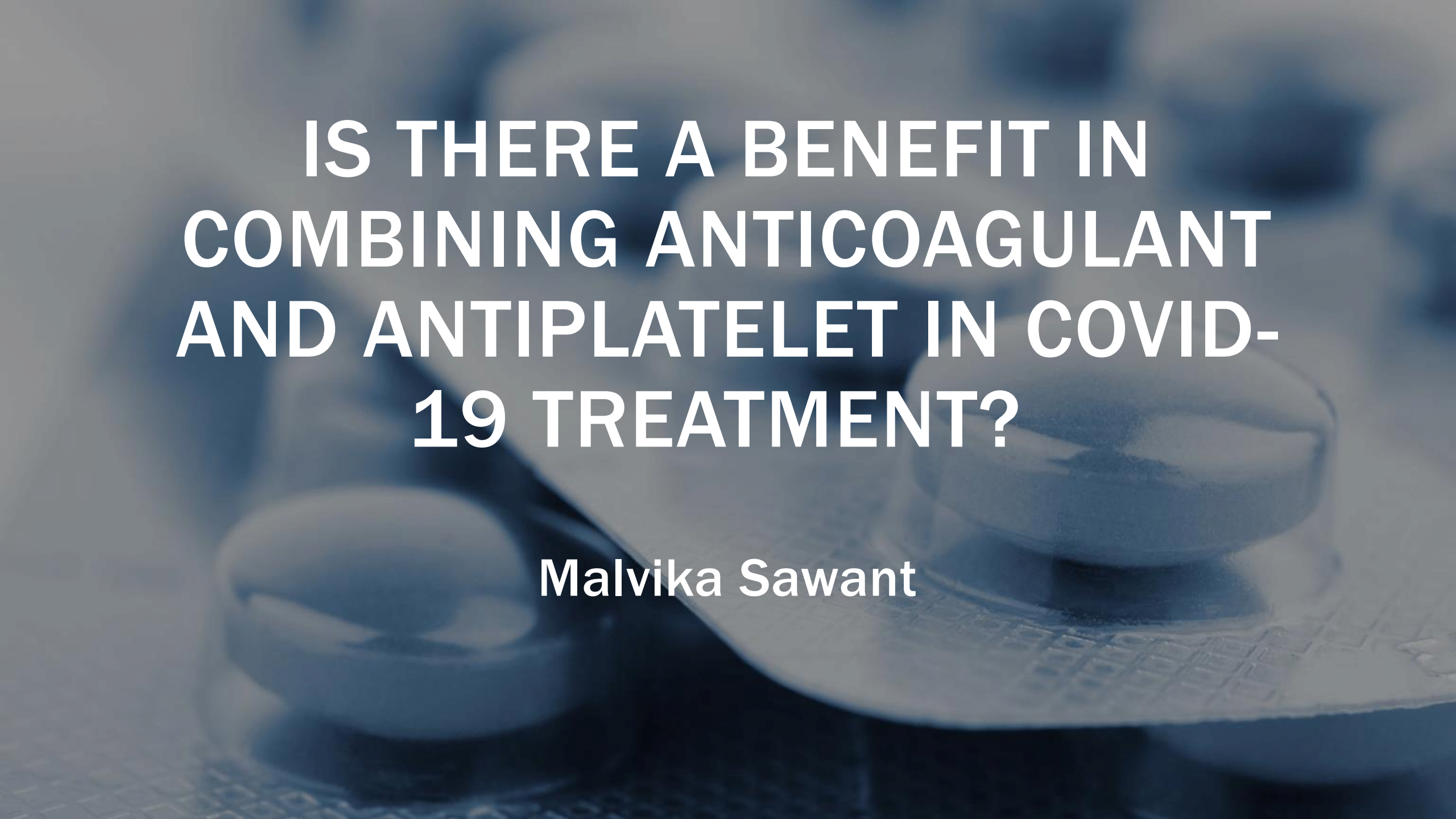


IS THERE A BENEFIT IN COMBINING ANTICOAGULANT AND ANTIPLATELET IN COVID-19 TREATMENT?

