Bilaga 1. Exkluderade studier

Studie	Exklusionsorsak
Abduljalil JM, Abduljalil BM. Epidemiology, genome, and clinical features of the pandemic SARS-CoV-2: a recent view. New Microbes New Infect 2020;35.	Studiedesign
Arachchillage DRJ, Laffan M. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18:1233-4.	Publikation Kommentar
Atallah B, Mallah SI, AlMahmeed W. Anticoagulation in COVID-19. Eur Heart J Cardiovasc Pharmacother 2020.	Publikation Letter
Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-up. J Am Coll Cardiol 2020;75:2950.	Studiedesign Guideline
Cattaneo M, Bertinato EM, Birocchi S, Brizio C, Malavolta D, Manzoni M, et al. Pulmonary Embolism or Pulmonary Thrombosis in COVID-19? Is the Recommendation to Use High-Dose Heparin for Thromboprophylaxis Justified? Thromb Haemost 2020.	Publikation Kommentar
Ciavarella A, Peyvandi F, Martinelli I. Where do we stand with antithrombotic prophylaxis in patients with COVID-19? Thromb Res 2020;191:29.	Studiedesign Inga patientdata
Danzi GB, Loffi M, Galeazzi G, Gherbesi E. Acute pulmonary embolism and COVID-19 pneumonia: a random association? Eur Heart J 2020;41:1858.	Studiedesign Fallstudie
Han H, Yang L, Liu R, Liu F, Wu KL, Li J, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. Clin Chem Lab Med 2020.	Ingår i inkluderad översikt
Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thrombosis Research 2020;191:145-7.	Studiedesign Ingen kontrollgrupp
Le Berre A, Marteau V, Emmerich J, Zins M. Concomitant acute aortic thrombosis and pulmonary embolism complicating COVID-19 pneumonia. Diagn Interv Imaging 2020;101:321-2.	Studiedesign Fallstudie /kommentar
Lee SG, Fralick M, Sholzberg M. Coagulopathy associated with COVID-19. Cmaj 2020.	Studiedesign Sammanfattar budskap ur 6 artiklar
Leisman DE, Deutschman CS, Legrand M. Facing COVID-19 in the ICU: vascular dysfunction, thrombosis, and dysregulated inflammation. Intensive Care Med 2020;46:1105-8.	Studiedesign Inga patientdata
Leonard-Lorant I, Delabranche X, Severac F, Helms J, Pauzet C, Collange O, et al. Acute Pulmonary Embolism in COVID-19	Publikation Letter

Patients on CT Angiography and Relationship to D-Dimer Levels. Radiology 2020:201561.	
Lillicrap D. Disseminated intravascular coagulation in patients with 2019-nCoV pneumonia. J Thromb Haemost 2020;18:786-7.	Publikation Kommentar
Liu ZH, Wei R, Wu YP, Lisman T, Wang ZX, Han JJ, et al. Elevated plasma tissue-type plasminogen activator (t-PA) and soluble thrombomodulin in patients suffering from severe acute respiratory syndrome (SARS) as a possible index for prognosis and treatment strategy. Biomed Environ Sci 2005;18:260-4.	Utfall
Llitjos JF, Leclerc M, Chochois C, Monsallier JM, Ramakers M, Auvray M, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost 2020.	Studiedesign Ingen kontrollgrupp
Lushina N, Kuo JS, Shaikh HA. Pulmonary, Cerebral, and Renal Thromboembolic Disease Associated with COVID-19 Infection. Radiology 2020:201623.	Studiedesign Fallstudie
Marone EM, Rinaldi LF. Upsurge of deep venous thrombosis in patients affected by COVID-19: Preliminary data and possible explanations. J Vasc Surg Venous Lymphat Disord 2020;8:694-5.	Publikation Brief report
Ng JJ, Choong A. Thromboembolic events in patients with SARS-CoV-2. J Vasc Surg 2020.	Publikation
Poissy J, Goutay J, Caplan M, Parmentier E, Duburcq T, Lassalle F, et al. Pulmonary Embolism in COVID-19 Patients: Awareness of an Increased Prevalence. Circulation 2020.	Studiedesign Ingen kontrollgrupp
Roncon L, Zuin M, Zonzin P. Age-adjusted D-dimer cut-off levels to rule out venous thromboembolism in COVID-19 patients. Thromb Res 2020;190:102	Publikation Kommentar
Scialpi M, Scialpi S, Piscioli I, Battista Scalera G, Longo F. Pulmonary thromboembolism in critical ill COVID-19 patients. Int J Infect Dis 2020;95:361-2.	Publication type Kommentar
Spyropoulos AC, Ageno W, Barnathan ES. Hospital-based use of thromboprophylaxis in patients with COVID-19. Lancet 2020;395:e75.	Publikation Kommentar
Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18:844-7.	Publikation Brief report
Ten Cate H. Thrombosis management in times of COVID-19 epidemy; a Dutch perspective. Thromb J 2020;18:7.	Publikation Kommentar
Testa S, Prandoni P, Paoletti O, Morandini R, Tala M, Dellanoce C, et al. Direct oral anticoagulant plasma levels' striking increase in severe COVID-19 respiratory syndrome patients treated with antiviral agents: The Cremona experience. J Thromb Haemost 2020;18:1320-3.	Studiedesign Ingen kontrollgrupp
Violi F, Perri L, Loffredo L. Should all acutely ill medical patients be treated with antithrombotic drugs? A review of the interventional trials. Thromb Haemost 2013;109:589-95.	Fel population Ej infektionssjukdom, akut sjuka

