



Table for included primary studies-
Question 2: What scientific studies are there on treatment of thromboembolic complications during infection with SARS-CoV 2, Sars-CoV-1 or Mers-CoV?

Author Year Country Study design Setting	Population	Intervention and control treatments	Outcome	Results	Aims Conclusions	Risk of bias Limitations
<p>Tang et al 2020 China</p> <p>Design: Retrospective observational study with control group</p> <p>Setting: All participants were enrolled from one university hospital in Wuhan, China.</p>	<p>Patients diagnosed with covid-19 and had severe symptoms</p> <p>Criteria's for severe covid-19 was one of the following: Respiratory rate ≥ 30 breaths/min; arterial oxygen saturation $\leq 93\%$ at rest; PaO₂/FiO₂ ≤ 300 mm Hg.</p> <p>Confirmed cases: 1786 Severe cases: 449 Age=65\pm12 % male=60%</p> <p>Exclusion criteria's: Bleeding diathesis, hospital stay <7 days, lack of information about coagulation parameters and medications, and age <18 years.</p>	<p>I: The intervention was Heparin treatment for 7 days or longer.</p> <p>99 of 449 (22%) participants, whereof 30 died within 28 days (30,3%).</p> <p>C: Control was patients w/o heparin treatment or treatment less than 7 days.</p> <p>350 of 449 (78%) participants, whereof 104 died within 28 days (29,7%).</p>	<p>The primary outcome was 28-day mortality.</p> <p>The multivariate analysis was adjusting for: Age; Gender; Underlying disease (Yes/no); Prothrombin time (Range: 11.5 to 14.5); Platelet count (Range 125 to 350); D-dimer (<0.5);</p> <p>Results were also stratified by SIC (Sepsis-Induced Coagulopathy) score and D-dimer ULN (upper limit of normal).</p>	<p>Mortality: (30.3% vs 29.7%, p=0.910)</p> <p>The heparin treat was associated with lower mortality in patients with high SIC-score but not in those with low.</p> <p>SIC score ≥ 4: OR 0.37; 95% CI, 0.15 to 0.90; p=0.03; SIC score <4: OR: 1,28; 95% CI, 0.70 to 2.36; p=0.419;</p> <p>For D-dimer result, the mortality in heparin users basically maintained at same level, but in nonusers, the mortality rose with the rising D-dimer.</p> <p>D-Dimer >4 ULN: OR 0.62; 95% CI, 0.35 to 1.13; p=0.09) D-Dimer >5 ULN: OR 0.56; 95% CI, 0.30 to 1.05; p=0.07) D-Dimer >6 ULN: OR 0.44; 95% CI, 0.23 to 0.87; p=0.02) D-Dimer >8 ULN: OR 0.41; 95% CI, 0,21 to 0.82; p=0.01)</p>	<p>Aim: To validate the usefulness of SIC score and other coagulation parameters, in screening out patients who can benefit from anticoagulant through retrospective analysis</p> <p>Conclusion: In conclusion, a relatively high mortality of severe covid-19 is worrying; our study suggests that anticoagulants may not benefit the unselected patients, instead, only the patients meeting SIC criteria or with markedly elevated D-dimer may benefit from anticoagulant therapy mainly with low molecular weight heparin. Further prospective studies are needed to confirm this result.</p>	Moderate risk of bias
<p>Liu et al 2020</p> <p>Design:</p>	<p>Patients diagnosed with covid-19 from two hospitals in China admitted</p>	<p>I: The intervention (n=14) was 50 mg Dipyridamole (DIP) oral tablets</p>	<p>Primary outcome: Clinical cure and remission rate.</p>	<p>Clinical cure and remission rate: (OR 23.75, p=0.06)</p> <p>Severely ill. Clinical cure/discharge:</p>	<p>Aim: To evaluate the therapeutic potential of DIP as an adjunctive therapy to promote</p>	Moderate risk of bias

