COVID-19 and Haemostasis

Selected Papers

COVID-19 and Haemostasis

COVID-19 and VTE/Anticoagulation: Frequently Asked Questions

Input from Drs. Lisa Baumann Kreuziger, Agnes Lee, David Garcia, Adam Cuker, Mary Cushman, Jean M. Connors

Available from: https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation

Practical guidance for the prevention of thrombosis and management of coagulopathy and disseminated intravascular coagulation of patients infected with COVID-19

Prof Beverley Hunt OBE, Dr Andrew Retter, Dr Claire McClintock

This guidance from Thrombosis UK gives information to manage thrombotic risk, coagulopathy, and DIC in patients with COVID-19. This guidance will be updated weekly.

Available from: https://thrombosisuk.org/covid-19-thrombosis.php

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Tang N, Bai H, Chen X, Gong J, Li D, Sun Z.

J Thromb Haemost 2020 Mar 27

The authors retrospectively investigate the effect of anticoagulation on COVID-19 outcomes included 449 patients, 22% received treatment with unfractionated heparin (UFH) or LMWH. They conclude that use of anticoagulant treatment was associated with better prognosis in severe COVID-19 patients meeting sepsis-induced coagulopathy criteria with a SIC score >4 or with D-dimer markedly elevated > 3 µg/L.

Available from: http://doi.wiley.com/10.1111/jth.14817

COVID-19 and Haemostasis

COVID-19: Anticoagulation Recommended Even After Discharge - Guidance from consensus group and others details on use across settings

Crystal Phend

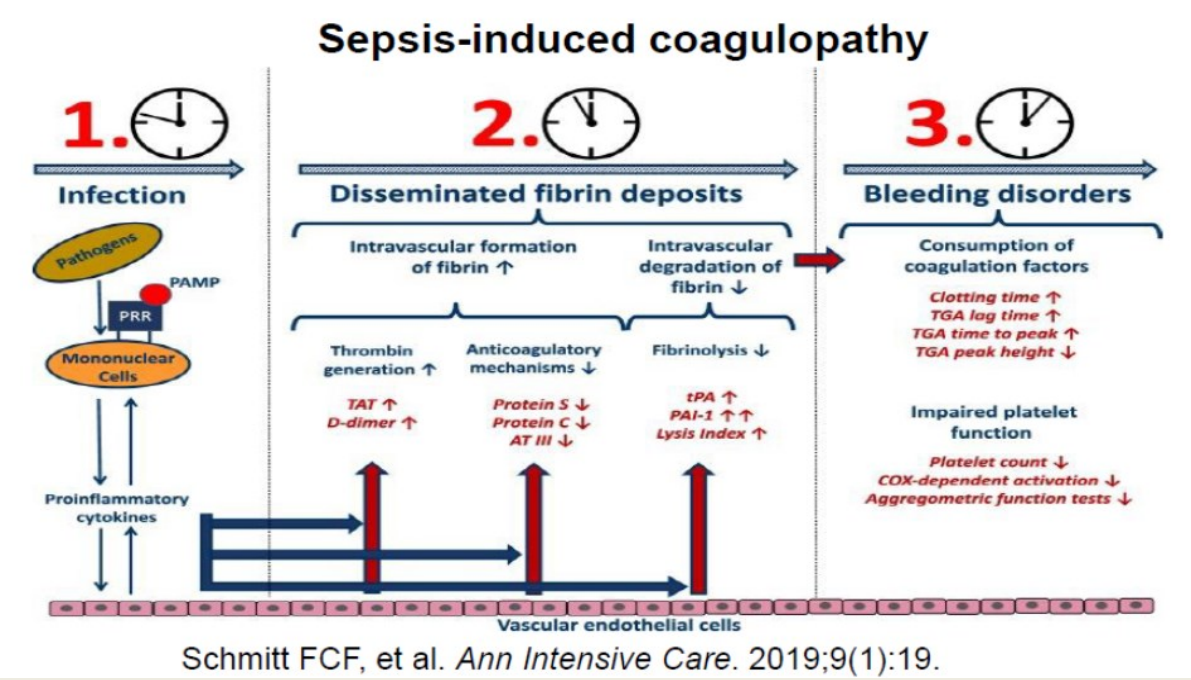
Whether coagulopathy in COVID-19 is a consequence or cause of what's happening in the lungs remains unclear. However, consensus has formed on anticoagulation treatment for hospitalized patients and sending them home with an empiric regimen.

Available from: https://thrombosisuk.org/covid-19-thrombosis.php

Coagulation tests In COVID-19

NingTang, Clinical laboratory of Tongjihospital

Many severe COVID-19 patients meet the sepsis criteria



Schmitt FCF, et al. *Ann Intensive Care*. 2019;9(1):19.