Wang T, Chen R, Liu C, Liang W, Guan W, Tang R, et al. Attention should be paid to venous thromboembolism prophylaxis in the management of COVID-19. Lancet Haematol 2020;7:e362-e363.	Publikation Kommentar
Wu YP, Wei R, Liu ZH, Chen B, Lisman T, Ren DL, et al. Analysis of thrombotic factors in severe acute respiratory syndrome (SARS) patients. Thromb Haemost 2006;96:100-1.	Publikation Kommentar
Xiang-Hua Y, Le-Min W, Ai-Bin L, Zhu G, Riquan L, Xu-You Z, et al. Severe acute respiratory syndrome and venous thromboembolism in multiple organs. Am J Respir Crit Care Med 2010;182:436-7.	Studiedesign Fallstudie
Xing C, Li Q, Du H, Kang W, Lian J, Yuan L. Lung ultrasound findings in patients with COVID-19 pneumonia. Crit Care 2020;24:174.	Publikation Research letter
Xiong M, Liang X, Wei YD. Changes in blood coagulation in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Br J Haematol 2020.	Publikation Research letter
Yang M, Li CK, Li K, Hon KL, Ng MH, Chan PK, et al. Hematological findings in SARS patients and possible mechanisms (review). Int J Mol Med 2004;14:311-5.	Studiedesign Ingen översikt
Yang M, Ng MH, Li CK. Thrombocytopenia in patients with severe acute respiratory syndrome (review). Hematology 2005;10:101-5.	Studiedesign Ingen översikt
Yang X, Yang Q, Wang Y, Wu Y, Xu J, Yu Y, et al. Thrombocytopenia and its association with mortality in patients with COVID-19. J Thromb Haemost 2020;18:1469-72.	Studiedesign Brief report
Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, et al. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19. N Engl J Med 2020;382:e38.	Publikation Letter

Bilaga 2

Koagulationspåverkan vid infektion med coronavirus (2020)

Bilaga 2 Tabell över ingående primärstudier för Fråga 1

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Author Year Study design Setting	Population	Intervention and control treatments	Outcome	Results	Aims Conclusions	Risk of bias Limitations
Lodigiani et al 2020 **Design:** Retrospective cohort study without comparison group **Setting:** One university hospital in Milan, Italy	Patients with covid-19 who were consecutive admitted to a university hospital in Milan between 13 February to 10 April 2020. Median age=66 % male=68%	**Participants:** n=388 ICU: n=61 General ward: n=327 **Thromboprophylaxis**: 61 (100%) patients in the ICU and 246 (75%) patients in the general ward received thromboprophylaxis	**Primary outcome:** Thromboembolic complications, such as venous thromboembolism (VTE), ischemic stroke, and acute coronary syndrome (ACS)/myocardial infarction (MI) **Secondary outcome:** Overt disseminated intravascular coagulation (DIC)	**Thromboembolic events**: Occurred in 28 of 362 closed cases for a rate of 7.7% (95% CI, 5.4% to 11.0%). **Overt DIC**: A total of 8 (2.1%) patients met the laboratory criteria for overt DIC Also presented D-dimer levels between survivors and non-survivors among hospitalization	**Aim**: To describe the rate of venous and arterial thromboembolic complications in hospitalized patients with covid-19 **Conclusion**: Hospitalized patients with covid-19 were characterized by substantial in-hospital mortality and a high rate of thromboembolic complications. Rapidly increasing D-dimer levels were observed in non-survivors, reflecting the inflammatory and procoagulant state of covid-19. The high number of arterial and venous thromboembolic events diagnosed within 24 h of admission and the high rate of positive VTE imaging tests suggest that there is an urgent need to improve specific VTE diagnostic strategies and investigate the efficacy and safety of thromboprophylaxis in ambulatory covid-19 patients.	Moderate risk of bias

