



## MEDICO RESEARCH CHRONICLES

ISSN NO. 2394-3971

DOI No. 10.26838/MEDRECH.2022.9.6.629

Contents available at [www.medrech.com](http://www.medrech.com)

### THROMBOEMBOLIC EVENTS AS A COMPLICATION OF COVID-19

<sup>1</sup> Dr. Dhiraj Giri, <sup>2</sup> Dr. Yogendra Sachdev, <sup>3</sup> Dr Ravindra Kawade, <sup>4</sup> Dr. Ganesh Vikhe

1. Junior Resident, Department of Radiodiagnosis, Rural Medical College, Loni

2. Prof. and HOD, Department of Radiodiagnosis, Rural Medical College, Loni

3. Professor, Department of Radiodiagnosis, Rural Medical College, Loni

4. Assistant Professor in the Department of Radiodiagnosis, Rural Medical College, Loni

#### ARTICLE INFO

#### ABSTRACT

#### CASE REPORT

##### Article History

Received: October 2022

Accepted: November 2022

**Key Words:** SARS-CoV2, thrombosis, hypercoagulability

##### Corresponding author

Dr. D. Giri\*

Coronavirus-2 (SARS-CoV2/ Severe Acute Respiratory Syndrome Corona Virus 2) infection has emerged as a global health crisis. The incidence of thromboembolic disease is very high in SARS- CoV2 disease and involves multiple organ systems ranging from cutaneous thrombosis to pulmonary embolism, stroke or coronary thrombosis sometimes with catastrophic outcomes. Evidence points towards a key role of thromboembolism, hypercoagulability and overproduction of proinflammatory cytokines mimicking a “cytokine storm” which leads to multiorgan failure

2022, [www.medrech.com](http://www.medrech.com)

#### INTRODUCTION:

Coronavirus disease 2019 (COVID-19) is a viral illness caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has been rapidly spreading throughout the world, causing a pandemic, involving >188 countries, >24 million cases, and >840,000 deaths. SARS-CoV-2 enters through angiotensin-converting enzyme 2 (ACE2) receptors, which are present in type 2 alveolar cells of the lung, myocardium, and proximal renal tubules. COVID-19 manifestations can range from asymptomatic infections to multiorgan failure and death. The respiratory system is involved in almost all cases. In both proven COVID-19 and COVID-like illness, fever, cough, dyspnea, chest pain, and oxygen desaturation upon exertion are

observed. These symptoms have been associated with increased D-dimer levels and pulmonary microangiopathy on necropsy. The kidneys can be involved, with a similar pathophysiology, presenting with hematuria and rapidly progressive renal failure with oliguria and death. There are various and diverse complications associated with SARS CoV-19 infection. Current data doesn't provide adequate information about the use of anticoagulants and management of thromboembolic events. Many authors suggest that a patient with high risk for development of thromboembolic state should be started with empirical anticoagulant treatment whereas some authors say that the use of full-dose anticoagulation should be done only in cases of confirmed thromboembolism.

## **PATHOGENESIS AND RISK FACTORS**

COVID-19 shows rise in pro and anti-inflammatory cytokines. There is evidence of complement activation in COVID-19 by direct endothelial infection which includes release of anaphylotoxin C5a. Complement activation as seen in COVID-19 not only drives neutrophil dysfunction leading to susceptibility to secondary infections but also activates the coagulation system thereby propagating a prothrombotic state. Coagulopathy associated with COVID-19 may be explained by the 'two way activation' theory, as seen by thrombocytopenia in critically ill patients (TICP) and the encompassing inflammatory and micro-thrombotic responses that occur when endothelial insult takes place. While the inflammatory pathway releases cytokines, the activation of microthrombotic pathway is mediated by release of large polymers of Von Willebrand factors (VWF). In the face of sepsis-induced endothelial injury, this reaction is aggravated causing enhanced platelet activation and consumption thrombocytopenia. In contrast to the typical consumptive coagulopathy and disseminated intravascular coagulation (DIC) profile observed in sepsis, patients with COVID-19 typically have relatively normal coagulation and platelet profiles. Progression to DIC occurs in a minority of patients, rarely developing in survivors. Therefore it seems that in keeping with Virchow's triad, thrombosis is driven both

by the activation of coagulation factors and endothelium. In-situ immune-thrombosis plays a key role to be the unifying mechanism explaining the micro and macrothrombotic manifestations of the disease. It should however be emphasized that in-situ microthrombosis has also been demonstrated in pulmonary and systemic tissue beds in ARDS and sepsis and therefore may not necessarily be unique to this population.

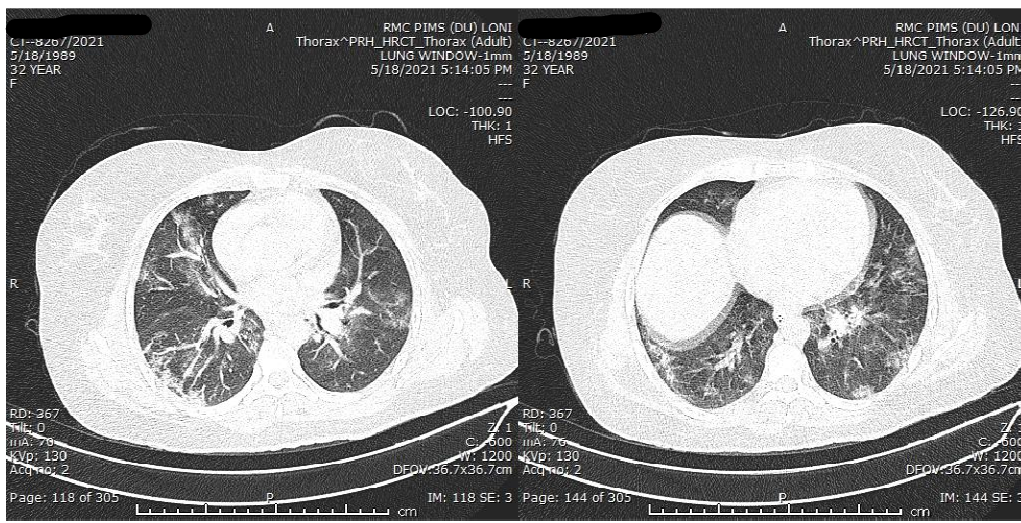
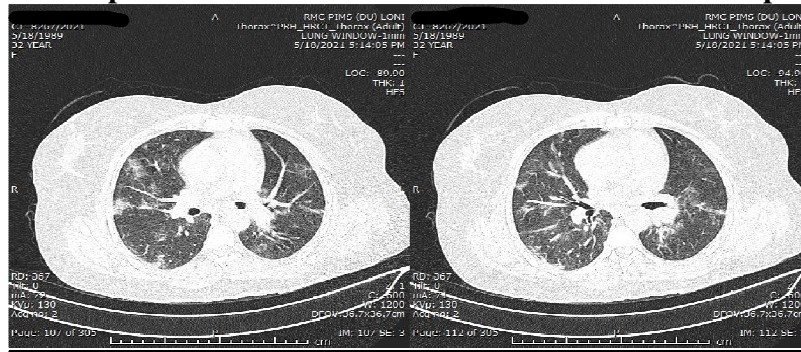
In addition to the factors mentioned above, these patients have additional risk factors for increased thrombosis, most notable among those being hypoxia, and immobility (made worse by frequent use of prone positioning). Although not systematically assessed, reduced staffing coupled with isolation precautions which limit frequent position changes and mobility may further predispose patients to a prothrombotic state

### **CASE REPORT 1:**

This is a case of a 32 yr female patient who was referred from outside to our hospital for a CT scan of Abdomen and Pelvis (Plain and contrast) with acute pain in abdomen to rule out intestinal perforation. The patient did not have fever, cough, cold, malaise or breathlessness since the beginning. The patient did not pass stools since 4 days. HRCT was done for the same as few ground glass opacities were noted in the visualized lung section during the abdomen scan.