In survivors only 0.6% patients meet the DIC criteria

Differential diagnosis of COVID-19 induced coagulopathy

Heparin interference:	TEG (heparinase), Anti-FXa
Vitamin K deficiency:	Coagulation factor II, VII, IX, X
TTP/HUS/ HIT:	ADAMTS13, CFH, Hep-PF4antibody..
APS/CAPS:	Antiphospholipidantibody

Conclusion:

Hypercoagulability has been found in (early) severe COVID-19, and indicates the ris- of DIC and VTE. Patients meeting SIC criteria or with markedly elevated D-dimer may benefit from anticoagulant therapy. The value of special coagulation tests on monito- ring and differential diagnosis of coagulopathy.

Available from:
https://academy.isth.org/isth/2020/covid-19/document?c_id=290512&type=journal_article

COVID-19 and Haemostasis

COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-up

Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, Nigoghossian CD, Ageno W, Madjid M, Guo Y, Tang LV, Hu Y, Giri J, Cushman M, Quéré I, Dimakakos EP, Gibson CM, Lippi G, Favaloro EJ, Fareed J, Caprini JA, Tafur AJ, Burton JR, Francese DP, Wang EY, Falanga A, McLintock C, Hunt BJ, Spyropoulos AC, Barnes GD, Eikelboom JW, Weinberg I, Schulman S, Carrier M, Piazza G, Beckman JA, Steg PG, Stone GW, Rosenkranz S, Goldhaber SZ, Parikh SA, Monreal M, Krumholz HM, Konstantinides SV, Weitz JI, Lip GYH

Journal of the American College of Cardiology (2020)

The authors review the current understanding of the pathogenesis, epidemiology, management and outcomes of patients with COVID-19 who develop venous or arterial thrombosis, and of those with preexisting thrombotic disease who develop COVID-19, or those who need prevention or care for their thrombotic disease during the COVID-19 pandemic

Available from: https://doi.org/10.1016/j.jacc.2020.04.031

Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia

Ning Tang, Dengju Li, Xiong Wang, Ziyong Sun

J Thromb Haemost. 2020;18:844–847.

The present study shows that abnormal coagulation results, especially markedly elevated D-dimer and FDP are common in deaths with NCP. DIC, mostly due to virus sepsis, appeared in most of the non-survivors.

Based on this publication the British Society of Haematology published a guidance in BSH Haemostasis and Thrombosis Task Force. 2020 Mar 18. This document indicates abnormal coagulation parameters can be a useful predictor of prognosis in pneumonia due to COVID-19.

Available from: https://onlinelibrary.wiley.com/doi/10.1111/jth.14768

Uncertainties on the prognostic value of D-dimers in COVID-19 patients

Christophe Gris, Isabelle Quéré, Antonia Pérez-Martin, Jean-Yves Lefrant, Albert Sotto.

JTH 2020 doi: 10.1111/JTH.14876

In this letter to the editor the authors comment on a possible selection bias and that impact of the modalities and intensities of the antithrombotic/anticoagulant treatments given to the patients on the D-dimer predictive value is not studied. The underlying meaning of increased D-dimer levels in COVID-19 patients must be clearly understood, the prevailing interpretation has been coagulation activation finally leading to DIC, which is probably true in the most severe patients and near fatal outcome but which is far to be demonstrated in the initial disease despite striking high D-Dimer levels. This has strong clinical consequences, as the observed high D-dimer levels have induced spontaneous therapeutic interventions and experts' recommendations increasing the antithrombotic/anticoagulant dosages, thus increasing the haemorrhagic risk. The mechanisms, determinants, roots and independent value of increased D-dimers in Covid-19 patients must be fully understood in order to propose the most pathophysiologically relevant treatments to test.

Available from: https://onlinelibrary.wiley.com/doi/epdf/10.1111/jth.14876

COVID-19 and Haemostasis

DIC in COVID-19: Implications for Prognosis and Treatment?

Rainer Seitz Wolfgang Schramm

JTH 2020 First published: 28 April 2020

In this letter to the editor the authors comment that it might be time for reconsidering the interaction and modulating of different connected systems e.g. coagulation, fibrinolysis, Kallikrein-Kinin, Complement and immunity (cytokine storm). A rationale for developing strategies for attenuating DIC in COVID-19. If such efforts would be successful, it might have immense benefit also for intensive care patients far beyond the current crisis.