Malvika Sawant

ABSTRACT

The COVID-19 pandemic has spread rapidly across the globe causing immense amounts of people to be hospitalized, furthermore, even causing deaths. Many clinicians are observing pathophysiological principles to diagnose patients and give them specific treatments that have been outlined. A therapeutic approach that has been observed to be quite beneficial is the antithrombotic treatment labelled by the combination of antiplatelets and anticoagulants. There have been multiple studies covering the increasing rates of the association between thrombosis and COVID-19. The mechanisms of the treatment cover the operations behind this specific therapeutic treatment and its positive results. However, there are risk factors that must be addressed, which are overcome through the proposed algorithm.

ANTICOAGULANT AND ANTIPLATELETS

- Anticoagulants: agents that are used to prevent the formation of blood clots; these are usually used if a blood clot blocks the flow of blood through a blood vessel and causes the affected part of the body to be starved of oxygen and stop working properly
- Antiplatelets: drugs that interfere with the binding of platelets, or the process that starts the formation of blood clots; it can be used to treat conditions such as heart disease, problems with blood circulation, abnormal heartbeat, and congenital heart defect

COVID-19 AND THROMBOSIS

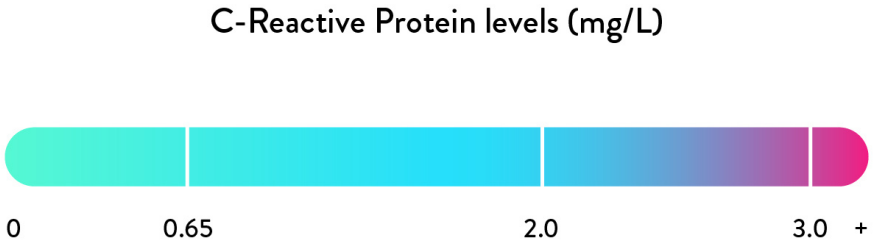
- COVID-19 causes a hypercoagulable state by altering the natural balance of circulating prothrombotic factors in severe infections
- A study conducted by Dr. Girish N. Nadkarni investigated the impact of prophylactic and therapeutic dose heparin or direct oral anticoagulants on the mortality of 2,859 COVID-19 patients as compared to 1,530 non-anticoagulant users in USA
- Based on the analysis, it was evident that all patients treated with an anticoagulant had a reduced mortality when compared to those not treated

HYPERCOAGULATION AND COVID-19

- SARS-CoV-2 patients and laboratory data exploring clotting system suggest the presence of a hypercoagulation state
- Hypercoagulation is commonly treated with blood thinners such as heparin
- The connection with treating hypercoagulation from the COVID-19 perspective is that many interventional trials have been conducted that state the efficacy of LMWH (low molecular weight heparin)

CONNECTION TO COAGULOPATHY

- Coagulopathy is often broadly defined as any derangement of hemostasis resulting in either excessive bleeding or clotting, although most typically it is defined as impaired clot formation
- Increased C-reactive protein levels reported in COVID-19 patients might reflect increased levels of systemic coagulopathy, along with increased inflammatory responses that could be attributed to endothelial dysfunction