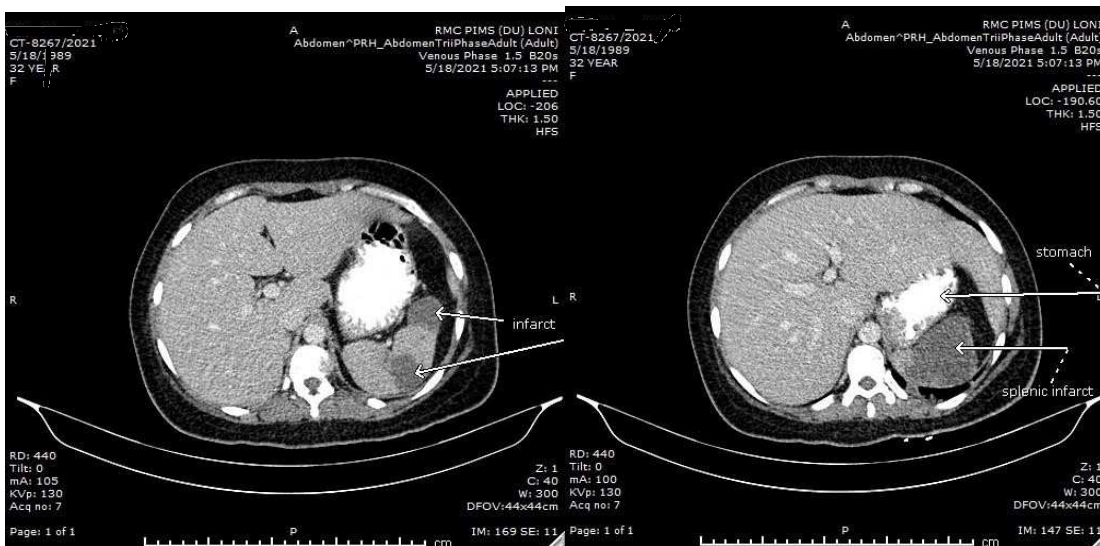
**INVESTIGATION:**

**CT scan of abdomen and pelvis and HRCT thorax was done for the same patient HRCT thorax**

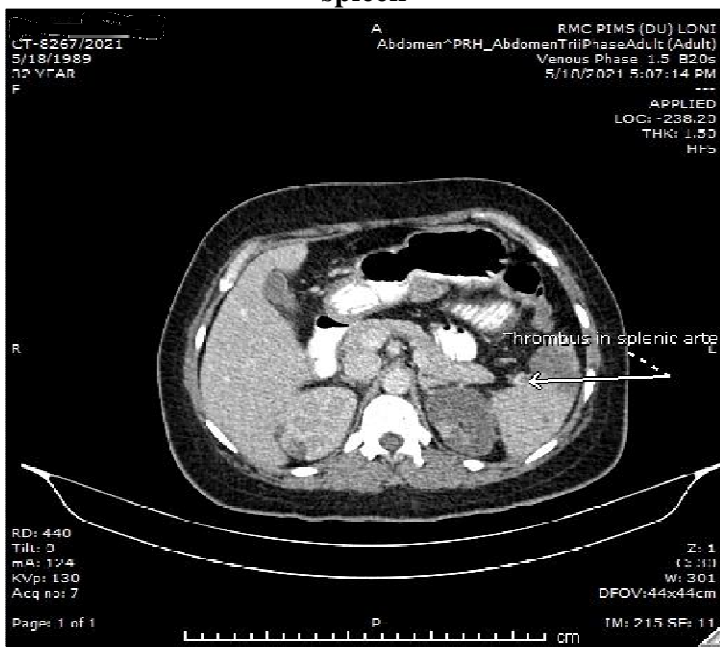


**ON HRCT findings were multiple subpleural and intrapulmonary ground glass opacities with interstitial septal thickening involving bilateral lung fields. It was typical for COVID- 19 (CORADS- V) and CT severity score was 12/25.**

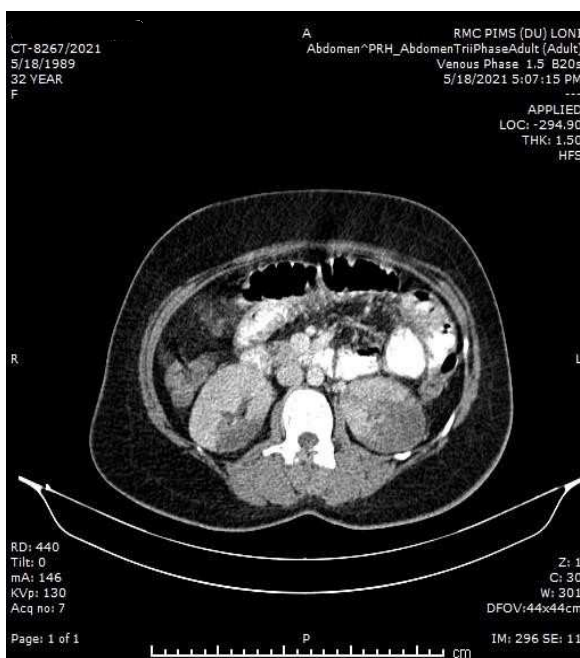
**CT ABDOMEN AND PELVIS**



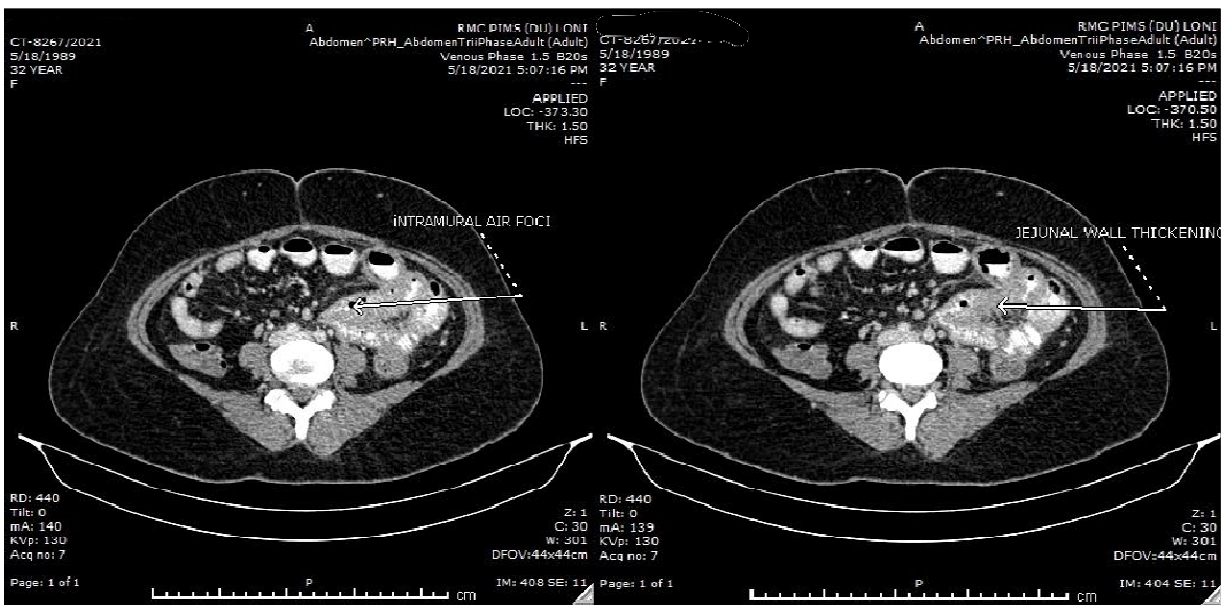
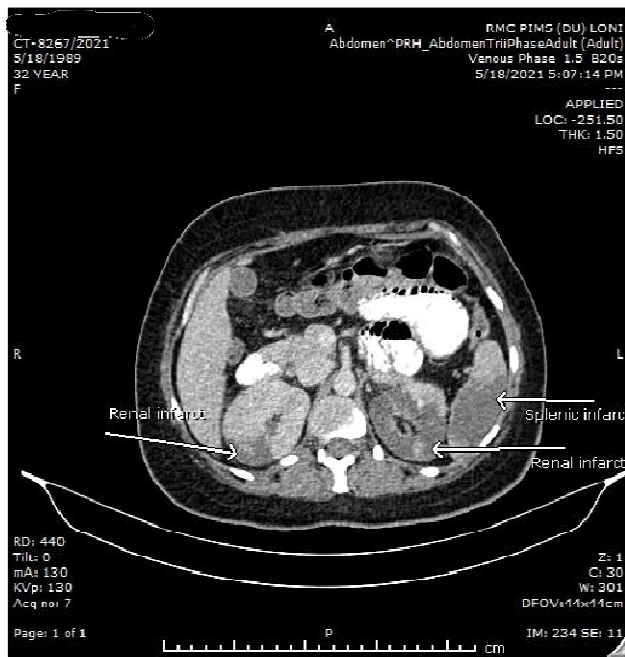
**Wedge shaped non enhancing hypodensities are noted at the upper pole and interpolar region of spleen**



**A hypodense filling defect is noted in the splenic artery which suggest thrombus with splenic infarct**



**Splenic and renal infarct**



In these images we can see jejunal wall thickening with intramural air foci with poor wall enhancement on post contrast study

