



www.mecs.com/

Multi-Knowledge Electronic Comprehensive Journal For Education
And Science Publications (MECSJ)

Issue (39),2020

ISSN: 2617-9563

MANAGING THE RISK OF VTE IN COVID-19 PATIENTS

DR. JALEEL M ABDULLA -CONSULTANT INTERNAL MEDICINE, PHCC, QATAR

drjaleelabdullah@gmail.com

DR. BABUR QAYYUM KHAN -CONSULTANT FAMILY MEDICINE, PHCC, QATAR

khanbabur@hotmail.com

DR. AZIZ UR REHMAN -GENERAL PRACTITIONER, PHCC, QATAR

aziz_azim2000@yahoo.com

1. ABSTRACT

This review article tries to address the relation of VTE and Covid-19 and attempts to clarify whether patients who suffer with Covid-19 should receive anticoagulation therapy. [1] The incidence of VTE in COVID-19 patients varies depending on the patient population, the severity of the symptoms, age, pre-existing medical conditions, co-morbidities, and previous history of VTE. Like most risk factors for VTE, such as being obese, having underlying cancer, or having suffered a VTE in the past, these patients are at a higher risk of developing VTE due to Covid-19 infection compared to fit and healthy individuals. Those who receive hospital admission and are subsequently admitted to an ICU are also at a higher risk of developing VTE than individuals who suffer with mild symptoms. [2] Studies have identified a wide range of Covid-19 suffers experiencing VTE from 1.1% in non-ICU hospital wards to 69% in ICU patients screened with lower extremity ultrasound. The risk of VTE following hospital discharge appears low, and patients who did not require hospitalization had no incidence of VTE reported.[3]

Keywords: Covid-19, Venous Thromboembolism, Thromboprophylaxis, Anticoagulants



www.mecsj.com/

Multi-Knowledge Electronic Comprehensive Journal For Education
And Science Publications (MECSJ)

Issue (39),2020

ISSN: 2617-9563

المخلص

هذه المقالة تحاول توضيح ما إذا كان المرضى الذين Covid-19 و VTE يحاول معالجة العلاقة بين في مرضى VTE يجب أن يتلقوا علاجًا مضادًا للتخثر. [1] يختلف معدل حدوث Covid-19 يعانون من اعتمادًا على عدد المرضى ، وشدة الأعراض ، والعمر ، والحالات الطبية الموجودة مسبقًا COVID-19 مثل معظم عوامل خطر الإصابة بالجلطات الدموية . VTE ، والأمراض المصاحبة ، والتاريخ السابق لـ في الماضي ، يكون VTE الوريدية ، مثل السمنة أو الإصابة بالسرطان الأساسي أو الإصابة بالتهاب مقارنة Covid-19 هؤلاء المرضى أكثر عرضة للإصابة بالجلطات الدموية الوريدية بسبب عدوى بالأفراد الأصحاء. أولئك الذين يتلقون دخولاً إلى المستشفى ويتم قبولهم لاحقاً في وحدة العناية المركزة هم أيضاً أكثر عرضة للإصابة بالجلطات الدموية الوريدية من الأفراد الذين يعانون من أعراض خفيفة. [2] من 1.1٪ في VTE الذين يعانون من Covid-19 حددت الدراسات مجموعة واسعة من المصابين بـ أجنحة المستشفيات غير وحدات العناية المركزة إلى 69٪ في مرضى وحدة العناية المركزة الذين تم فحصهم باستخدام الموجات فوق الصوتية في الأطراف السفلية. يبدو أن خطر الإصابة بالجلطات الدموية الوريدية بعد الخروج من المستشفى منخفضاً ، والمرضى الذين لم يحتاجوا إلى دخول المستشفى لم يكن لديهم حالات حدوث VTE

الكلمات الرئيسية: كوفيد-19 ، الجلطات الدموية الوريدية ، الوقاية من التخثر ، مضادات التخثر



www.mecsj.com/

Multi-Knowledge Electronic Comprehensive Journal For Education
And Science Publications (MECSJ)