Zhang et al 2020 **Design:** Nonrandomized retrospective cohort study with a comparison group **Setting:** One hospital in Wuhan, China	Adult patients with covid-19 were enrolled in Wuhan Asia General Hospital from 12 January to 15 March 2020. Median age=62 % male=49.3%	**Participants**: n=343 Participants were stratified by D-dimer level	**Primary outcome:** Mortality	**Mortality:** D-dimer <2.0 µg/ml: 1 of 276 patients (0.4%) died D-dimer >2.0 µg/ml: 12 of 67 patients (15.8%) died **Optimum cut-off value:** D-dimer: 2.0 µg/ml with a sensitivity of 92.3% and a specificity of 83.3%. D-dimer: C-index 0.883 (95% CI, 0.842 to 0.916) **Predictive value:** D-dimer level ≥2.0µg/ml was the significant predictor of death after adjusting for gender, age and underlying diseases (HR:22 .4; 95% CI, 2.86 to 175.7, p=0.003)	**Aim:** Evaluate whether elevated D-dimer levels could predict mortality in patients with covid-19. **Conclusion:** D-dimer on admission greater than 2.0 µg/mL could effectively predict in-hospital mortality in patients with covid-19, which indicated D-dimer could be an early and helpful marker to improve management of covid-19 patients.	Moderate risk of bias
Zou et al 2020 **Design:** Nonrandomized retrospective cohort study with a comparison group **Setting:** One hospital in Shanghai	Adult patients with confirmed covid-19 who were admitted to the Shanghai Public Health Clinical Center between 20 January to 24 February 2020. Median age=51 % male=52%	**Participants**: n=303 patients of 324 were included in the study The patients were then put into two groups in terms of the severity of the disease **Mild:** 277 participants with mild (n=1) or moderate covid-19 (n=276) were assigned to the "mild group"	**Primary outcomes.** Coagulation parameters, such as PT, D-dimer, fibrinogen, abnormal APTT, FDP and INF	**Abnormal coagulation parameters** (Severe: 100% vs. mild: 66.1%) 209 (69%) of the participants had abnormal coagulation parameters in a total of at admission **Proportion of abnormal fibrinogen:** (Severe: 80.8% vs. mild: 62.8%), **Proportion of abnormal D-dimer**: (Severe: 80.8% vs. mild: 39.0%), **Proportion of abnormal APTT:** (Severe: 34.6% vs. mild: 20.6%), **Proportion of abnormal PT:** (Severe: 38.5% vs. mild: 16.6%),	**Aim:** To investigate the correlation between coagulopathy and covid-19 by comparing baseline coagulation functions of patients with different disease severity. **Conclusion:** That coagulopathy is common among covid-19 patients and that DIC-related parameters are significantly elevated in patients with severe cases compared to those with mild cases	Moderate risk of bias