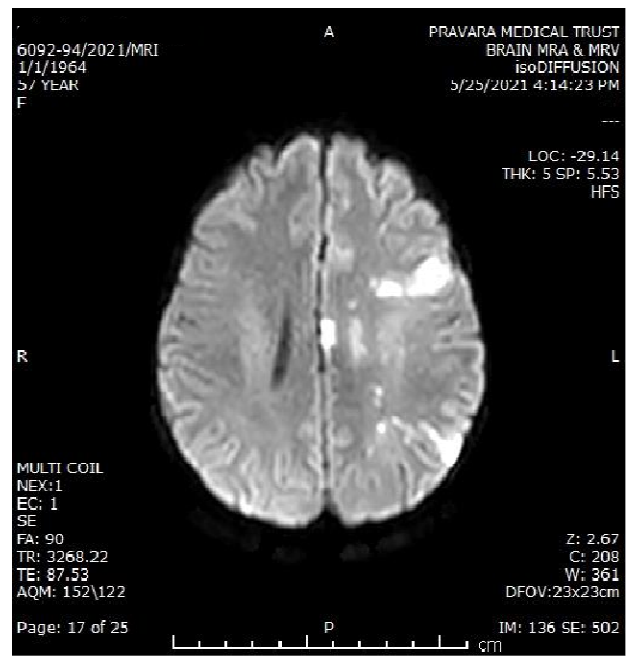
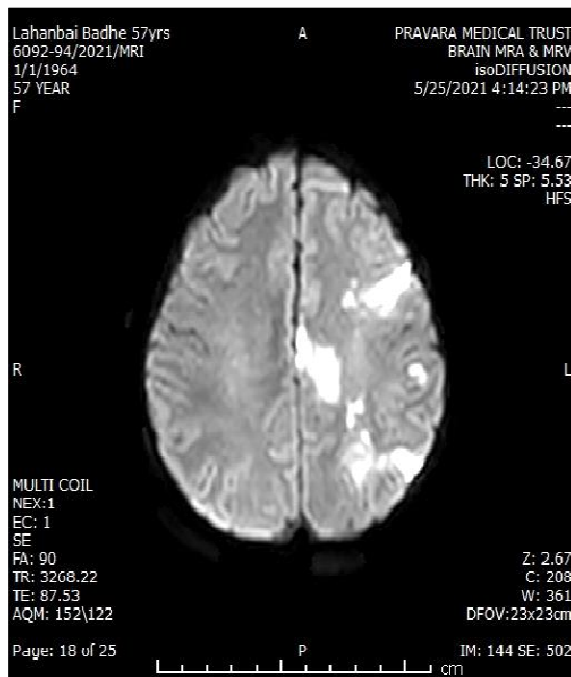
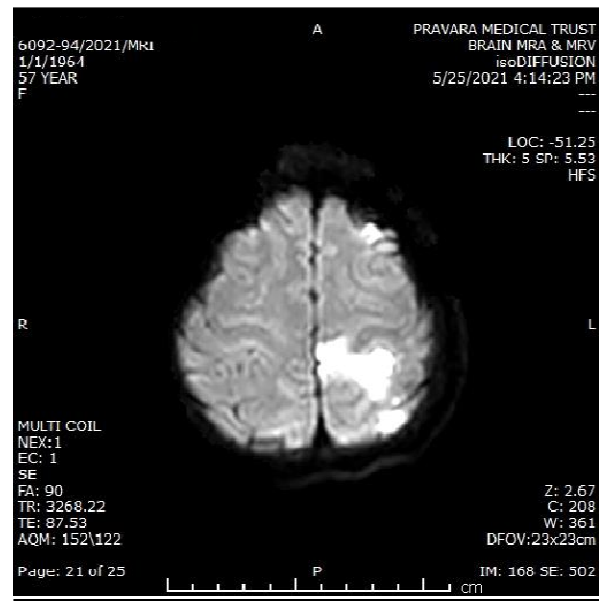
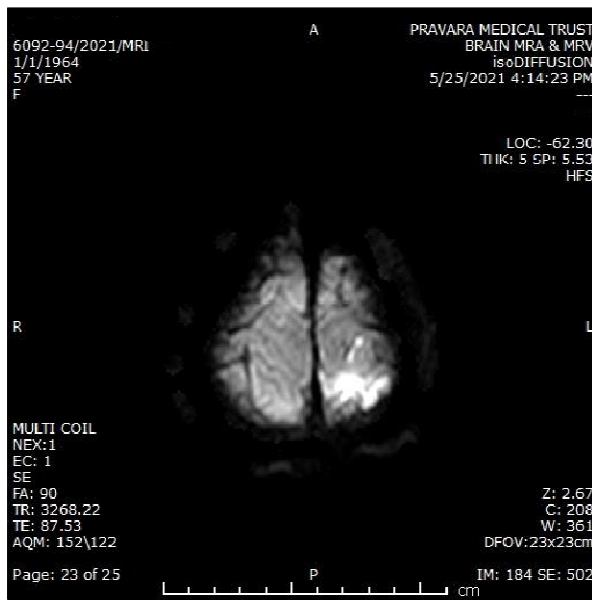
**TREATMENT:**

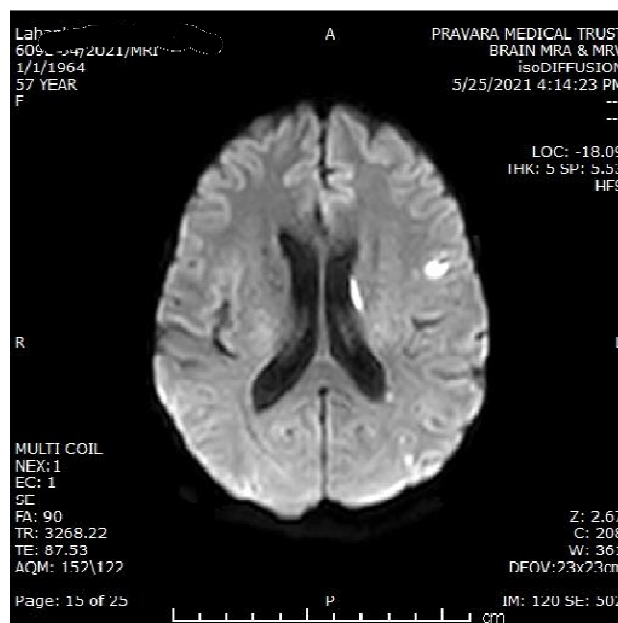
The patient was referred to different hospital after the scan where the patient was given antithrombotics

**CASE REPORT 2:****INVESTIGATION :**

**MRI brain revealed multiple infarcts in left fronto-parieto-temporal region**

This is a case of 57 yr female patient who came for MRI brain with complaints of right sided weakness since morning. She was a known case of COVID-19, 15 days ago.





### CASE REPORT 3:

A case of 30 year female patient who came for CT Abdomen and pelvis (Plain and contrast) with complaints of pain in right flank and iliac fossa since 15-20 days.

HRCT thorax of the same patient was done as she also had complaints of fever and cough since 15 days

### INVESTIGATION:

Blood investigation:

WBC- 14,460 (Increased)

CRP-70.9 (Increased) Urine analysis:

Appearance- clear

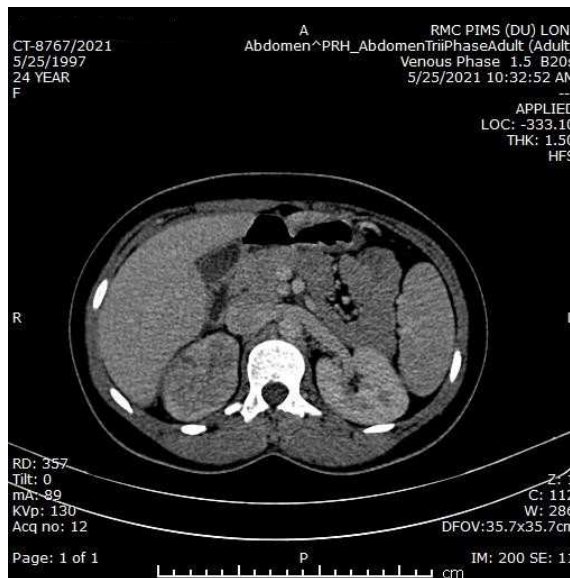
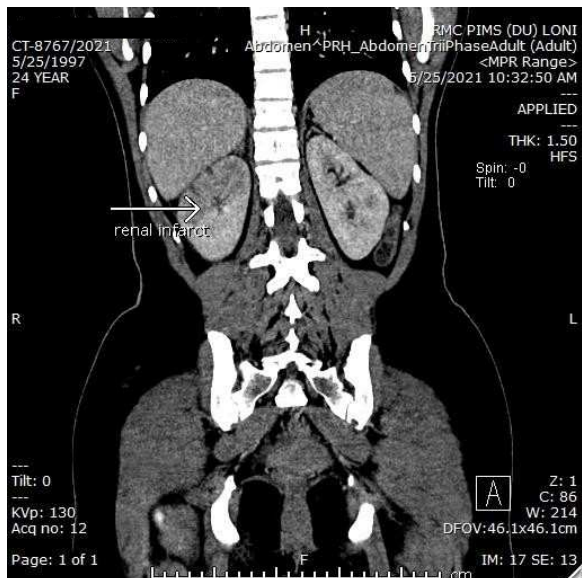
Deposits-absent

Rbc- 2-3 (Normal)

WBC- 3-4 (0-5)