UFH-LMWH AND COVID-19 TREATMENT

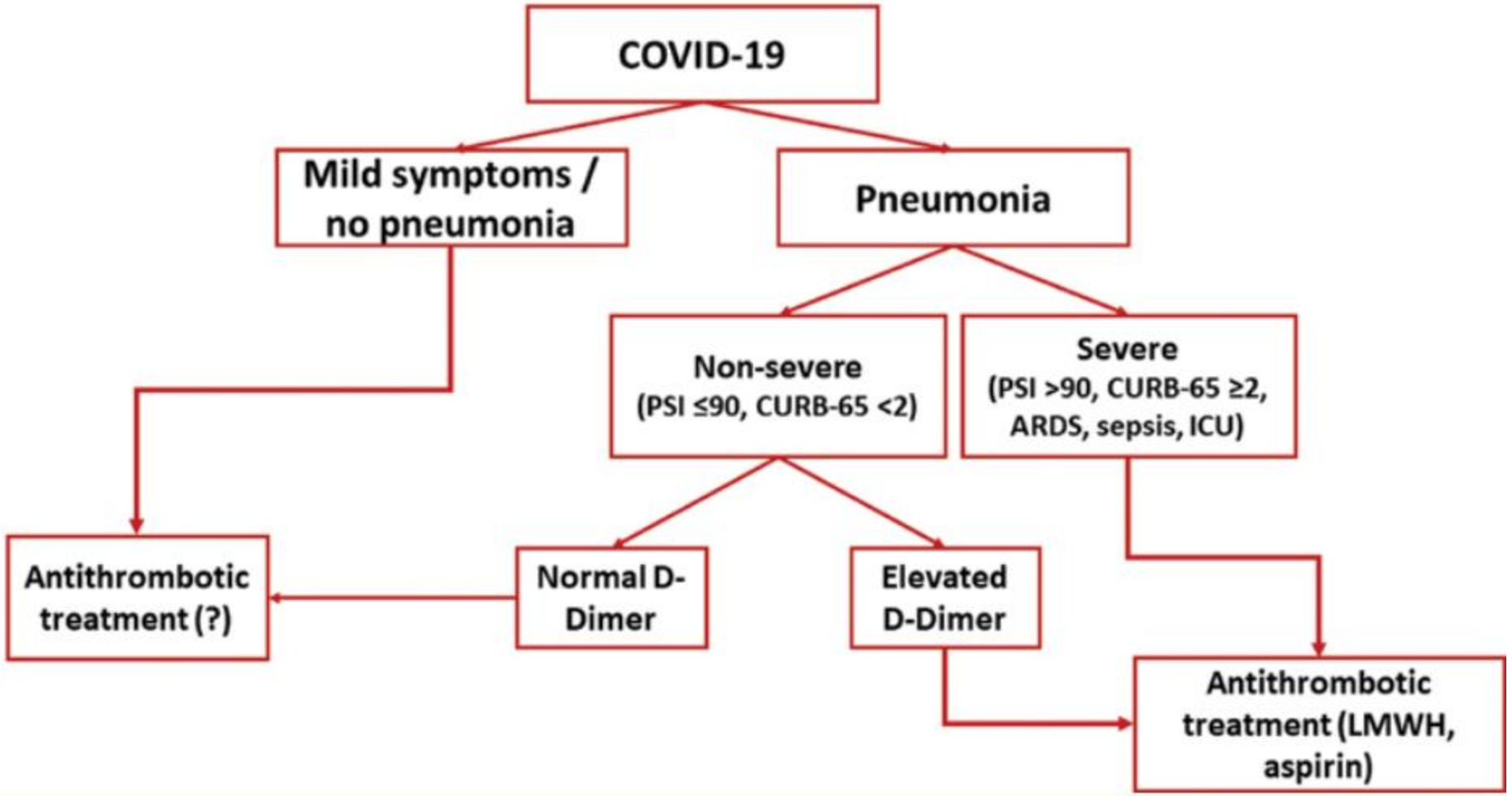
- Unfractioned heparin and low molecular weight heparins (LMWH) can be candidates for targeting protease cleavage and cellular entrance of SARS-CoV2
- The prophylactic use of minidose or prophylactic doses of LMWH can be used for hospitalized non-ICU patients with a normal coagulation profile and normal platelet counts in order to decrease viral load of host cells and prevent the involvement of lower respiratory tract

DEVELOPMENT WITH OTHER DISEASES

- Hyperinflammation and macrophage activating syndrome (MAS) is complicating COVID infection leading to capillary leakage and Acute Respiratory Distress Syndrome (ARDS)
- COVID-19 has the potential to result in severe illness such as ARD- because of their anti inflammatory and antiproliferative functions; usage of unfractioned heparin, tinzaparin and dalteparin can be beneficial
- COVID-19 infects the host cells via proteases, unfractioned heparin and LMWH can be potential inhibitors of multiple endoproteases