Available from: https://doi.org/10.1111/jth.14878

Laboratory haemostasis monitoring in COVID-19

Jecko Thachil, Ning Tang, Satoshi Gando, Anna Falanga, Marcel Levi, Cary Clark, Toshiaki Iba

JTH 2020 doi: 10.1111/JTH.14866

The authors comment on the criticisms about laboratory monitoring of haemostatic variables.They still believe that the use of simple and easily available laboratory markers both at admission and whilst in the hospital is necessary in the management of COVID-19 patients.

Available from: https://onlinelibrary.wiley.com/doi/epdf/10.1111/jth.14866

ISTH interim guidance on recognition and management of coagulopathy in COVID-19

Jecko Thachil, Ning Tang, Satoshi Gando, Anna Falanga, Marco Cattaneo, Marcel Levi, Cary Clark, Toshiaki Iba

J Thromb Haemost. 22020;18:1023–1026.

The authors address the need of measuring coagulation markers at admission and their monitoring. The guidance recommends measuring D-dimer, prothrombin time and platelet count in all patients suspected of COVID-19 infection, in order to stratify risk of developing coagulopathy and to help in management. One of the commonest laboratory findings noted in COVID-19 patients requiring hospitalization has been the increase in D-dimers. An algorithm based on simple coagulation tests is proposed, including measurement of fibrinogen which may help to assess disseminated intravascular coagulation (DIC) in these patients. Finally, low molecular weight heparin (LMWH) treatment may be used in some COVID-19 patients.

Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14810

Chinese expert consensus on diagnosis and treatment of coagulation dysfunction in COVID-19

Song JC, Wang G, Zhang W, et al.

Military Medical Research (2020) 7:19. DOI: 10.1186/s40779-020-00247-7

This consensus includes an overview of COVID-19-related coagulation dysfunction, tests for coagulation, anticoagulation therapy, replacement therapy, supportive therapy and prevention. The consensus produced 18 recommendations which are being used to guide clinical work.

Available from:
https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-00247-7

DIC in COVID-19: Implications for Prognosis and Treatment?

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Available from: https://doi.org/10.1111/jth.14878

Direct oral anticoagulant plasma levels striking increase in severe COVID-19 respiratory Syndrome patients treated with antiviral agents. The Cremona experience

Testa S, Prandoni P, Paoletti O et al.

J Thromb Haemost. 2020 Apr 23

The authors showed in this paper that DOAC patients treated with antiviral drugs show an alarming increase in DOAC plasma levels, with C-trough levels 6.14 times higher during hospitalization than in pre-hospitalization period. They recommend to replace DOAC with alternative parenteral antithrombotic strategies for as long as antiviral agents are deemed necessary and until discharge.

Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14871

COVID 19 Coagulopathy in Caucasian patients

Fogarty H, Townsend L, Ni Cheallaigh C.

Br J Haematol 2020 Apr 24. doi: 10.1111/bjh.16749.

This paper shows haemostasis parameters depicting the coagulopathy in Caucasian patients (until now, most of reports reports were from Chinese patients).

Authors conclude that:

- Race and ethnicity have major effects upon thrombotic risk, with significantly lower risk in Chinese compared to Caucasian individuals.
- Severe COVID-19 infection is associated with a significant coagulopathy in Caucasian patients that correlates with disease severity.
- Despite significantly increased D-dimers, progression to overt DIC in Caucasian COVID-19 patients maintained on prophylactic dose LMWH is rare.

Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.16749

COVID-19 and Haemostasis

COVID-19 and TTP

COVID-19 and Thrombotic Thrombocytopenic Purpura: Frequently Asked Questions

Input from Drs. Spero Cataland, Paul Coppo, Marie Scully, Masanori Matsumoto, James George, Bernhard Lämmle, Flora Peyvandi, and Ravi Sarode

Available from: https://www.hematology.org/covid-19/covid-19-and-ttp

Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis

Giuseppe Lippia, Mario Plebanib,1, Brandon Michael Henryc,☐,1

a Section of Clinical Biochemistry, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy
b Department of Laboratory Medicine, University Hospital of Padova, Padova, Italy
c Cardiac Intensive Care Unit, The Heart Institute, Cincinnati Children's Hospital Medical Center, OH, USA

Clinica Chimica Acta 506 (2020) 145–148

In this study was investigated whether platelet count could differentiate between COVID-19 patients with or without severe disease. Additionally, was evaluated if thrombocytopenia is associated with severe COVID-19. It was concluded that low platelet count is associated with increased risk of severe disease and mortality in patients with COVID-19, and thus should serve as clinical indicator of worsening illness during hospitalization.