**CT scan Abdomen and pelvis (Plain and contrast):**

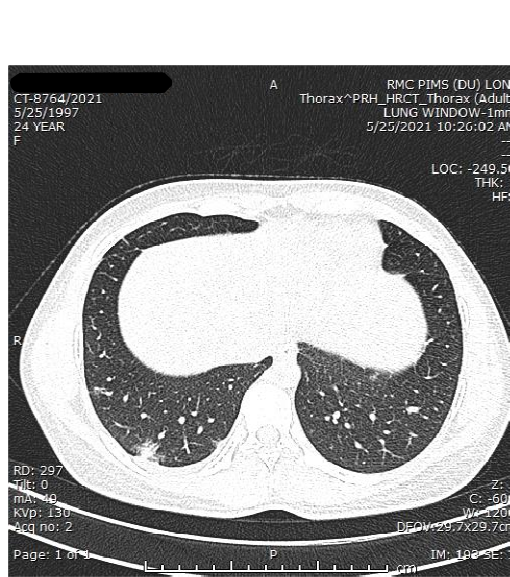
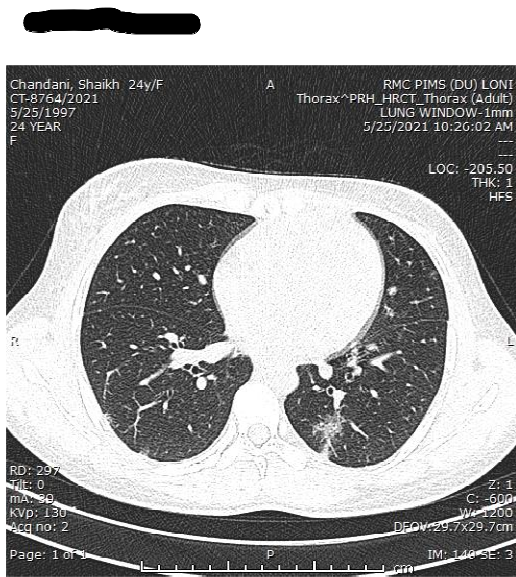
**CT scan revealed a hypodense non enhancing area involving cortex and medulla of upper**



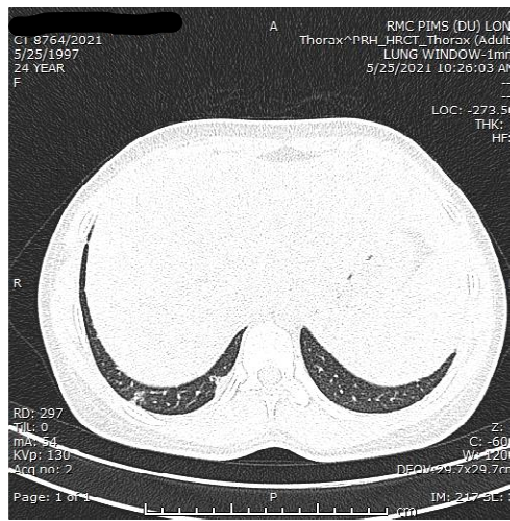
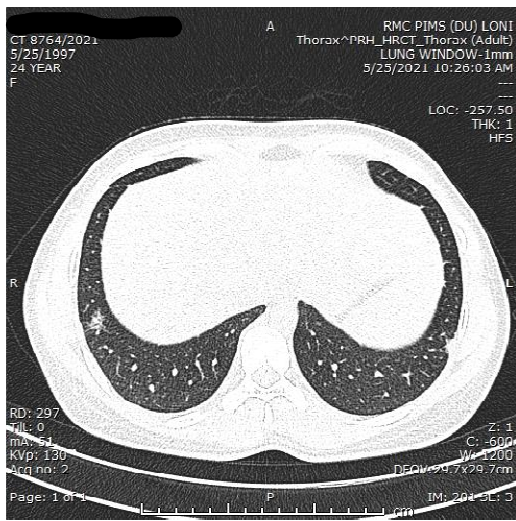
**and midpolar region of left kidney**

**HRCT thorax revealed multiple subpleural and intrapulmonary ground glass opacities in bilateral lung fields with CT severity score of 5/25**

**CT SCAN ABDOMEN AND PELVIS (PLAIN AND CONTRAST) HRCT THORAX**



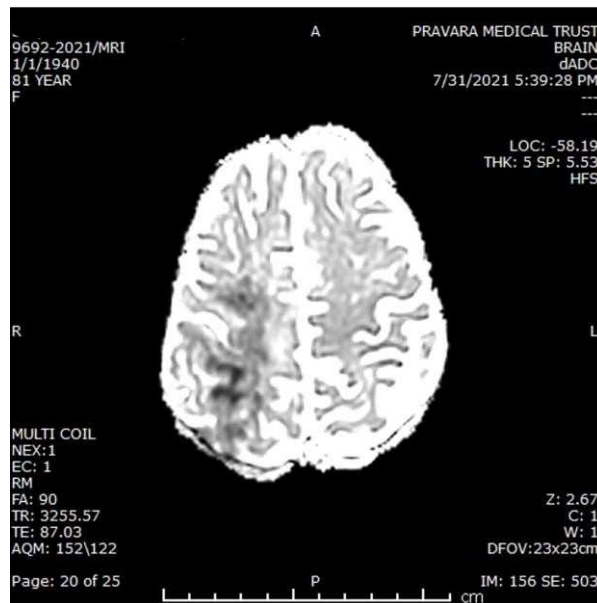
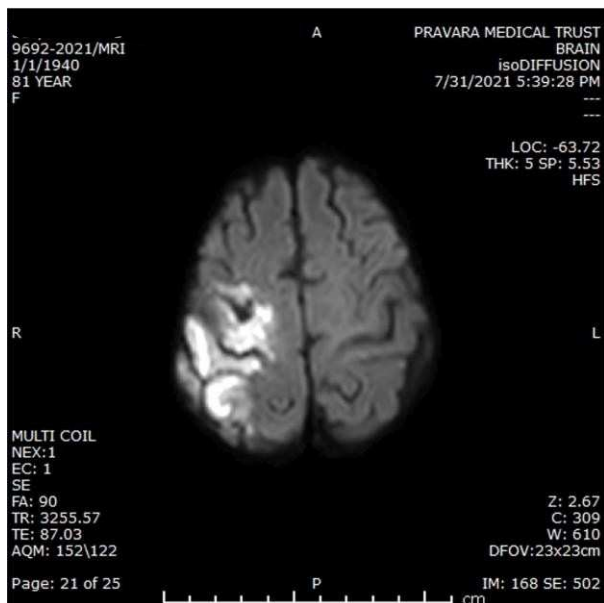


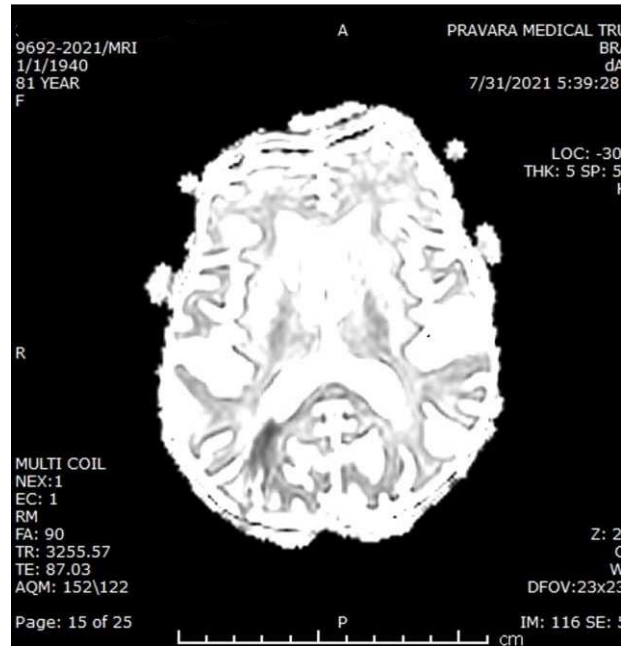
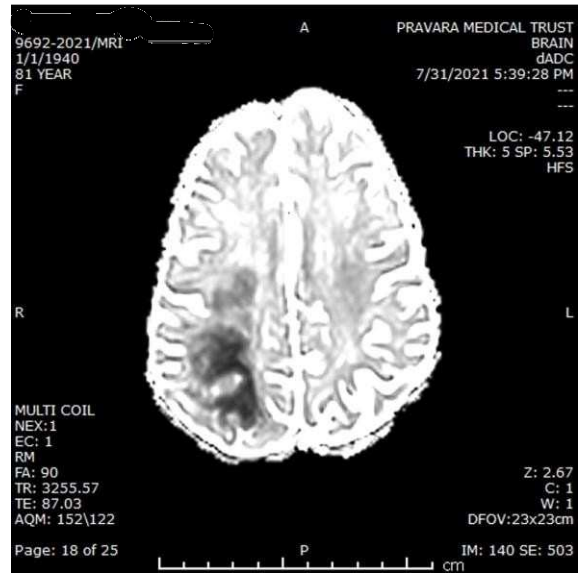
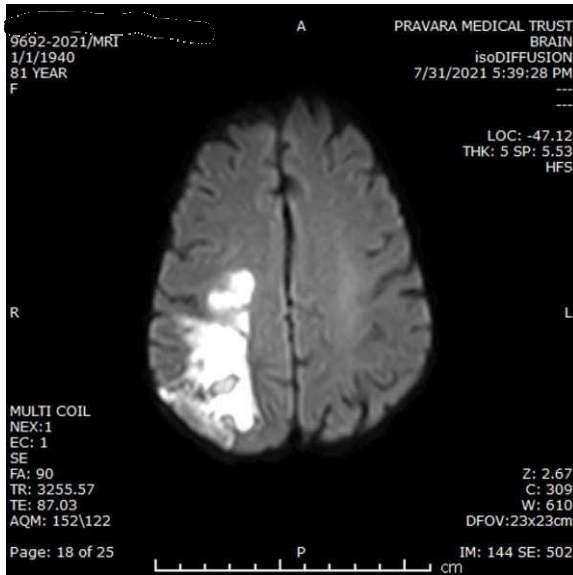