SPECIFIC MECHANISMS

- The mechanism behind the combination of antiplatelet and anticoagulant therapy, antithrombotic therapy, in COVID-19 patients can be understood as subcutaneous low-molecular-weight heparin or with short-acting novel anticoagulant drugs in dosing schemes like those used in outpatient thromboprophylaxis
- In a retrospective study of 2773 inpatients with COVID-19, 28% received anticoagulant therapy within 2 days of admission, and despite being used in more severe cases, anticoagulant administration was associated with a reduction in mortality


COVID-19
Mild symptoms / no pneumonia
Pneumonia
Non-severe (PSI ≤90, CURB-65 <2)
Severe (PSI >90, CURB-65 ≥2, ARDS, sepsis, ICU)
Antithrombotic treatment (?)
Normal D-Dimer
Elevated D-Dimer
Antithrombotic treatment (LMWH, aspirin)

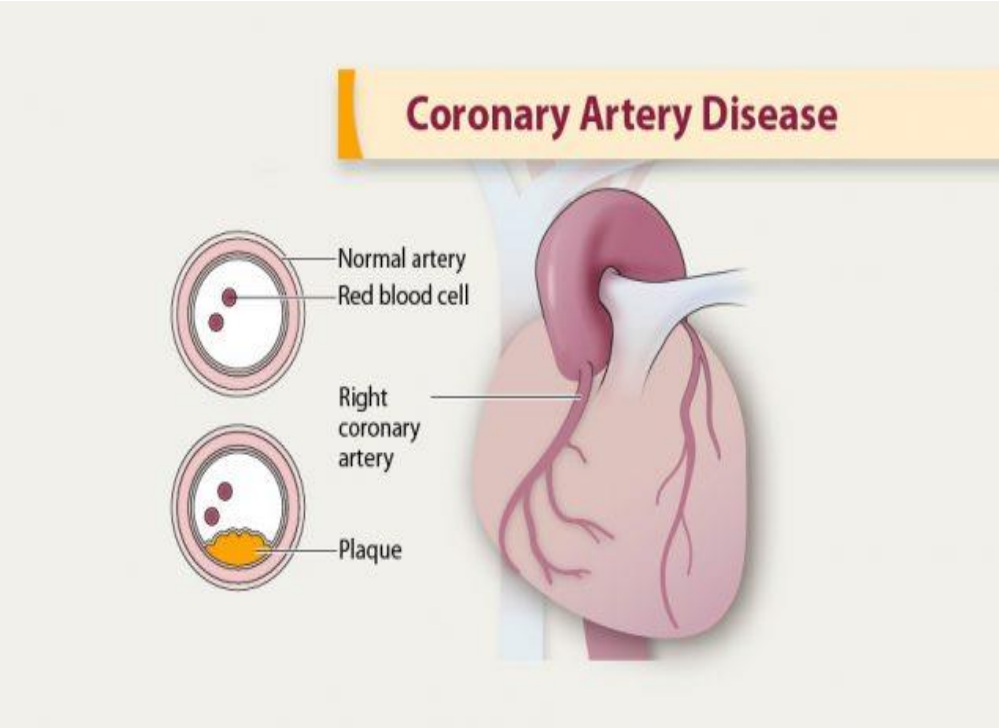
D DIMER CORRELATION WITH COVID-19

- “More than one-quarter of patients with COVID-19 had elevated D-dimer levels up to 4 months after diagnosis”
- “Elucidating the biological mechanisms responsible for sustained D-dimer increases may be of relevance in long COVID-19 pathogenesis and has implications for clinical management of these patients”

- Liam Townsend, PhD candidate in the department of infectious diseases at St. James’s Hospital in Dublin

RELATIONSHIP WITH CORONARY DISEASES

- COVID-19 patients may experience thrombotic events in coronary and cerebral trees or in other circulatory districts including lung and kidney
- There has been intense research done detecting that patients with coronary artery disease (CAD) have indications for intense antiplatelet therapy and anticoagulant therapy