		Severe: 26 participants with severe (n=10) or critical (n=16) covid-19 were assigned to the "severe group"		**Proportion of abnormal FDP:** (Severe: 19.2% vs. mild: 5.1%)		
Gao et al 2020 **Design:** Nonrandomized retrospective cohort study with a comparison group. **Setting:** One hospital in china.	Adults patients with confirmed covid-19 who were admitted to the Fuyang Second People's Hospital between 23 January and 2 February 2020. Mean age=44±12 % male=61%	**Participants:** n=43 patients were included in the study The patients were then put into two groups in terms of the severity of the disease **Mild:** 28 patients **Severe:** 15 patients	**Primary outcomes:** White blood cell (WBC) count, lymphocyte count (LYM), mononuclear count (MONO), neutrophils count (NEU), aspartate aminotransferase (AST), alanine aminotransferase (ALT), glucose (GLU), urea, creatinine (Cr), cystatin (Cys-c), uric acid (UA), C-reactive protein (CRP), D-dimer, thrombin time (TT), PT, FIB, APTT and Procalcitonin (PCT)	**Clinical laboratory data:** GLU, CRP, IL-6, TT, FIB, and D-dimer were significantly higher in the severe group compared to the mild group. WBC, LYM, NEU, MONO counts were not significantly different between the severe group and the mild group. **Predictive values:** **IL-6**: AUC: 0.795 (95% CI, 0.645 to 0.903; p<0.000) **D-dimer:** AUC: 0.750 (95% CI, 0.595 to 0.869; p=0.005) **D-dimer + IL-6:** AUC: 0.840 (95% CI, 0.697 to 0.934; p<0.000) AUC of TT, GLU, CRP, and FIB were below 0.750. **Optimal cut-off values:** **IL-6** 24.3 µg/L. Sensitivity of 73.3% and a specificity of 89.3% **D-dimer:** 0.28 µg/L, Sensitivity of 86.7% and a specificity of 82.1% **IL-6 or D-dimer:** Sensitivity: 93.3, Specificity: 75.0 **IL-6 and D-dimer:** Sensitivity: 66.7, Specificity: 96.4	**Aim**: Assess the hematological characteristics of covid-19 patients. Also, determine the correlation between clinical laboratory data and the severity of covid-19 in adult patients. Moreover, determine the predictive value of clinical laboratory data for the severity of covid-19 **Conclusion:** In conclusion, our findings suggest that IL-6 and d -D levels can be used to estimate the severity of covid-19. If necessary, the levels of IL-6 and d-D should be measured, as they can help diagnose the severity of adult covid-19 patients	Moderate risk of bias

Chen et al 2020 **Design:** Retrospective case series **Setting:** One hospital in Wuhan, China	Patients with confirmed covid-19 who either was dead or had recovered (13 January – 12 February 2020) at Tongji Hospital Median age=62 % male=62%	113 deceased patients (from a cohort of 799 patients, where 274 were included in the study). Of these, 161 patients had recovered and 113 deceased	Laboratory findings (such as white blood cell count, neutrophil, platelet count etc.), abnormalities on chest radiographs, arterial blood gases, complications, primary interventions.	The median age of deceased patients was significantly older than that of recovered patients Male sex was more predominant in patients who died than in those who recovered Chronic hypertension and other cardiovascular comorbidities were more frequent among deceased patients than recovered patients Symptoms related to hypoxemia were more common in deceased patients than in recovered patients Deceased patients more often developed systematic inflammation and multi-organ dysfunction than did recovered patients The indicators of cardiac injury showed more frequent or prominent abnormalities in deceased patients than in recovered patients	**Aim:** To delineate clinical characteristics of patients with covid-19 who died. **Conclusion:** Severe acute respiratory syndrome coronavirus 2 infection can cause both pulmonary and systemic inflammation, leading to multi-organ dysfunction in patients at high risk. Acute respiratory distress syndrome and respiratory failure, sepsis, acute cardiac injury, and heart failure were the most common critical complications during exacerbation of covid-19	Moderate risk of bias
Helms et al 2020 **Design:** Retrospective cohort study with historical control	All patients referred to 4 intensive care units (ICUs) due to covid-19 between March 3rd and 31st 2020 were included Median age=63	**I:** 150 patients with both covid-19 and ARDS were in the covid-19 group and in the matched comparison analysis 77 patients from this group were included	**Primary outcome:** Occurrence of any thrombotic event **Secondary outcome:** Renal replacement therapy (RRT) filter coagulation, the	**Thromboembolic complications (%)** OR: 2.6 (95% CI, 1.1 to 6.1) p=0.035 Most of which was pulmonary embolism. **RRT and lifespan:**	**Aim:** Assess thrombotic risk in severe forms of SARS-CoV-2 infection **Conclusion:** Despite anticoagulation, a high number of patients with	Moderate risk of bias

Setting: Intensive care units in French tertiary hospitals	% male=81.3%	**C:** A historical prospective cohort of "non-covid-19 ARDS" patients (n=233) included between 2014 and 2019 was used for the comparison. In the matched comparison analysis 145 patients from this group were included. The covid-19 and non-covid-19 patients were paired 1:3 on propensity scores based on baseline characteristics that were unbalanced between groups or had clinical relevance as the independent variables (age, sex, medical history of malignancies, cardiovascular diseases, cerebrovascular diseases, venous thrombo-embolic event, immune diseases, chronic liver diseases, chronic renal diseases, respiratory diseases, SAPS II, SOFA, PaO2/ FiO2 on ICU admission, anticoagulant treatment and ECMO)	median lifespan of each RRT circuit, the occurrence of ECMO oxygenator coagulation, hemorrhagic complications and the results of coagulation tests.	The number of RRT circuits per dialyzed patient was higher in covid-19 patients and their median lifespan shorter. **Coagulation parameters:** Prothrombin time, antithrombin, fibrinogen and platelets were significantly higher in covid-19 patients compared to non-covid-19 patients aPTT and D-dimers were significantly lower in covid-19 patients	ARDS and covid-19 develop life-threatening thrombotic complications. The monitoring of anticoagulant treatment should be achieved through anti-Xa measurement, owing to changes of standard hemostasis parameters in this particular pathology. Although Tang et al suggested that anticoagulant therapy mainly with LMWH appears to be associated with better prognosis in severe covid-19 patients meeting SIC criteria or with markedly elevated D-dimer, higher anticoagulation targets than usual should probably be taken into consideration	