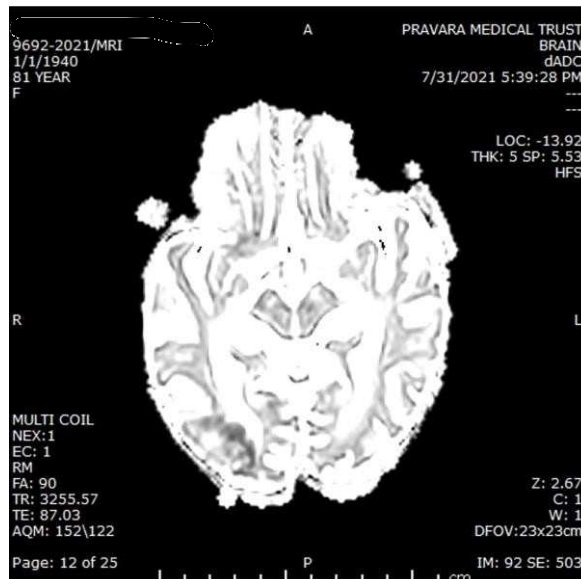
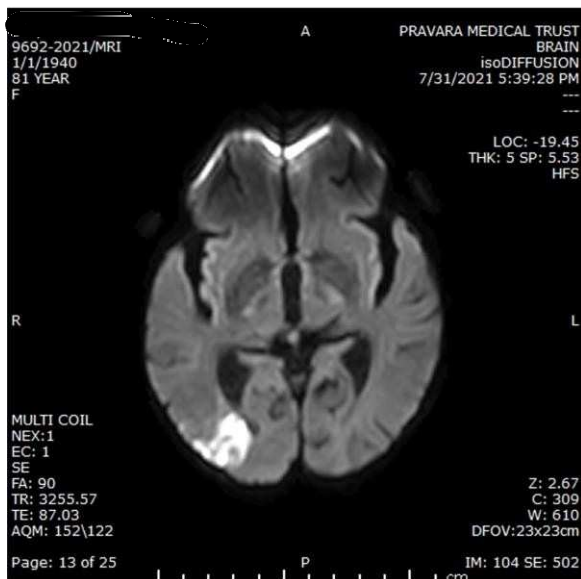
**Case no 4**

This is a case of 81 yr old female patient with a history of COVID-19 10 days back. The patient came with complaints of left sided weakness and disorientation. There was no known

comorbidity documented. The patient came for MRI Brain. Here are the diffusion and ADC images of the brain suggesting infarct on right side secondary to thromboembolic effect of COVID 19 infection.



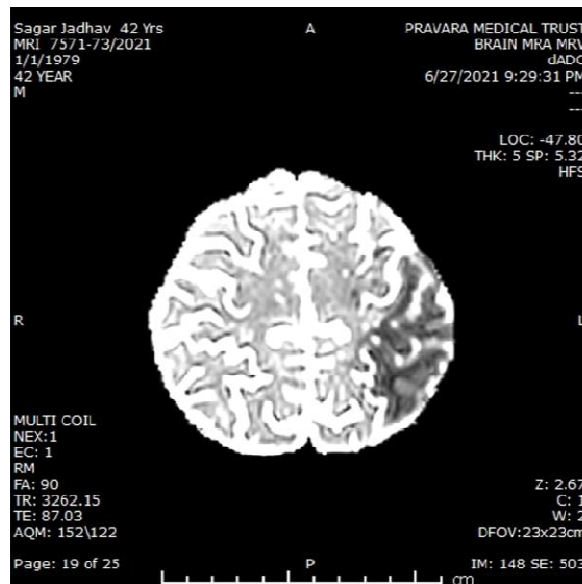
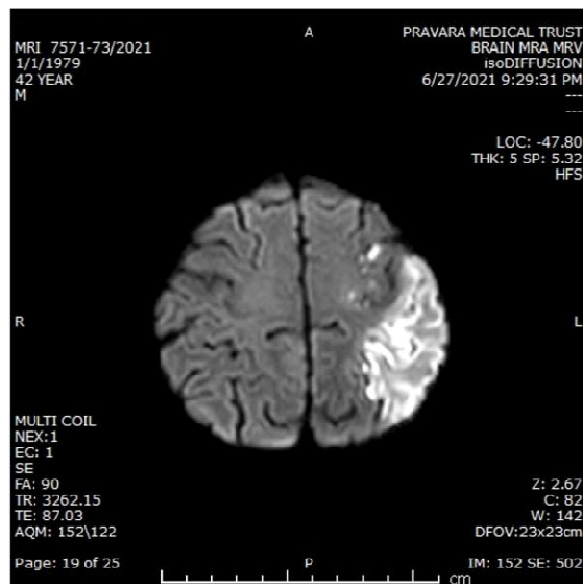


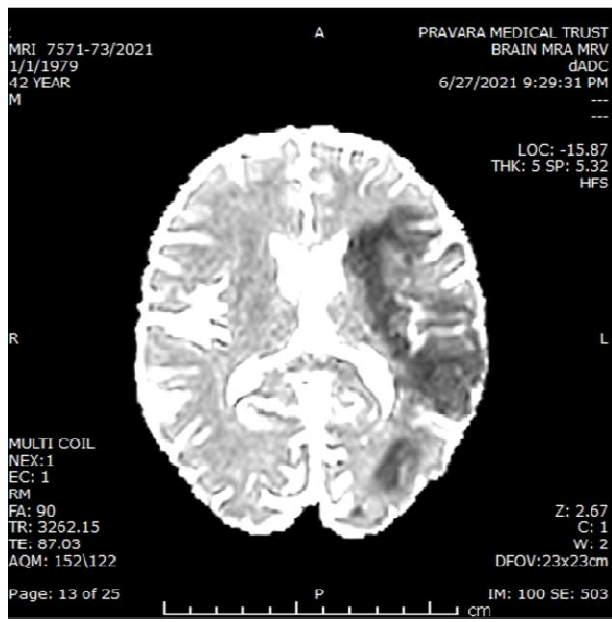
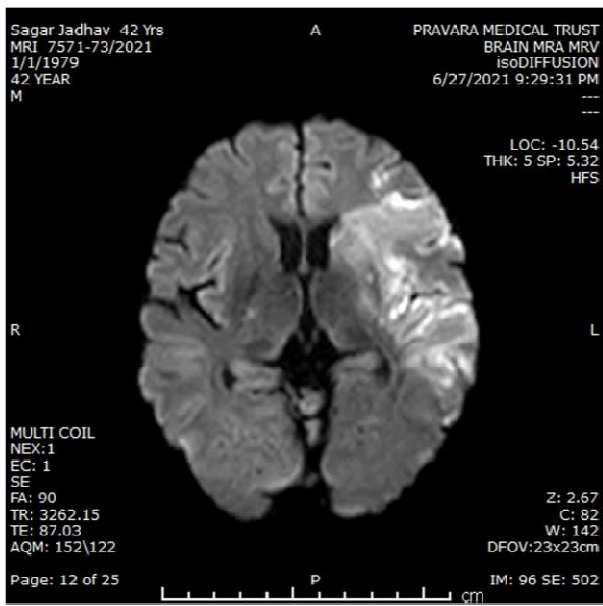
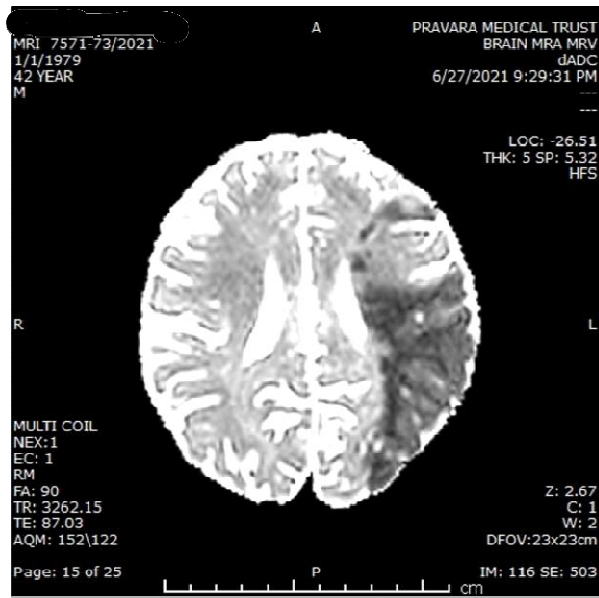
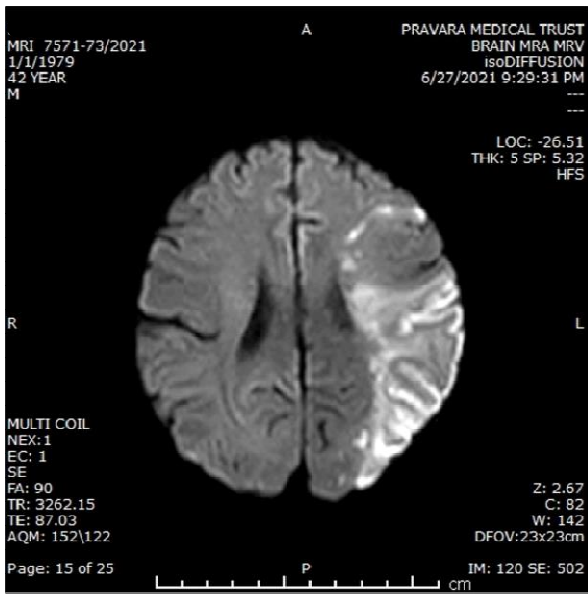