<p>A multicenter parallel randomized controlled clinical trial</p> <p>Setting: The participants were enrolled from two hospitals in China (Xiaogan and Wuhan)</p>	<p>between February 3 to March 8, 2020</p> <p>The diagnosis of severe case was made if patients met any of the following criteria: (1) respiratory rate ≥ 30 breaths/min; (2) SpO₂ $\leq 93\%$ while breathing room air; (3) PaO₂/FiO₂ ≤ 300 mmHg.</p> <p>Mean age 56 years</p>	<p>administered thrice daily for 14 days.</p> <p>8 of 14 patients in the intervention group were severely ill.</p> <p>C: The control (n=17) was patients from other wards without DIP adjunctive Therapy.</p> <p>12 of 17 patients in the intervention group were severely ill.</p>	<p>Mortality.</p> <p>Secondary outcomes: Counts of lymphocyte Counts of platelet. Virus clearance D-Dimer.</p> <p>Results were also stratified by non-severe and severely ill patients.</p>	<p>Intervention: 7 of 8 discharged (88%) Control: 4 of 12 discharged (33%)</p> <p>Severely ill. Remission: Intervention: 1 of 8 in remission (12,5%) Control: 2 of 12 in remission (16,7%)</p> <p>Severely ill. Mortality: Intervention: 0 of 8 dead (0%) Control: 2 of 12 dead (17%)</p> <p>Were unable to accurately determine the effects of DIP to viral clearance.</p> <p>The severely ill patients from both the intervention (50%) and control group (42%) had increased baseline concentrations of D-dimer</p> <p>The dynamic changes for each patient were calculated with reference to their own baseline value. Which showed that D-dimer rose continuously in the control group, whereas they were decreased in the DIP-treated group.</p>	<p>virus clearance and reduce the risk of hypercoagulability</p> <p>Conclusion: DIP supplementation was associated with significantly decreased concentrations of D-dimers (p<0.05), increased lymphocyte and platelet recovery in the circulation, and markedly improved clinical outcomes in comparison to the control patients.</p> <p>In particular, all 8 of the DIP-treated severely ill patients showed remarkable improvement: 7 patients (87.5%) achieved clinical cure and were discharged from the hospitals while the remaining 1 patient (12.5%) was in clinical remission.</p>	
<p>Yin et al 2020</p> <p>Design: Retrospective observational study with control group</p> <p>Setting: The participants were enrolled</p>	<p>Patients with severe covid-19 who were consecutive admitted to Tongji hospital between 1 January to 13 February 2020.</p> <p>The diagnosis of severe case was made if patients met any of the following criteria:</p>	<p>I: The intervention group (n=449) was patients with severe covid-19.</p> <p>The intervention was heparin treatment for at least 7 days, where 99 (22.0%) from the intervention group was included.</p>	<p>Primary outcome: Mortality and differences in clinical features.</p> <p>Clinical features: prothrombin time, platelet count and D-dimer.</p>	<p>Mortality: The 28-day mortality in covid group was approximately twofold of mortality in non-covid group (29.8% vs. 15.4%, p=0.003)</p> <p>Mortality between heparin users and nonusers: I: (30.3% vs. 29.7%, p=0.910) C: (13.6% vs. 15.9%, p=0.798).</p>	<p>Aim: To compare the coagulation parameters between severe covid-19 and severe pneumonia induced by other pathogens. Also, to evaluate if patients with elevated D-dimer could benefit from anticoagulant treatment.</p> <p>Conclusion: In conclusion, patients with severe pneumonia induced by</p>	<p>Moderate risk of bias</p>

from one hospital in Wuhan China.	Respiratory rate ≥ 30 breaths/min; Arterial oxygen saturation $\leq 93\%$ at rest; PaO ₂ /FiO ₂ ≤ 300 mmHg	C: The control group (n=104) was patients with severe pneumonia induced by other pathogens. 22 (21,6%) patients from the control group received heparin treatment.		Results were also stratified by D-dimer. When D-dimer exceeding 3.0 $\mu\text{g/mL}$ (6 ULN), significantly lower mortality in heparin users than nonusers was found in covid group (32.8% vs. 52.4%, $p=0.017$). But, no difference on mortality between heparin users than nonusers were found in non-covid group when stratified	SARS-CoV2 had higher platelet count than those induced by non-SARS-CoV2, and only the former (SARS-CoV2) with markedly elevated D-dimer may benefit from anticoagulant therapy mainly with low molecular weight heparin. .	
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