Issue (39),2020

ISSN: 2617-9563

2. INTRODUCTION

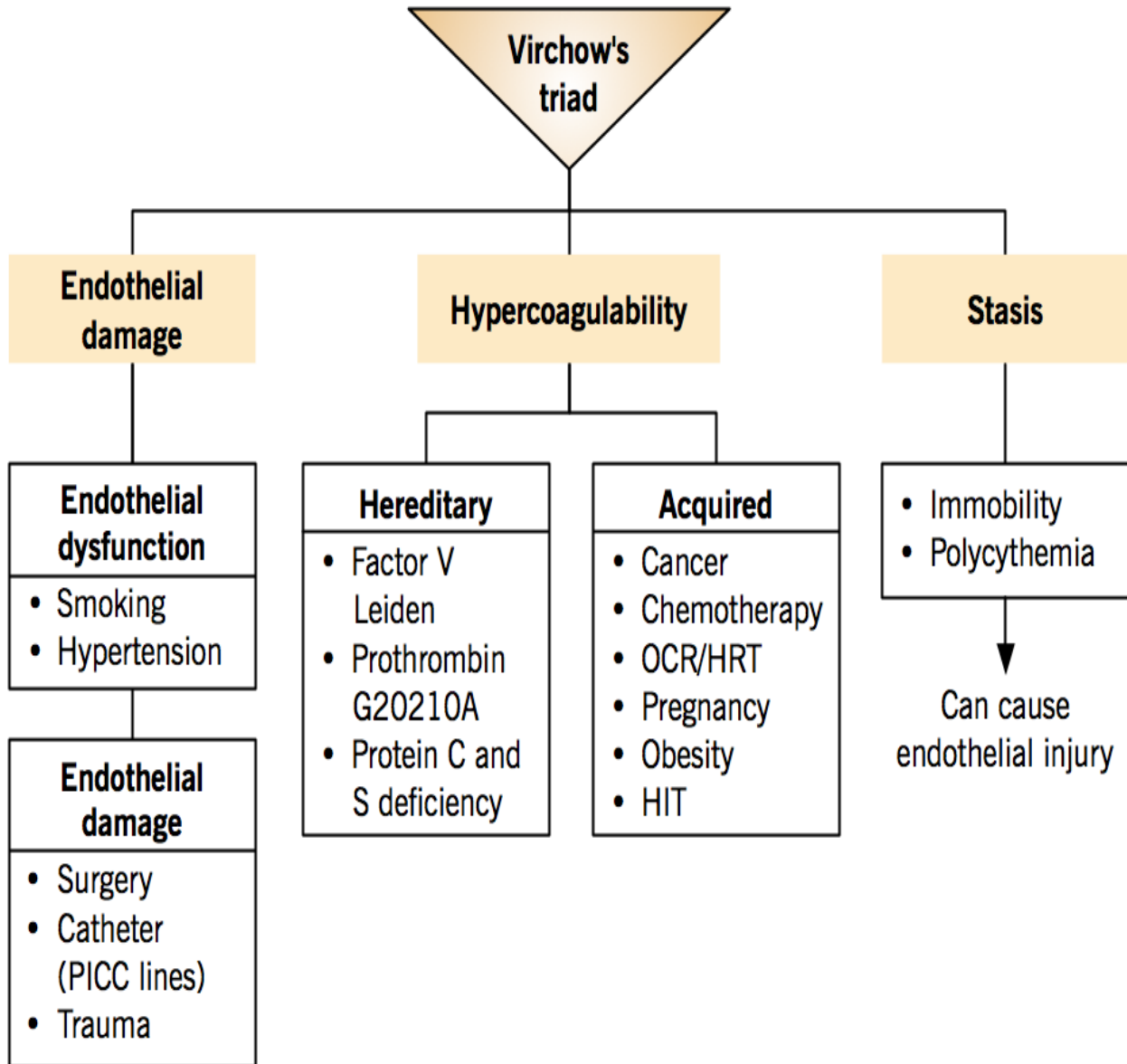
Research on Covid-19 is revealing more about this deadly virus than was known at the beginning of the pandemic. Researchers worldwide have developed new strategies and approaches to managing these patients from those who present with mild symptoms to those who are critical and end up on ICU. It is understood that Covid-19 infection can be complicated with coagulopathy, namely disseminated intravascular coagulation that leads to a high risk of VTE. It is understood that patients admitted to the ICU are at a higher risk of developing VTE. [4]

Based on these findings it has been suggested that all hospitalized patients should receive thromboprophylaxis with LMWH, unless the risk of bleeding outweighs the risk of thrombosis. Those who are on the ICU and who present with more severe symptoms could be offered full therapeutic intensity anti-coagulation depending on the local therapeutic guidelines, however due to the lack of quality published evidence, an intermediate-intensity protocol which includes administering the usual daily LMWH dose twice daily has been widely adopted. In those where anticoagulants are contraindicated or not available, the use of mechanical thromboprophylaxis such as pneumatic compression devices can be used.