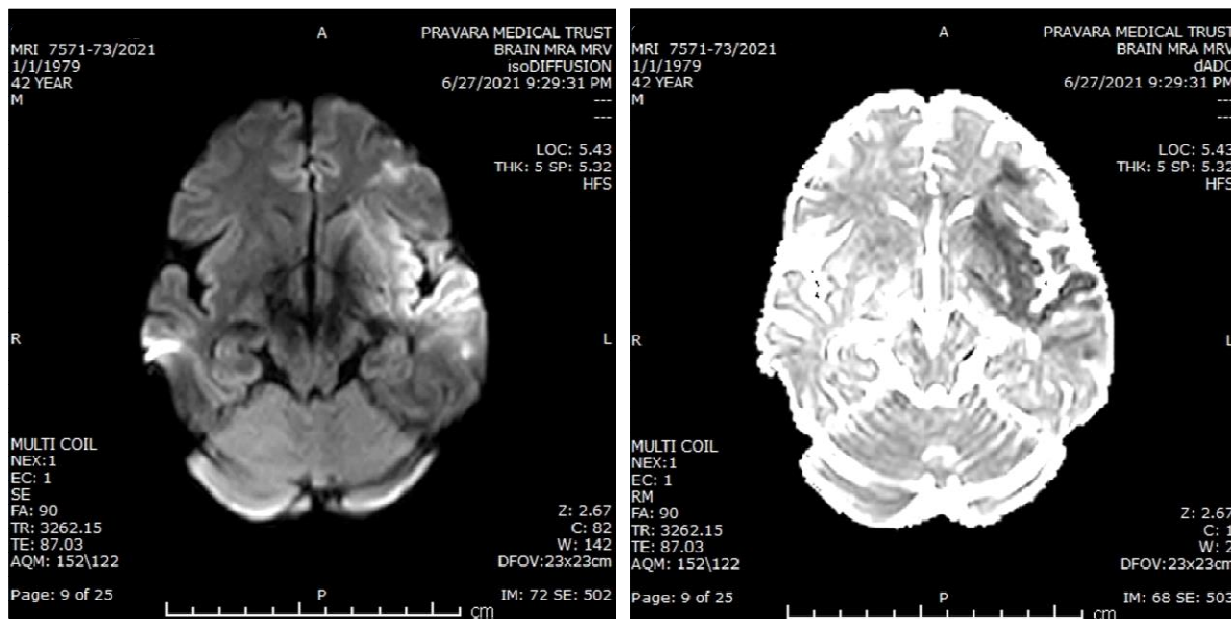
**Case no 5**

This is a case of 42 yr male patient with a history of COVID-19 infection. The patient came with complaints of right sided weakness since 1 day. No known comorbidities were

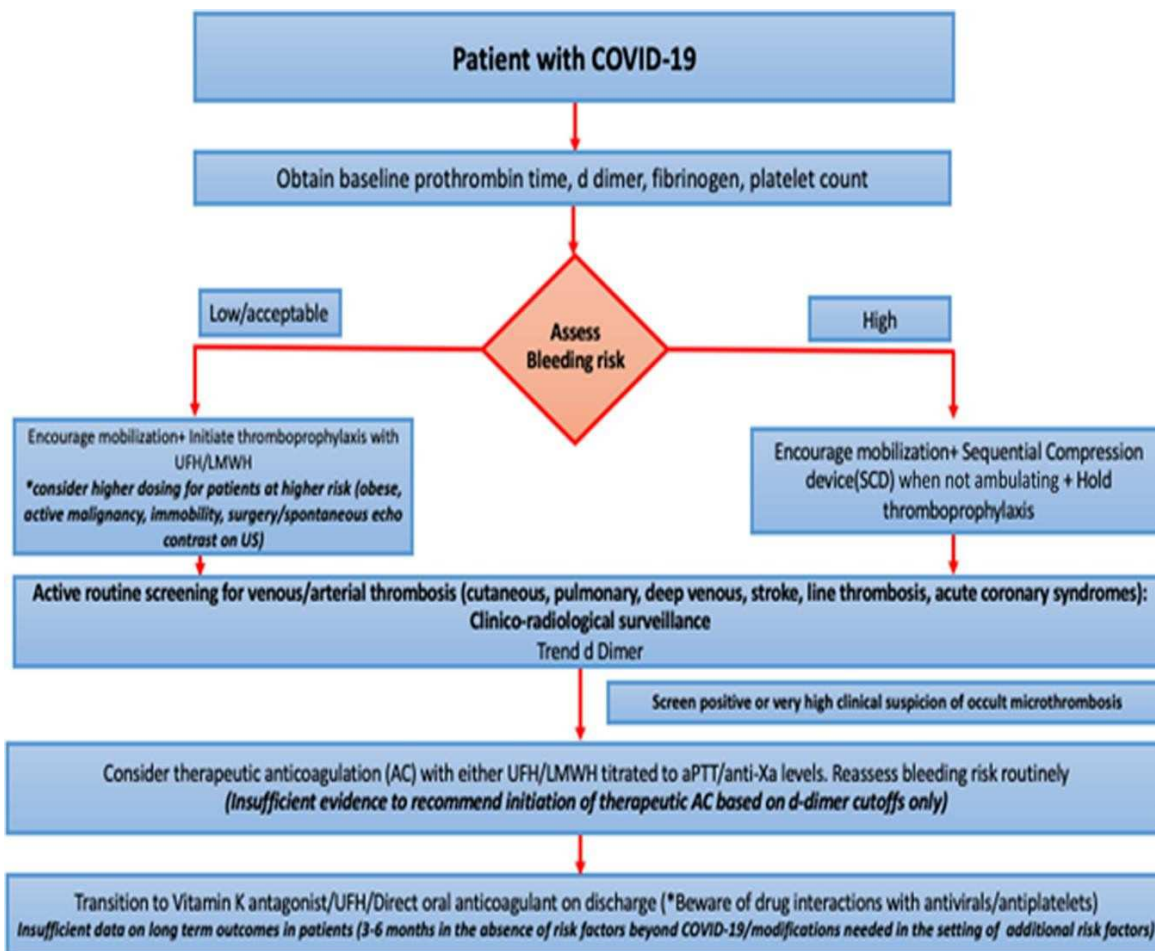
documented. The patient came for MRI Brain to rule out infarct. Here are the diffusion and ADC images of the patient representing left sided infarct. The patient was strated with thrombolytics immediately after the MRI







**Protocol for treatment of thromboembolic event in COVID-19 pateint**



## MANAGEMENT OF ANTICOAGULATION

The optimal approach to management of anticoagulation in these patients remains unclear in absence of well conducted trials. There remains major uncertainty in the optimal management of immune-thrombosis as commonly seen in COVID-19. In asymptomatic and mildly symptomatic patients who do not require hospital admission, ambulation should continue to be the mainstay of thromboprophylaxis. It is advisable to institute, at minimum, prophylactic anticoagulation in admitted patients without clinical contraindications. Unfractionated heparin and low molecular weight heparin (LMWH) have been successfully used in these patients both prophylactically and therapeutically. Higher doses should be considered for those with higher risk patients (eg, obese, active malignancy, prolonged immobility or recent surgery). As a caveat, it must be noted a high incidence of VTE has been noted even on patients on either prophylactic and therapeutic anticoagulation which makes routine surveillance extremely important.

In addition to the usual indications such as obesity or active malignancy where higher intensity dosing of prophylactic anticoagulation may be warranted, patients with COVID-19 who demonstrate SEC on surveillance imaging may be considered for augmented dosing although high quality data to support routine use of this strategy is currently unavailable. Although some retrospective studies have demonstrated systemic anticoagulation to be associated with improved outcomes in hospitalized patients

## CONCLUSION

Systemic thrombosis is frequently associated with critically ill COVID-19 patients and may lead to fatal outcomes if not diagnosed and managed appropriately. Thrombotic risk commonly persists despite initiation of anticoagulation. Until more information is

available, providers should consider prophylactic versus therapeutic anticoagulation based on a combination of patient specific criteria including laboratory results, imaging, clinical suspicion and careful balance of thrombotic and bleeding risks. Routine active surveillance guided by clinical and/or radiological assessment is recommended to either pre-empt or aid prompt diagnosis of macrothrombotic events which may be beneficial in guiding anticoagulation strategies. Larger, well designed prospective studies are urgently needed to further elucidate optimal management strategies to mitigate the thrombotic risks associated with COVID-19.

