SARS-CoV-2 test by RNA detection	Median (IQR):68 (51.5,74.5)	76.92	3.84	26.92	Median (IQR):1750 (1130,2850)	26.92	NR	8	NR (not 'therapeutic intensity')	Medium
Lodigiani 2020	Retrospective cohort	Italy, Milan, February 13 to April 10, 2020	ICU only	Critically ill patients requiring intensive care	Symptomatic with laboratory-proven COVID-19	Median (IQR):61 (55,69)	80.33	0.00	3.30	NR	NR	NR	48	NR, as labeled by authors	Medium
Longchamp 2020	Other	Switzerland, Sion, March 8 and April 4, 2020	ICU only	Critically ill patients admitted to ICU for hypoxemic respiratory failure	Positive result on a reverse transcriptase–polymerase chain reaction assay of a specimen collected from a nasopharyngeal swab, sputum, or bronchial aspirate	Mean (SD):68 (11.00)	64	0.00	8.00	Median (IQR):2071 (953,3606)	8.00	NR	25	Heparin, 5000 IU SC TID) or (Enoxaparin, 4000 IU SC OD	Low
Maatman 2020	Retrospective cohort	USA, Indianapolis, March 12 to March 31, 2020	ICU only	Patients with laboratory-confirmed SARS-CoV-2 infection. Admitted to three Indianapolis area hospitals	Confirmed Dx, Positive SARS-CoV-2 test only	Mean (SD):61 (16.00)	56.88	NR	NR	Median (IQR):84506 (321,973)	2.75	3.66	109	5,000 U subcutaneous heparin every 8 hours, 40 mg enoxaparin daily, or	Low

														30 mg enoxaparin bid.		
Mei 2020	Retrospective cohort	China, Hubei, January 1 to March 23, 2020	ICU only	Critically ill patients requiring ventilator support	Symptomatic with laboratory-proven COVID-20	NR		NR	NR		NR	NR	NR	45	NR, as labeled by authors	Low
Nougier 2020	Retrospective cohort	France, Lyon, NR	ICU only	Adult patients with a positive COVID-19 PCR	PCR	Mean (SD):62.8 (13.10)	NR	NR	NR		Mean (SD):3456 (2641.00)	NR	NR	48	Enoxaparin, 40 mg once daily if 50-100 kg and 40 mg twice daily [BID] if >100 kg or fibrinogen >8 g/L or D-dimer >3000 ng/mL or subcutaneous unfractionated heparin, (5000 IU BID) according to their renal status.	Medium
Pavoni 2020	Retrospective cohort	Italy, Bagno a Ripoli, February 28 to April 10, 2020	ICU only	Adult patients (≥ 18 years old) with severe COVID-19 admitted to ICU	Diagnosis of severe COVID-19 pneumonia was according to World Health Organization (WHO) [12] interim guidance and it was confirmed by RNA detection of the SARS-CoV-2 in clinical laboratory of Santa Maria Annunziata Hospital (Bagno a Ripoli, Italy).	Mean (SD):61 (13.00)	60	NR	NR		Mean (SD):1556 (1090.00)	NR	NR	40	Enoxaparin 30 mg (3000 units) SC BID (for BMI >40 kg/m ²); Enoxaparin 40 mg (4000 units) SC OD	Mortality: Low Other outcomes: Medium
Trigonis 2020	Retrospective cohort	USA, Indianapolis, March 23 to April 8, 2020	ICU only	Patients hospitalized at international units Health Methodist Hospital with severe acute respiratory syndrome coronavirus 2 requiring intubation between March 23, 2020, and April 8, 2020, (...) all who underwent ultrasound evaluation for DVT were included.	Patients with confirmed SARS-CoV-2	Mean (SD):60.8 (14.90)		NR	NR		NR	NR	NR	33	LMWH 30 mg, 40 mg, UFH 5000 U	Low
Wright 2020	Prospective cohort	USA, Colorado, March 1 to April 20, 2020	ICU only	Critically ill patients with covid-19	Patients with documented COVID-19	Median (IQR):54 (42,59)	63.63	NR	NR		Median (IQR):1840 (935,4085)	NR	NR	44	Enoxaparin, between 40 and 60 mg/d or UFH between 10,000 and 15,000 units/d.	Medium

Supplement – Anticoagulation Intensity studies – PICO 1a (Critically ill – Intermediate Intensity)

Study ID	Study design	Country, City Study Period	Population	COVID-19 diagnosis	Age	Male (%)	Prior VTE (%)	Anticoagulation prior to study entry (%)	D-dimer	Still in ICU at end of study (%)	Still in hospital at end of study (%) May include ICU, if not specified	Anticoagulation Group (N)	Anticoagulation intensity description (drug, dose, duration)	Risk of bias
INSPIRATION 2021	Parallel RCT group	Iran, multiple cities, July 29, 2020 to November 19, 2020	"Patients admitted to the ICU with polymerase chain reaction testing–confirmed COVID-19 within 7 days of the index hospitalization were eligible for inclusion. Patients with life expectancy less than 24 hours, an established indication for therapeutic-dose anticoagulation, weight less than 40 kg, pregnancy, history of heparin-induced thrombocytopenia, platelet count less than 50 ×103/μL, or overt bleeding were excluded.	Polymerase chain reaction testing–confirmed COVID-19 within 7 days of the index hospitalization	Median (IQR): 62 (50,71)	57.80	0%	0%	Mean (SD): 972 (394)	39%	NR	Prophylactic intensity (N=286)	Enoxaparin, 40mg daily	Probably Low
												Intermediate intensity (N=276)	For patients who weighed less than 120 kg and had a creatinine clearance greater than 30 mL/min, enoxaparin, 1 mg/kg daily	