Spiezia et al 2020 **Design:** Nonrandomized prospective case control with matched control group **Setting:** Intesive care unit (ICU) at one hospital in Italy	All consecutive patients admitted to the intensive care unit (ICU) of Padua University Hospital between March 7 and 19, 2020 for acute respiratory distress syndrome (ARDS) due to covid-19	**I:** 22 patients with ARDS due to covid-19 were enrolled in the study. **C:** 44 healthy, age-, sex-, and body weight-matched subjects served as controls for laboratory data.	**Outcomes:** Thromboelasteometry profiles using a ROTEM delta Apparatus. Clotting time, clot formation time (CFT), maximum clot firmness (MCF) and area under the curve (mm 100) Hemoglobin, platelet count, prothrombin time/international normalized ratio, activated partial thromboplastin time, fibrinogen, antithrombin, and D-dimer	**ROTEM Profiles:** covid-19 patients had a significantly shorter CFT in INTEM (p=0.000) and EXTEM (p=0.01) covid-19 patients had a significantly higher MCF in INTEM, EXTEM, and FIBTEM (p<0.001 in all comparisons). Fibrinogen and D-dimer plasma levels were significantly higher in covid-19 patients than controls (p<0.000 in both comparisons)	**Aim:** To better characterize covid-19-related coagulation changes **Conclusion:** covid-19 patients with acute respiratory failure present a severe hypercoagulability rather than consumptive coagulopathy. Fibrin formation and polymerization may predispose to thrombosis and correlate with a worse outcome.	Moderate risk of bias
Chen et al 2006 **Design:** Nonrandomized prospective case control with age-matched control group **Setting:** One hospital in Taipei in Taiwan	Patients, family caregivers and health care workers (n=15) who were previously healthy and developed SARS in a cluster outbreak from one index case were enrolled (2–17 May, 2003) Age range: 23 to 45	15 participants who developed SARS from one index case were enrolled in the study. **C:** 15 healthy age-matched adults that had not been exposed to SARS were recruited as control.	**Leukocytes, lymphocytes, neutrophil, monocytes, platelet counts, APTT, PT:** Levels of soluble vascular cell adhesion molecule-1 (sVCAM-1), Levels of plasma soluble Fas ligand (sFasL), intracellular cleaved caspase-3 levels	Patients with SARS had significantly lower lymphocyte (p<0.001) and platelet counts (p<0.001) and significantly higher sVCAM-1 (p=0.003) and sFasL levels (p=0.039(compared to healthy controls. sVCAM-1 levels correlated negatively with total leukocytes (p=0.047) and platelet counts (p=0.031), but positively with plasma sFasL levels (p=0.023) Intracellular cleaved caspase-3 expression was also significantly	**Aim:** To explore the relationship of lymphopenia, thrombocytopenia and clinical manifestations to plasma sFasL and sVCAM-1 levels, as well as intracellular cleaved caspase-3 levels in SARS patients. **Conclusion:** Lymphopenia and thrombocytopenia in SARS patients may be caused, in part, by enhanced vascular sequestration associated with	Moderate risk of bias

				higher in lymphocytes from SARS patients in acute phase than in convalescent stage.	increased sVCAM-1 levels. However, lymphopenia may be due to enhanced cell death. Inhibition of cell adhesion and caspase-3 activation could, therefore, have prevented SARS patients from developing thrombocytopenia and lymphopenia.	