## REFERENCES

- Medicine JHU. Corona Virus Resource Center. 04.28.2020 ed. Baltimore, USA 2020.
- Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. JAMA 2020.
- Meduri GU, Kohler G, Headley S, Tolley E, Stentz F, Postlethwaite A. Inflammatory cytokines in the BAL of patients with ARDS. Persistent elevation over time predicts poor outcome. Chest. 1995;108:1303–14.
- Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus 5.
- Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS- CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med 2020.
- Llitjos JF, Leclerc M, Chochois C, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost. 2020.
- Klok FA, Kruip M, van der Meer NJM, et al. Incidence of thrombotic complications in

- critically ill ICU patients with COVID-19. *Thromb Res.* 2020;191:145–7.
- Klok FA, Kruip M, van der Meer NJM, et al. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: An updated analysis. *Thromb Res.* 2020;191:148–50.
  - Yang Y SC, Li J, Yuan J, Yang M et al. Exuberant elevation of IP-10, MCP-3 and IL-1ra during SARS-CoV-2 infection is associated with disease severity and fatal outcome. medRxiv 2020.
  - Faix JD. Biomarkers of sepsis. *Crit Rev Clin Lab Sci.* 2013;50:23–36.
  - Gao T HM, Zhang X, Li H, Zhu L et al. Highly pathogenic coronavirus N protein aggravates lung injury by MASP-2-mediated complement over-activation. medRxiv 2020.
  - Chang JC. Hemostasis based on a novel 'two-path unifying theory' and classification of hemostatic disorders. *Blood Coagul Fibrinolysis.* 2018;29:573–84.
  - Chang JC. Sepsis and septic shock: endothelial molecular pathogenesis associated with vascular microthrombotic disease. *Thromb J.* 2019;17:10.
  - Gupta N, Zhao YY, Evans CE. The stimulation of thrombosis by hypoxia. *Thromb Res.* 2019;181:77–83.
  - Kollias A, Kyriakoulis KG, Dimakakos E, Poulakou G, Stergiou GS, Syrigos K. Thromboembolic risk and anticoagulant therapy in COVID-19 patients: emerging evidence and call for action. *Br J Haematol.* 2020.
  - Yao XH, Li TY, He ZC, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies. *Zhonghua Bing Li Xue Za Zhi.* 2020;49:E009.
  - Barton LM, Duval EJ, Stroberg E, Ghosh S, Mukhopadhyay S. COVID-19 Autopsies. USA. *Am J Clin Pathol: Oklahoma;* 2020.
  - Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. *Transl Res.* 2020;220:1–13.
  - Ciceri F, Beretta L, Scandroglio AM, et al. Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis. *Crit Care Resusc.* 2020;22:95–7.
  - Dolhnikoff M, Duarte-Neto AN, de Almeida Monteiro RA, et al. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19. *J Thromb Haemost.* 2020.
  - Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res.* 2020;191:9–14.
  - Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost.* 2020.
  - 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.
  - Wichmann D, Sperhake JP, Lutgehetmann M, et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. *Ann Intern Med.* 2020.
  - Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost.* 2020.
  - Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. *N Engl J Med.* 2020.
  - Demelo-Rodriguez P, Cervilla-Munoz E, Ordieres-Ortega L, et al. Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and

- elevated D-dimer levels. *Thromb Res.* 2020;192:23–6.
- Zhang L, Feng X, Zhang D, et al. Deep Vein Thrombosis in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) in Wuhan, China: Prevalence, Risk Factors, and Outcome. *Circulation* 2020.
  - Ren B, Yan F, Deng Z, et al. Extremely High Incidence of Lower Extremity Deep Venous Thrombosis in 48 Patients with Severe COVID-19 in Wuhan. *Circulation.* 2020.
  - Stoneham SM, Milne KM, Nuttal E, et al. Thrombotic risk in COVID-19: a case series and case-control study. *Clin Med (Lond).* 2020.
  - Voicu S, Bonnin P, Stepanian A, et al. High prevalence of deep vein thrombosis in mechanically ventilated COVID-19 patients. *J Am Coll Cardiol.* 2020.
  - Desborough MJR, Doyle AJ, Griffiths A, Retter A, Breen KA, Hunt BJ. Image-proven thromboembolism in patients with severe COVID-19 in a tertiary critical care unit in the United Kingdom. *Thromb Res.* 2020;193:1–4.
  - Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID and Coagulation: Bleeding and Thrombotic Manifestations of SARS-CoV2 Infection. *Blood.* 2020.
  - Fraisse M, Logre E, Pajot O, Mentec H, Plantefeve G, Contou D. Thrombotic and hemorrhagic events in critically ill COVID-19 patients: a French monocenter retrospective study. *Crit Care.* 2020;24:275.
  - 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.
  - Baldacini M, Pop R, Sattler L, et al. Concomitant hemorrhagic syndrome and recurrent extensive arterial thrombosis in a patient with COVID-19 and acute promyelocytic leukemia. *Br J Haematol.* 2020.
  - Giacomelli E, Dorigo W, Fargion A, Calugi G, Cianchi G, Pratesi C. Acute thrombosis of an aortic prosthetic graft in a patient with severe COVID-19 related pneumonia. *Ann Vasc Surg.* 2020.
  - Lacour T, Semaan C, Genet T, Ivanec F. Insights for increased risk of failed fibrinolytic therapy and stent thrombosis associated with COVID-19 in ST-segment elevation myocardial infarction patients. *Catheter Cardiovasc Interv.* 2020.
  - de Barry O, Mekki A, Diffre C, Seror M, Hajjam ME, Carlier RY. Arterial and venous abdominal thrombosis in a 79-year-old woman with COVID-19 pneumonia. *Radiol Case Rep.* 2020.
  - Mulvey JJ, Magro CM, Ma LX, Nuovo GJ, Baergen RN. Analysis of complement deposition and viral RNA in placentas of COVID-19 patients. *Ann Diagn Pathol.* 2020;46:151530.
  - Griffin DO, Jensen A, Khan M, et al. Pulmonary Embolism and Increased Levels of d-Dimer in Patients with Coronavirus Disease. *Emerg Infect Dis.* 2020;26.
  - Zhou B, She J, Wang Y, Ma X. Venous thrombosis and arteriosclerosis obliterans of lower extremities in a very severe patient with 2019 novel coronavirus disease: a case report. *J Thromb Thrombolysis.* 2020.
  - Zhou B, She J, Wang Y, Ma X. A Case of Coronavirus Disease 2019 With Concomitant Acute Cerebral Infarction and Deep Vein Thrombosis. *Front Neurol.* 2020;11:296.
  - Dominguez-Erquicia P, Dobarro D, Raposeiras-Roubin S, Bastos-Fernandez G, Iniguez-Romo
  - Multivessel coronary thrombosis in a patient with COVID-19 pneumonia. *Eur Heart J.* 2020.
  - Martinelli I, Ferrazzi E, Ciavarella A, et al. Pulmonary embolism in a young pregnant woman with COVID-19. *Thromb Res.* 2020;191:36–7.



- Bozzani A, Arici V, Franciscone MM, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Infection and the Upper Limb Deep Vein Thrombosis Risk. *Ann Vasc Surg.* 2020.
- Poggiali E, Bastoni D, Ioannilli E, Vercelli A, Magnacavallo A. Deep Vein Thrombosis and Pulmonary Embolism: Two Complications of COVID-19 Pneumonia? *Eur J Case Rep Intern Med.* 2020;7:001646.
- Hughes C, Nichols T, Pike M, Subbe C, Elghenzai S. Cerebral Venous Sinus Thrombosis as a Presentation of COVID-19. *Eur J Case Rep Intern Med.* 2020;7:001691.
- Kashi M, Jacquin A, Dakhil B, et al. Severe arterial thrombosis associated with Covid-19 infection. *Thromb Res.* 2020;192:75–7.
- Garaci F, Di Giuliano F, Picchi E, Da Ros V, Floris R. Venous cerebral thrombosis in COVID-19 patient. *J Neurol Sci.* 2020;414:116871.
- Lax SF, Skok K, Zechner P, et al. Pulmonary Arterial Thrombosis in COVID-19 With Fatal Outcome: Results From a Prospective. *Clinicopathologic Case Series. Ann Intern Med: Single-Center;* 2020.
- Mestres G, Puigmacia R, Blanco C, Yugueros X, Esturrica M, Riambau V. Risk of peripheral arterial thrombosis in COVID-19. *J Vasc Surg.* 2020.
- Gomez-Arbelaez D, Ibarra-Sanchez G, Garcia-Gutierrez A, Comanges-Yeboles A, Ansuategui-Vicente M, Gonzalez-Fajardo JA. Covid-19-Related Aortic Thrombosis: A Report of Four Cases. *Ann Vasc Surg.* 2020.
- Davoodi L, Jafarpour H, Taghavi M, Razavi A. COVID-19 Presented With Deep Vein Thrombosis: An Unusual Presenting. *J Investig Med High Impact Case Rep.* 2020;8:2324709620931239.
- Viguier A, Delamarre L, Duplantier J, Olivot JM, Bonneville F. Acute ischemic stroke complicating common carotid artery thrombosis during a severe COVID-19 infection. *J Neuroradiol.* 2020.
- Rey JR, Valero SJ, Pinedo DP, Llorens JLM, Lopez-Sendon JL, Caro-Codon J. [COVID-19 and simultaneous thrombosis of two coronary arteries]. *Rev Esp Cardiol* 2020.
- Bhayana R, Som A, Li MD, et al. Abdominal Imaging Findings in COVID-19: Preliminary Observations. *Radiology.* 2020;201908.
- Hemasian H, Ansari B. First case of Covid-19 presented with cerebral venous thrombosis: A rare and dreaded case. *Rev Neurol (Paris).* 2020;176:521–3.
- Fara MG, Stein LK, Skliut M, Morgello S, Fifi JT, Dhamoon MS. Macrothrombosis and stroke in patients with mild Covid-19 infection. *J Thromb Haemost.* 2020.
- Azouz E, Yang S, Monnier-Cholley L, Arrive L. Systemic arterial thrombosis and acute mesenteric ischemia in a patient with COVID-19. *Intensive Care Med.* 2020.
- Nauka PC, Oran E, Chekuri S. Deep venous thrombosis in a non-critically ill patient with novel COVID-19 infection. *Thromb Res.* 2020;192:27–8.
- Seif S, Ayuna A, Kumar A, Macdonald J. Massive coronary thrombosis caused primary percutaneous coronary intervention to fail in a COVID-19 patient with ST-elevation myocardial infarction. *Catheter Cardiovasc Interv.* 2020.
- Morales MH, Leigh CL, Simon EL. COVID-19 infection with extensive thrombosis: A case of phlegmasia cerulea dolens. *Am J Emerg Med.* 2020.
- Kaur P, Qaqa F, Ramahi A, et al. Acute upper limb ischemia in a patient with COVID-19. *Hematol Oncol Stem Cell Ther.* 2020.
- Fox SE, Akmatbekov A, Harbert JL, Li G, Quincy Brown J, Vander Heide RS. Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. *Lancet Respir Med.* 2020.