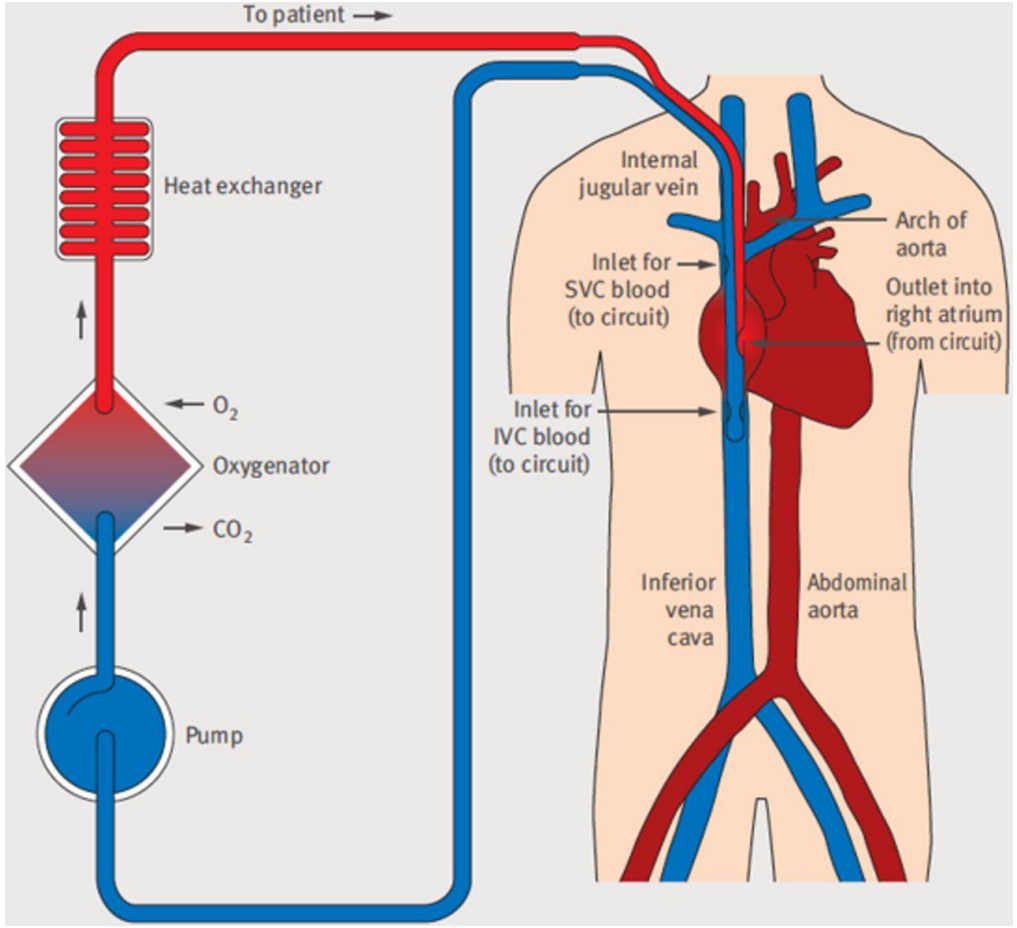


PRIOR USAGE

- Patients with COVID-19 who require extracorporeal membrane oxygenation or continuous renal replacement therapy or who have thrombosis of catheters or extracorporeal filters should be treated with antithrombotic therapy as per the standard institutional protocols for those without COVID-19.