3. PATHOPHYSIOLOGY OF VTE

Venous thromboembolism is associated with **Virchow's triad**: three conditions that predispose to thrombus formation.[5]

1. Hypercoagulability
2. Stasis
3. Endothelial damage



4. Clinical Presentation of VTE

Symptomatic VTE can cause either a deep vein thrombosis or a pulmonary embolism and present as follows

DVT symptoms include:



www.mecs.com/

Multi-Knowledge Electronic Comprehensive Journal For Education
And Science Publications (MECSJ)

Issue (39),2020

ISSN: 2617-9563

- Pain or tenderness in your arm or leg, usually in the thigh or calf
- Swollen leg or arm
- Skin that red or warm to the touch
- Red streaks on the skin

With a pulmonary embolism, you could notice:

- Shortness of breath you can't explain
- Fast breathing
- Chest pain under your rib cage that can get worse when you take a deep breath
- Rapid heart rate
- Feeling lightheaded or passing out

5. DIAGNOSIS

To rule out VTE, the following investigations need to be performed

D-dimer: This looks for levels of D-dimer

Duplex ultrasound. Checks the veins in the lower extremities or upper extremities for any signs of a clot

Pulse oximetry: This is often the first test. A low level could indicate respiratory disease due to covid-19 or due to a PE.

Arterial blood gas: This would provide more information of the pH, oxygen saturation, type 1 and type 2 respiratory failure.

Chest X-ray: This test helps rule out a clot show up on which does not show up on an X-rays, but other conditions, like pneumonia or pleural effusion will do.

Ventilation perfusion (V/Q) scan: To check the lungs for air flow (ventilation, or V) and blood flow (perfusion, or Q).



www.mecsj.com/

Multi-Knowledge Electronic Comprehensive Journal For Education
And Science Publications (MECSJ)

Issue (39),2020

ISSN: 2617-9563

Spiral computed tomography: This is a special version of a CT scan in which the scanner rotates to create a cross-section view of the lungs.

Pulmonary angiogram: This is an invasive test where a catheter is placed into the vein and guide it to the veins and arteries around the heart. They'll use it to inject a dye that shows up on an X-ray. This helps them see if there's a clot in your lungs.

6. TYPES OF ANTICOAGULANTS

Anticoagulants generally include non-VKA oral anticoagulants (NOACs), heparins and vitamin K antagonists.

Vitamin K Antagonists (Warfarin, Coumarins)

Vitamin K Antagonists (VKA) like Warfarin are a group of substances that reduce blood clotting by reducing the action of vitamin K. Vitamin K in turn is needed for the proper synthesis of certain clotting factors in the liver.

Non-VKA Oral Anticoagulants (NOACs)

Rivaroxaban, Edoxaban, and Apixaban

These are all a direct Factor Xa inhibitor oral anticoagulant and work by inhibiting Factor Xa, a protein that helps blood clots form.

Dabigatran

By contrast to the NOACs listed above, Dabigatran is a direct thrombin inhibitor oral anticoagulant. Dabigatran works by inhibiting the action of thrombin, a protein that helps blood clots form.



www.mecsaj.com/

Multi-Knowledge Electronic Comprehensive Journal For Education
And Science Publications (MECSJ)

Issue (39),2020

ISSN: 2617-9563

Heparin

Heparin works immediately, preventing further clotting and is available in two forms

- Standard (unfractionated) heparin- can be administered either through an intravenous or subcutaneous injection or an intravenous infusion/drip.
- Low-molecular-weight heparin (LMWH)- include **dalteparin**, **enoxaparin**, and **tinzaparin**, are usually given as subcutaneous injections.

7. PATHOPHYSIOLOGY OF VTE IN COVID 19 PATIENTS

It is understood that hospitalized patients have predisposing factors for VTE, namely being bed bound, or immobile and as a result are considered for thromboprophylaxis. However, it appears that in COVID-19 patients' additional mechanisms might contribute to increased VTE risk, including endothelial damage, microvascular thrombosis and occlusion, or even autoimmune mechanisms. More studies are needed to elaborate on the possible mechanisms underlying this association.[6]

8. THERAPEUTIC -INTENSITY ANTICOAGULATION IN SERIOUSLY ILL COVID 19 PATIENTS IN THE ABSENSE OF CONFIRMED OR SUSPECTED VTE

There have not been enough reliable studies to suggest that all critically ill Covid-19 patients should receive therapeutic intensity anticoagulation in the absence of confirmed or suspected VTE. [7] There are multiple randomized controlled trials being conducted to investigate the effects of different doses of heparin on patients' outcomes and until these studies are available it is not recommended to apply a blanket policy of treating all critically ill covid-19 patients with therapeutic-intensity anticoagulation.



www.mecs.com/

Multi-Knowledge Electronic Comprehensive Journal For Education
And Science Publications (MECSJ)

Issue (39),2020

ISSN: 2617-9563

9. INDICATION FOR POST DISCHARGE THROMBOPROPHYLAXIS

Studies indicate that patients hospitalized for acute medical illness are at an increased risk of VTE for up to 90 days after discharge. Covid-19 sufferers should be perceived to be at a similar risk of VTE. Post-discharge prophylaxis is being investigated in clinical trials. A decision on whether to continue thromboprophylaxis post-discharge should be made on the individuals VTE risk factors which include, but are not limited to any pre-existing comorbidities, mobility, age, previous history of VTE, obesity, and consider whether there is an increased bleeding risk especially in the elderly who are prone to falls. [8]