Available from: https://doi.org/10.1016/j.cca.2020.03.022

Immune Thrombocytopenic Purpura in a Patient with Covid-19

Abrar Ahmad Zulfiqar et al

N Engl J Med 2020; 382:e43

Available from: https://www.nejm.org/doi/full/10.1056/NEJMc2010472

Thrombocytopenia and its association with mortality in patients with COVID-19

Xiaobo Yang. Qingyu Yang, Yaxin Wang, Yongran Wu, Jiqian Xu, Yuan Yu, You Shang

J Thromb Haemost. 2020;00:1–4.

Thrombocytopenia is common in patients with COVID-19, and it is associated with increased risk of in-hospital mortality. The lower the platelet count, the higher the mortality becomes.

Available from: https://onlinelibrary.wiley.com/journal/15387836

COVID-19 and Haemostasis

Decreased ADAMTS-13 (A disintegrin-like and metalloprotease with thrombospondin type 1 repeats) is associated with a poor prognosis in sepsis-induced organ failure

Kenneth Martin, et al. Crit Care Med 2007; 35:2375–2382

Low ADAMTS-13 activity and antigen in severe sepsis and in other conditions associated with organ dysfunction was observed. ADAMTS-13 levels were significantly associated with differences in morbidity, mortality, and variables of inflammation and endothelial dysregulation only in severe sepsis patients. This suggests that ADAMTS-13 deficiency may have a pathophysiological relevance specific to severe sepsis.

Available from: https://journals.lww.com/ccmjournal/Abstract/2007/10000/Decreased_ADAMTS_13__A_disintegrin_like_and.21.aspx

Decreased ADAMTS 13 Activity is Associated With Disease Severity and Outcome in Pediatric Severe Sepsis

Jainn-Jim Lin, MD, Oi-Wa Chan, MD, Hsiang-Ju Hsiao, MD, Yu Wang, MD, Shao-Hsuan Hsia, MD, and Cheng-Hsun Chiu, MD, PhD. Medicine 2016, 95(16):e3374

ADAMTS 13 activity is strongly negatively correlated with the severity of pediatric sepsis. Lower ADAMTS 13 activity on day 1 of admission is associated with increased risk of mortality. Therefore, analysis of ADAMTS 13 activity in pediatric sepsis may offer help in evaluating the status and outcome of patients.

Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4845826/pdf/medi-95-e3374.pdf

COVID-19 and Thrombingeneration

Detecting hypercoagulability in sepsis: thromboelastometry vs thrombomodulin - modified thrombin generation test

Osovskikh et al
Intensive Care Medicine Experimental 2015, 3(Suppl 1):A786

Available from: http://www.icm-experimental.com/content/3/S1/A786

The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome

Ranucci M, Ballotta A, Di Dedda U, et al.
J THromb Haemost, 17 April 2020.

Prospective observational study aimed to characterize the coagulation profile

of COVID-19 ARDS patients with standard and viscoelastic coagulation tests, and to evaluate their changes after establishment of an aggressive thromboprophylaxis. The authors confirmed the pro-coagulant pattern of these patients that may justify the thromboembolic complications (pulmonary embolism) during the course of the disease. Further studies are needed to assess the best prophylaxis and treatment of this condition.

Available from : https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14854

COVID-19 and Haemostasis

COVID-19 and Fibrinolytic Abnormalities

Fibrinolytic abnormalities in acute respiratory distress syndrome (ARDS) and versatility of thrombolytic drugs to treat COVID-19

Whyte CS, Morrow GB, Mitchell JL et al.
J Thromb Haemost. 2020 Apr 23.

In this review, the authors discuss the repurposing of tissue-type plasminogen activator (tPA), to treat COVID-19 associated ARDS. tPA is an approved intravenous thrombolytic treatment, and the nebulizer form has been shown to be effective in plastic bronchitis and is currently in Phase II clinical trial. Nebulizer plasminogen activators may provide a targeted approach in COVID-19 patients to degrade fibrin and improving oxygenation in critically ill patients.

Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14872

Tissue Plasminogen Activator (tPA) Treatment for COVID-19 Associated Acute Respiratory Distress Syndrome (ARDS): A Case Series

Wang J, Hajizadeh N, Moore EE et al.
J Thromb Haemost. 2020 Apr 8.

3 cases of using tissue plasminogen activator (t-PA) in critically ill, mechanically ventilated COVID-19 positive patients with ARDS are reported. They report clinical improvement in these patients with a decrease in hypoxemia as long as the tPA infusion lasted. These preliminary data, subject to confirmation in independent study, provide insights for improving the anticoagulant and fibrinolytic strategy in critically ill COVID-19 patients. The risk of catastrophic bleeding from use of tPA must be considered in the context of patient treatment.

Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14828

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