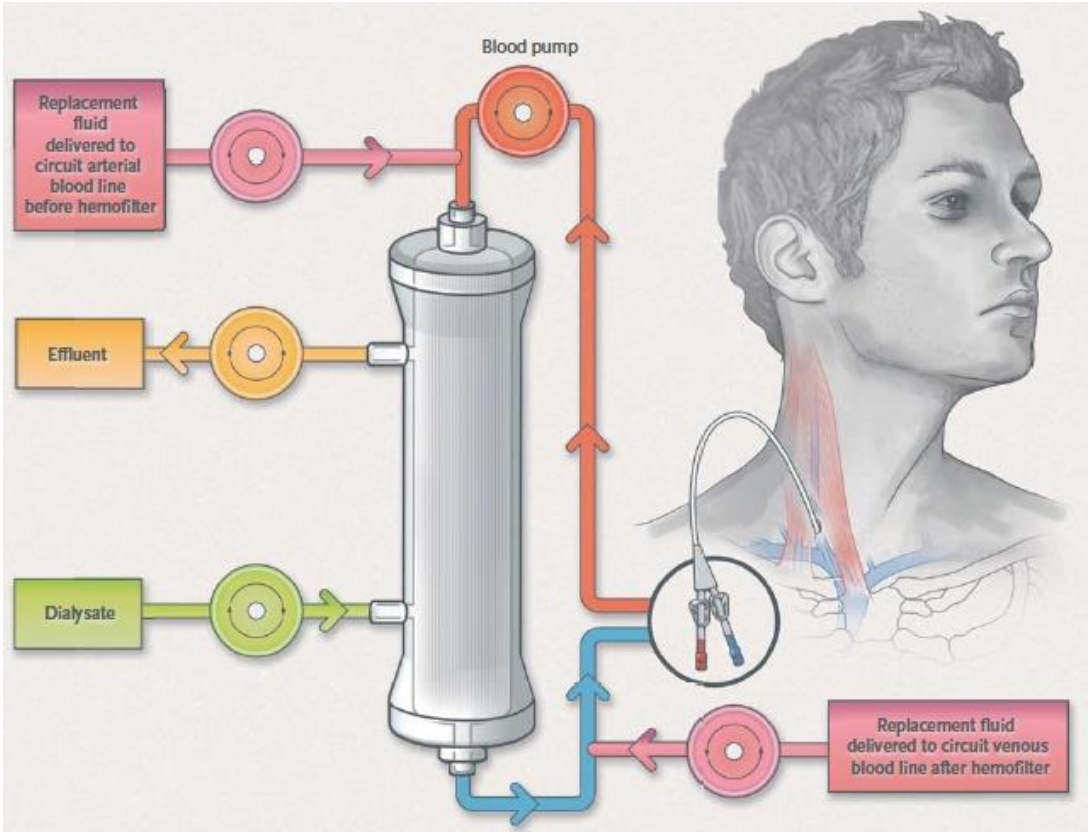
PRIOR USAGE

Extracorporeal Membrane Oxygenation:



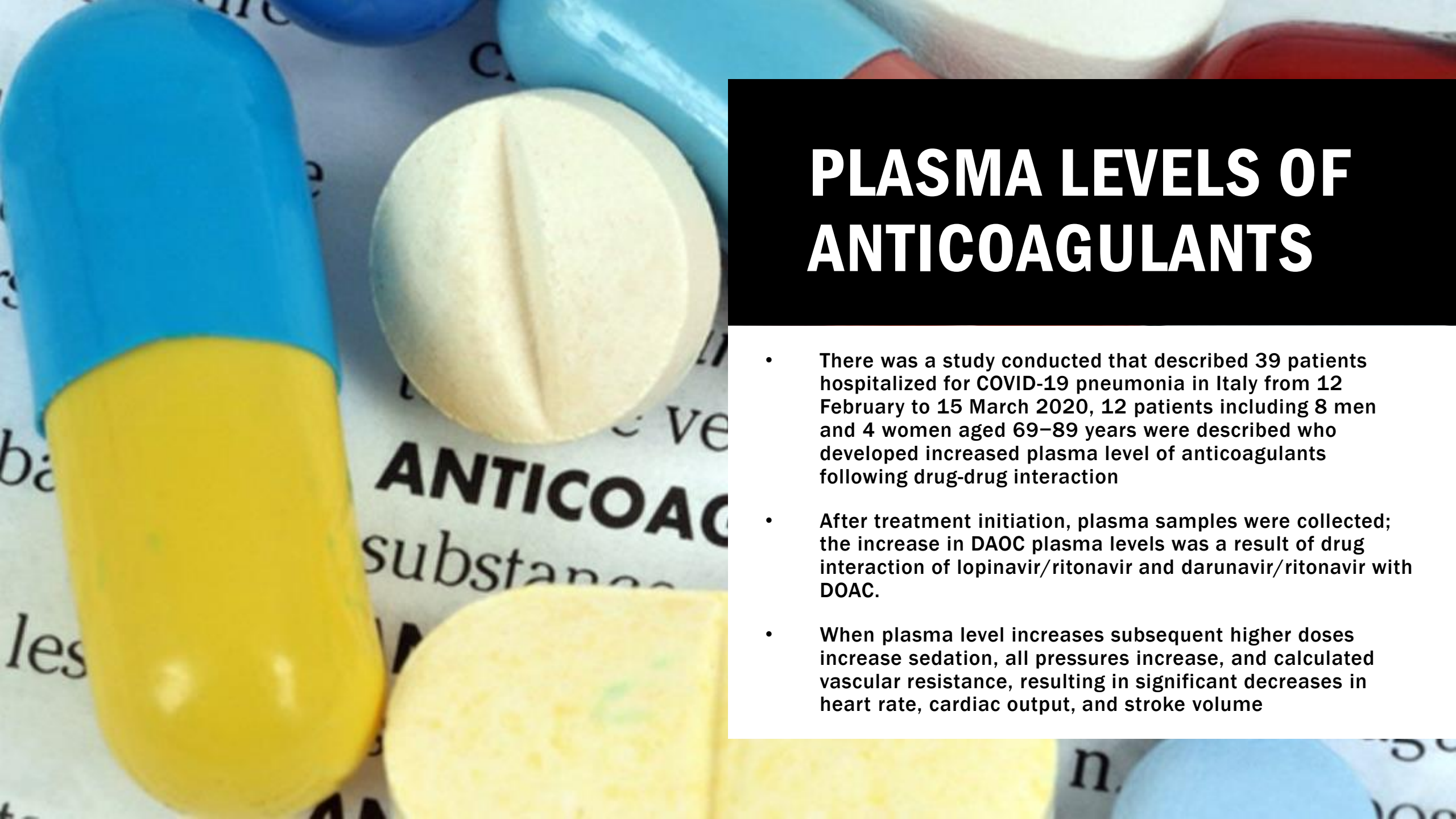
PRIOR USAGE

Continuous Renal Replacement Therapy:



ANTITHROMBOTIC DRUG INTERACTIONS WITH COVID-19 TREATMENT

- There’s interest in hydroxychloroquine as a COVID-19 treatment because early studies in the lab showed promise; they found that the drug had some antiviral effect on the cells infected with SARS-CoV-2
- The connection with this drug and antithrombotic treatments is that this drug works as an antithrombotic treatment and therefore renders that there is a link between antithrombotic therapies and a positive COVID-19 treatment
- This drug actively helps in preventing blood clots; however, there has been no data stating that this drug actually clinically benefitted hospitalized patients