10. CHOICE OF ANTICOAGULANT IN COVID 19

Recent approaches to the management of Covid-19 has included the used of multiple medications, which can lead to drug-drug interactions and this needs to be considered before deciding which anticoagulant to use.[9] An example of this is the Cytochrome P450 enzyme activity is increased by Actemra and Kevzara and can therefore not be used with Apixiban or Rivaroxaban. These antivirals may also increase the doses of warfarin required. A full list of Covid-19 drug-drug interactions can be found at www.covid19-drug-interactions.org LMWH or UFH in hospitalized critically ill patients is preferred because of the shorter half-life and fewer drug-drug interactions compared with direct oral anticoagulants. Regular warfarin users who are unable to get INR monitoring during isolation or national lockdowns may be candidates for direct oral anticoagulants, such as Rivaroxaban or Apixiban. [10] Those in whom direct anticoagulants are not indicated such as those with mechanical heart valves, ventricular assist devices, valvular atrial fibrillation, antiphospholipid antibody syndrome, or lactation should generally continue treatment with warfarin therapy. LMWH or UFH remain the anticoagulants of choice in pregnancy.[11]



Aspirin has been studied for VTE prophylaxis in low-risk patients after hip or knee arthroplasty and is currently being investigated for COVID-19 post-discharge thromboprophylaxis. Patients should be educated on the signs and symptoms of VTE at hospital discharge and advised to seek urgent medical attention should these develop.

11. SUMMARY

As with all hospitalized patients, Covid-19 patients should be considered at a higher risk of VTE due to the combined factors of being bed bound, isolated, and in addition due to the mechanisms of endothelial damage and microvascular thrombosis. It is **recommended** to consider thromboprophylaxis in Covid-19 patients admitted to hospital. The choice of anticoagulant should be based on other medication being taken to avoid drug-drug interaction. Consider post-discharge thromboprophylaxis in those patients who are at a higher risk of VTE, such as the elderly, obese patients, and those who have suffered a previous VTE. This is an area that should be researched in the future to improve the clinical outcomes of those who suffer with Covid-19.

12. REFERENCES

1. Wiersinga, W. J., Rhodes, A., Cheng, A. C., Peacock, S. J., & Prescott, H. C. (2020). Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *Jama*, 324(8), 782-793.
2. Geerts, W. H., Bergqvist, D., Pineo, G. F., Heit, J. A., Samama, C. M., Lassen, M. R., & Colwell, C. W. (2008). Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, 133(6), 381S-453S.
3. Dobesh, P. P., & Trujillo, T. C. (2020). Coagulopathy, Venous Thromboembolism, and Anticoagulation in Patients with COVID-19. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*.
4. Bikdeli, B., Madhavan, M. V., Gupta, A., Jimenez, D., Burton, J. R., Der Nigoghossian, C., ... & Sethi, S. (2020). Pharmacological agents targeting



- thromboinflammation in COVID-19: review and implications for future research. *Thrombosis and haemostasis*, 120(7), 1004.
5. Fraser, E. P., & Geddes, C. C. (2008). Acute pulmonary embolism. *The New England journal of medicine*, 358(25), 2744-author.
 6. Kollias, A., Kyriakoulis, K. G., Dimakakos, E., Poulakou, G., Stergiou, G. S., & Syrigos, K. (2020). Thromboembolic risk and anticoagulant therapy in COVID-19 patients: emerging evidence and call for action. *British journal of haematology*, 189(5), 846-847.
 7. Barnes, G. D., Burnett, A., Allen, A., Blumenstein, M., Clark, N. P., Cuker, A., ... & Kaatz, S. (2020). Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. *Journal of Thrombosis and Thrombolysis*, 1.
 8. White, J. J., Khan, W. S., & Smitham, P. J. (2011). Perioperative implications of surgery in elderly patients with hip fractures: an evidence-based review. *Journal of Perioperative Practice*, 21(6), 192-197.
 9. Zhai, Z., Li, C., Chen, Y., Gerotziafas, G., Zhang, Z., Wan, J., ... & Wang, C. (2020). Prevention and treatment of venous thromboembolism associated with coronavirus disease 2019 infection: a consensus statement before guidelines. *Thrombosis and haemostasis*, 120(6), 937.
 10. Burnett, A. E., Mahan, C. E., Vazquez, S. R., Oertel, L. B., Garcia, D. A., & Ansell, J. (2016). Guidance for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment. *Journal of thrombosis and thrombolysis*, 41(1), 206-232.
 11. Hillis, C. M., & Crowther, M. A. (2015). Acute phase treatment of VTE: Anticoagulation, including non-vitamin K antagonist oral anticoagulants. *Thrombosis and Haemostasis*, 113(06), 1193-1202.