APTT = Activated partial thromboplastin time; **DIC** = Disseminated intravascular coagulation; **FDP** = Fibrin degradation products; **FIB** = Fibrinogen; **PT** = Prothrombin time

Bilaga 3

Koagulationspåverkan vid infektion med coronavirus (2020)

Bilaga 3 Tabell över ingående primärstudier för Fråga 2

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Author Year Country Study design Setting	Population	Intervention and control treatments	Outcome	Results	Aims Conclusions	Risk of bias Limitations
Tang et al 2020 **China** **Design:** Retrospective observational study with control group **Setting:** All participants were enrolled from one university hospital in Wuhan, China.	Patients diagnosed with covid-19 and had severe symptoms Criteria's for severe covid-19 was one of the following: Respiratory rate ≥30 breaths/min; arterial oxygen saturation ≤93% at rest; PaO2/ FiO2 ≤300 mm Hg. Confirmed cases: 1786 Severe cases: 449 Age=65±12 % male=60% Exclusion criteria's: Bleeding diathesis, hospital stay <7 days, lack of information about coagulation parameters and medications, and age <18 years.	**I:** The intervention was Heparin treatment for 7 days or longer. 99 of 449 (22%) participants, whereof 30 died within 28 days (30,3%). **C:** Control was patients w/o heparin treatment or treatment less than 7 days. 350 of 449 (78%) participants, whereof 104 died within 28 days (29,7%).	The primary outcome was 28-day mortality. 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); Results were also stratified by SIC (Sepsis-Induced Coagulopathy) score and D-dimer ULN (upper limit of normal).	**Mortality**: (30.3% vs 29.7%, p=0.910) The heparin treat was associated with lower mortality in patients with high SIC-score but not in those with low. **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; 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. **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)	**Aim:** To validate the usefulness of SIC score and other coagulation parameters, in screening out patients who can benefit from anticoagulant through retrospective analysis **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.	Moderate risk of bias

Liu et al 2020 **Design:** A multicenter parallel randomized controlled clinical trial **Setting:** The participants were enrolled from two hospitals in China (Xiaogan and Wuhan)	Patients diagnosed with covid-19 from two hospitals in China admitted between February 3 to March 8, 2020 The diagnosis of severe case was made if patients met any of the following criteria: (1) respiratory rate ≥30 breaths/min; (2) SpO2 ≤93% while breathing room air; (3) PaO2/FiO2 ≤300 mmHg. Mean age 56 years	**I:** The intervention (n=14) was 50 mg Dipyridamole (DIP) oral tablets administered thrice daily for 14 days. 8 of 14 patients in the intervention group were severely ill. **C:** The control (n=17) was patients from other wards without DIP adjunctive Therapy. 12 of 17 patients in the intervention group were severely ill.	**Primary outcome:** Clinical cure and remission rate. Mortality. **Secondary outcomes:** Counts of lymphocyte Counts of platelet. Virus clearance D-Dimer. Results were also stratified by non-severe and severely ill patients.	**Clinical cure and remission rate:** (OR 23.75, p=0.06) **Severely ill. Clinical cure/discharge:** Intervention: 7 of 8 discharged (88%) Control: 4 of 12 discharged (33%) **Severely ill. Remission:** Intervention: 1 of 8 in remission (12,5%) Control: 2 of 12 in remission (16,7%) **Severely ill. Mortality:** Intervention: 0 of 8 dead (0%) Control: 2 of 12 dead (17%) Were unable to accurately determine the effects of DIP to viral clearance. The severely ill patients from both the intervention (50%) and control group (42%) had increased baseline concentrations of D-dimer 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.	**Aim:** To evaluate the therapeutic potential of DIP as an adjunctive therapy to promote virus clearance and reduce the risk of hypercoagulability **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. 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.	Moderate risk of bias
Yin et al 2020 **Design:** Retrospective observational study with control group	Patients with severe covid-19 who were consecutive admitted to Tongji hospital between 1 January to 13 February 2020. The diagnosis	**I:** The intervention group (n=449) was patients with severe covid-19. The intervention was heparin treatment for at	**Primary outcome:** Mortality and differences in clinical features. **Clinical features:**	**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) **Mortality between heparin users and nonusers:**	**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	Moderate risk of bias

Setting: The participants were enrolled from one hospital in Wuhan China.	of severe case was made if patients met any of the following criteria: Respiratory rate ≥30 breaths/min; Arterial oxygen saturation ≤93% at rest; PaO2/FiO2 ≤300 mmHg	least 7 days, where 99 (22.0%) from the intervention group was included. **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.	prothrombin time, platelet count and D-dimer.	**I:** (30.3% vs. 29.7%, p=0.910) **C**: (13.6% vs. 15.9%, p=0.798). Results were also stratified by D-dimer. When D-dimer exceeding 3.0 µg/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	benefit from anticoagulant treatment. **Conclusion:** In conclusion, patients with severe pneumonia induced by 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. .	