PLASMA LEVELS OF ANTICOAGULANTS

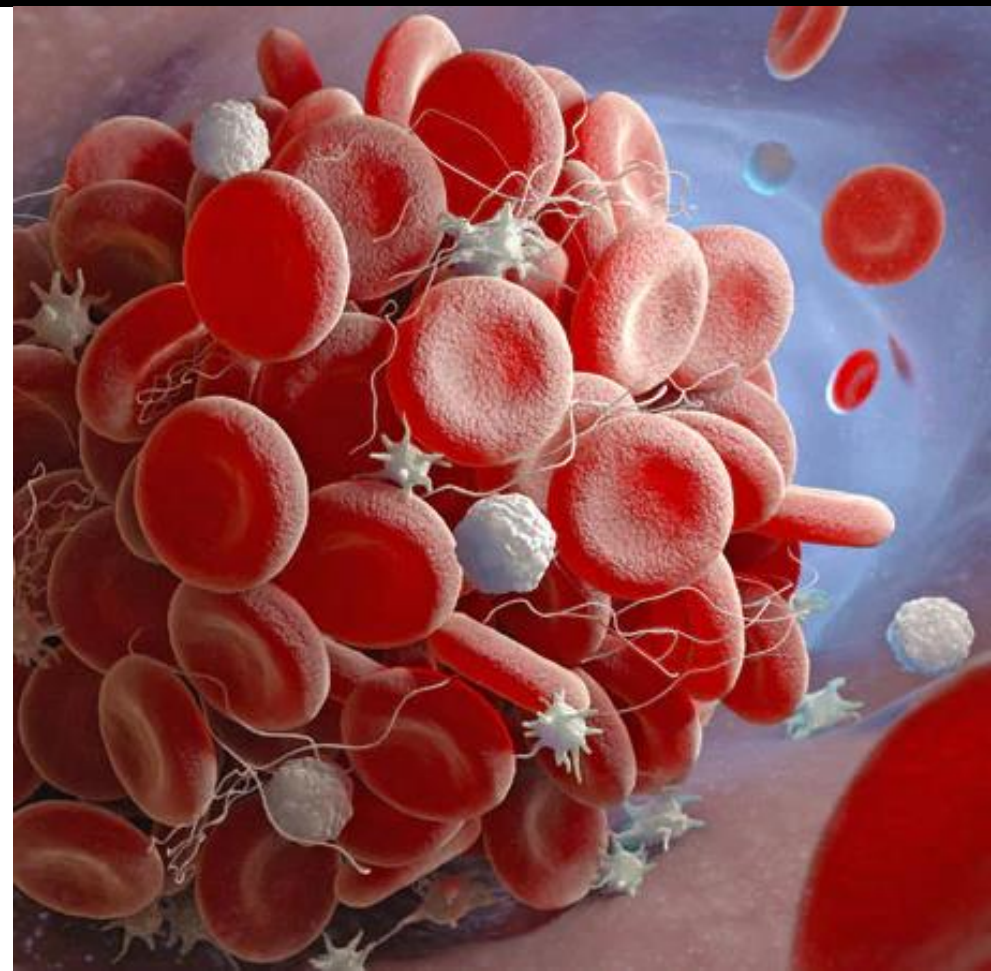
- There was a study conducted that described 39 patients hospitalized for COVID-19 pneumonia in Italy from 12 February to 15 March 2020, 12 patients including 8 men and 4 women aged 69–89 years were described who developed increased plasma level of anticoagulants following drug-drug interaction
- After treatment initiation, plasma samples were collected; the increase in DAOC plasma levels was a result of drug interaction of lopinavir/ritonavir and darunavir/ritonavir with DOAC.
- When plasma level increases subsequent higher doses increase sedation, all pressures increase, and calculated vascular resistance, resulting in significant decreases in heart rate, cardiac output, and stroke volume

ROLE OF COMBINING ANTICOAGULANT AND ANTIPLATELET AGENTS IN COVID-19 TREATMENT

- On the whole, combined antiplatelet and anticoagulant therapy increased patient survival and alleviated respiratory symptoms secondary to PE, which indicates an advantage for combination therapy over antiplatelet or anticoagulant therapy alone
- Moreover, therapeutic dose anticoagulation seems to reduce endothelial cell lesion which could also reduce the thromboembolic risk of COVID-19, suggesting another therapeutic target for anticoagulants

CONCLUSION

- The benefits of combining antiplatelet and anticoagulant treatments into an antithrombotic treatment for the beneficiary of treating COVID-19 are immense
- It is critical that pathophysiological principles are applied to develop a treatment that is aimed at reducing the risk of hospitalizations and death
- COVID-19 has proven to provide a great range of clinical severity and therefore the proposed algorithm of an antithrombotic therapy based on the key principles described must be put into effect



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