- Hinterseer M, Zens M, Wimmer RJ, et al. Acute myocardial infarction due to coronary stent thrombosis in a symptomatic COVID-19 patient. *Clin Res Cardiol.* 2020.
- Vulliamy P, Jacob S, Davenport RA. Acute aorto-iliac and mesenteric arterial thromboses as presenting features of COVID-19. *Br J Haematol.* 2020.
- L AB, Pacioni C, Ponton S, Francavilla S, Cuzzoli A. Arterial Mesenteric Thrombosis as a Complication of SARS-CoV-2 Infection. *Eur J Case Rep Intern Med.* 2020;7:001690.
- Faggiano P, Bonelli A, Paris S, et al. Acute pulmonary embolism in COVID-19 disease: Preliminary report on seven patients. *Int J Cardiol.* 2020.
- Szekely Y, Lichter Y, Taieb P, et al. The Spectrum of Cardiac Manifestations in Coronavirus Disease 2019 (COVID-19) - a Systematic Echocardiographic Study. *Circulation.* 2020.
- Harari R, Bangalore S, Chang E, Shah B. COVID-19 complicated by acute myocardial infarction with extensive thrombus burden and cardiogenic shock. *Catheter Cardiovasc Interv.* 2020.
- Andrea V, Gianluca F, Rodolfo P, Paolo T, Alessandro P, Mauro G. Unheralded Lower Limb Threatening Ischemia in a COVID-19 Patient. *Int J Infect Dis.* 2020.
- La Mura V, Artoni A, Martinelli I, et al. Acute Portal Vein Thrombosis in SARS-CoV-2 Infection: A Case Report. *Am J Gastroenterol.* 2020.
- Horowitz JM, Yuriditsky E, Henderson IJ, Stachel MW, Kwok B, Saric M. Clot in Transit on Transesophageal Echocardiography in a Prone Patient with COVID-19 Acute Respiratory Distress Syndrome. *CASE (Phila).* 2020.
- Buja LM, Wolf DA, Zhao B, et al. The emerging spectrum of cardiopulmonary pathology of the coronavirus disease 2019 (COVID-19): Report of 3 autopsies from Houston, Texas, and review of autopsy findings from other United States cities. *Cardiovasc Pathol.* 2020;48:107233.
- Qanadli SD, Gudmundsson L, Rotzinger DC. Catheter-directed thrombolysis in COVID-19 pneumonia with acute PE: Thinking beyond the guidelines. *Thromb Res.* 2020;192:9–11.
- Vitali C, Minniti A, Caporali R, Del Papa N. Occurrence of pulmonary embolism in a patient with mild clinical expression of COVID-19. *Thromb Res.* 2020;192:21–2.
- Zayet S, Klopfenstein T, Kovacs R, Stancescu S, Hagenkotter B. Acute Cerebral Stroke with Multiple Infarctions and COVID-19, France, 2020. *Emerg Infect Dis.* 2020;26.
- Baergen RN, Heller DS. Placental Pathology in Covid-19 Positive Mothers: Preliminary Findings. *Pediatr Dev Pathol.* 2020;23:177–80.
- Malentacchi M, Gned D, Angelino V, et al. Concomitant brain arterial and venous thrombosis in a COVID-19 patient. *Eur J Neurol.* 2020.
- Ding S, Lin Q, Zhu T, et al. Is there a correlation between inflammatory markers and coagulation parameters in women with advanced ovarian endometriosis? *BMC Womens Health.* 2019;19:169.
- Zhang L, Yan X, Fan Q, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. *J Thromb Haemost.* 2020;18:1324–9.
- Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. *Blood.* 2020;135:2033–40.
- Seirafianpour F, Sodagar S, Mohammad AP, et al. Cutaneous manifestations and considerations in COVID-19 pandemic: A systematic review. *Dermatol Ther.* 2020.
- Spiezia L, Boscolo A, Poletto F, et al. COVID-19-Related Severe Hypercoagulability in Patients Admitted to Intensive Care Unit for Acute Respiratory Failure. *Thromb Haemost.* 2020;120:998–1000.

- Panigada M, Bottino N, Tagliabue P, et al. Hypercoagulability of COVID-19 patients in Intensive Care Unit. A Report of Thromboelastography Findings and other Parameters of Hemostasis. *J Thromb Haemost* 2020.
- Dugar S, Duggal A, Bassel A, Soliman M, Moghekar A. Spontaneous echo contrast in venous ultrasound of severe COVID-19 patients. *Intensive Care Med*. 2020.
- Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-up. *J Am Coll Cardiol*. 2020.
- Thachil J, Tang N, Gando S, et al. Type and dose of heparin in COVID-19. *J Thromb Haemost*. 2020.
- Belen-Apak FB, Sarialioglu F. The old but new: Can unfractionated heparin and low molecular weight heparins inhibit proteolytic activation and cellular internalization of SARS-CoV2 by inhibition of host cell proteases? *Med Hypotheses*. 2020;142:109743.
- Paranjpe I, Fuster V, Lala A, et al. Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19. *J Am Coll Cardiol*. 2020.
- Streiff MB, Agnelli G, Connors JM, et al. Guidance for the treatment of deep vein thrombosis and pulmonary embolism. *J Thromb Thrombolysis*. 2016;41:32–67.
- Kumar P, Mediwake R, Rhead C. A matter of time: duration and choice of venous thromboprophylaxis in patients diagnosed with COVID-19. *Br J Hosp Med (Lond)*. 2020;81:1–2.
- Testa S, Prandoni P, Paoletti O, 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.
- Marullo AG, Cavarretta E, Biondi-Zoccai G, et al. Extracorporeal membrane oxygenation for critically ill patients with coronavirus-associated disease 2019: an updated perspective of the European experience. *Minerva Cardioangiol*. 2020.
- Zochios V, Brodie D, Charlesworth M, Parhar KK. Delivering extracorporeal membrane oxygenation for patients with COVID-19: what, who, when and how? *Anaesthesia*; 2020.
- Koeckerling D, Pan D, Mudalige NL, Oyefeso O, Barker J. Blood transfusion strategies and ECMO during the COVID-19 pandemic. *Lancet Respir Med*. 2020.
- Lukito P, Wong A, Jing J, et al. Mechanical circulatory support is associated with loss of platelet receptors glycoprotein Ibalpha and glycoprotein VI. *J Thromb Haemost*. 2016;14:2253–60.
- Horiuchi H, Doman T, Kokame K, Saiki Y, Matsumoto M. Acquired von Willebrand Syndrome Associated with Cardiovascular Diseases. *J Atheroscler Thromb*. 2019;26:303–14.
- Hashmi NK, Ghadimi K, Srinivasan AJ, et al. Three-factor prothrombin complex concentrates for refractory bleeding after cardiovascular surgery within an algorithmic approach to haemostasis. *Vox Sang*. 2019;114:374–85.
- Piacente C, Martucci G, Miceli V, et al. A narrative review of antithrombin use during veno-venous extracorporeal membrane oxygenation in adults: rationale, current use, effects on anticoagulation, and outcomes. *Perfusion*. 2020;267659120913803.
- Kurihara C, Walter JM, Karim A, et al. Feasibility of veno-venous extracorporeal membrane oxygenation without systemic anticoagulation. *Ann Thorac Surg* 2020.
- Chen L, Li Q, Zheng D, et al. Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan. *China N Engl J Med*. 2020.

- Dashraath P, Wong JLJ, Lim MXK, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. Am J Obstet Gynecol. 2020;222:521–31.
  - Simcox LE, Ormesher L, Tower C, Greer IA. Thrombophilia and Pregnancy Complications. Int J Mol Sci. 2015;16:28418–28.
-