

[Home](#) › [COVID-19](#) › [COVID-19 and Thrombosis in Cancer Patients: The Clot Thickens](#)



FOCUS ON: COVID-19, THROMBOSIS AND CANCER [f](#) [t](#) [in](#)

COVID-19 and Thrombosis in Cancer Patients: The Clot Thickens

March 2021 marks a full year since the WHO officially declared the coronavirus disease 2019 (COVID-19) outbreak a global pandemic. Patients with active cancer represent a population with unique susceptibilities to infection. Early in the pandemic, initial studies suggested that COVID-19 patients with hematologic malignances or actively receiving chemotherapy may be at higher risk of more severe complications or death.¹

In contrast, more recent data suggest that there may not be a link to poorer outcomes in cancer. A cohort study matched COVID-19 patients with and without cancer and found that patients with COVID-19 and cancer had similar outcomes compared with matched patients without cancer.² Similarly, a large cohort study of 22,900 Veterans Affairs (VA) patients in the USA with a history of cancer found that individuals who had received recent cancer therapy had, in fact, a lower prevalence of COVID-19 and similar mortality compared with those who had not.³

A prospective consortium study of 928 cancer patients in the USA, Canada and Spain did not show an association between cancer site or timing of therapy with mortality from COVID-19.⁴ On the other hand, the mortality in hematopoietic stem cell transplant patients after a diagnosis of COVID-19 reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) is high, which highlights that at least certain

cancer subpopulations are at significantly higher risk than others and strategies to manage them must be individualized.⁵

Hypercoagulability of COVID-19

The hypercoagulability of COVID-19 was a relatively early observation with increased micro- and macro-vascular thrombosis.⁶ This thromboinflammatory phenomenon has been linked to systemic inflammation with circulating cytokines, neutrophil extracellular trap formation, increased prothrombotic microparticles formation, elevated coagulation factors, endothelial activation, complement protein and platelet activation.⁷⁻¹⁰ In addition to the increased thrombotic complications, numerous reports have described that rates of bleeding in hospitalized COVID-19 patients range from 2 to 4.8%.^{11,12}

Cancer is an independent risk factor for thrombosis and bleeding, but data exploring the impact of malignancy on the thrombotic and bleeding in COVID-19 patients are limited. A single healthcare center study of 3,808 patients showed an over four-fold higher risk of venous thromboembolism (VTE) for hospitalized COVID-19 patients with cancer compared to those without (OR: 4.4, 95% CI: 2.4–7.9).¹³ A multicenter cohort study of 1,629 hospitalized cancer patients with COVID-19 found the incidence of in-hospital VTE was 9.3% on the regular floor and 13.4% in the critical care setting.

Factors associated with increased risk included recent anti-cancer therapy (OR: 2.1, 95% CI: 1.5–3.0), progressive disease (OR: 2.7, 95% CI: 1.7–4.3), high-risk VTE cancer subtypes (pancreatic, gastro-esophageal; OR: 2.7, 95% CI: 1.2–5.6), and ICU admission (OR: 2.2, 95% CI: 1.5–3.2), whereas pre-admission anticoagulant/antiplatelet therapy was associated with decreased risk.¹⁴ Bleeding rates in cancer patients are not well described. A single center retrospective study found similarly high rates of thrombosis and bleeding in COVID-19 patients with and without cancer, with a cumulative incidence of major bleeding of 20.8% (95% CI: 12.1–31.0%) in the non-cancer group and 19.5% (95% CI: 5.5–39.8%) in the cancer cohort.¹⁵

Strategies and recommendations for anticoagulation

Strategies and recommendations for anticoagulation have evolved over pandemic and have relied on expertise and relatively weak retrospective observations thus far, leading to significant variation in societal guidelines and institutional practices.¹⁶ Recently, interim results from three multicenter (ATTACC NCT04372589, REMAP-CAP NCT02735707, and ACTIV-4 NCT04505774), randomized, open-label trials were announced and suggested that empiric therapeutic anticoagulation improves outcomes in moderately ill, but not critically ill patients, provided bleeding risk is reasonably low.¹⁷

These results have not been officially published or peer-reviewed but once verified represent an important step towards evidence-based management of hospitalized COVID-19 patients. Patients with cancer were not excluded from the randomized studies (apart from intracranial metastasis) but the number of cancer patients included and generalizability to cancer patients, which have unique bleeding and thrombotic risks, will need to be assessed. Data to guide anticoagulation decisions in other clinical settings, such as ambulatory patients or post-hospitalization are very limited and have not been reported separately for patients with malignancies.

Currently, empiric anticoagulation in these patients are not routinely recommended based on low incidence of thrombosis^{18,19} and if used would be individualized by treating

physicians based on personalized risks of bleeding and thrombosis. Recent guidelines for cancer-associated thrombosis in 2021 recommend considering thromboprophylaxis in ambulatory cancer patients receiving systemic therapies that have at least an intermediate risk for thrombosis, although how COVID-19 modulates this risk is yet to be elucidated.²⁰

The emergence of the novel SARS-CoV-2

Since the emergence of the novel SARS-CoV-2, more than 2.5 million lives have been lost globally, and healthcare has faced more challenges than ever before. There has also been an unprecedented pace of progress in the understanding of the disease, preventative and management strategies, including high-risk populations, such as patients with active malignancies. The coagulopathy of COVID-19 in cancer patients is an important area of investigation to guide clinicians caring for these patients. With the ongoing pandemic and our improved understanding, there remains the need to rapidly generate and disseminate accurate information, implement evidence-based discoveries and simultaneously identify impactful questions that need to be answered including thrombosis and bleeding in cancer patients with COVID-19.

References

- Tian J, Yuan X, Xiao J, et al. Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study. *Lancet Oncol.* 2020;21(7):893-903.
2. Brar G, Pinheiro LC, Shusterman M, et al. COVID-19 Severity and Outcomes in Patients With Cancer: A Matched Cohort Study. *J Clin Oncol.* 2020;38(33):3914-3924.
 3. Fillmore NR, La J, Szalat RE, et al. Prevalence and outcome of COVID-19 infection in cancer patients: a national Veterans Affairs study. *Journal of the National Cancer Institute.* 2020.
 4. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet.* 2020;395(10241):1907-1918.
 5. Sharma A, Bhatt NS, St Martin A, et al. Clinical characteristics and outcomes of COVID-19 in haematopoietic stem-cell transplantation recipients: an observational cohort study. *Lancet Haematol.* 2021;8(3):e185-e193.
 6. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. *J Thromb Haemost.* 2020.
 7. Iba T, Levy JH, Levi M, Thachil J. Coagulopathy in COVID-19. *J Thromb Haemost.* 2020.
 8. Abou-Ismael MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. *Thromb Res.* 2020;194:101-115.
 9. 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.
 10. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet.* 2020;395(10234):1417-1418.
 11. Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID and Coagulation: Bleeding and Thrombotic Manifestations of SARS-CoV2 Infection. *Blood.* 2020.
 12. Nadkarni GN, Lala A, Bagiella E, et al. Anticoagulation, Bleeding, Mortality, and Pathology in Hospitalized Patients With COVID-19. *Journal of the American College of Cardiology.* 2020;76(16):1815-1826.
 13. Ananthula A, Tran D, Thomas K, et al. Association and prevalence of venous thromboembolism (VTE) in cancer patients with COVID-19: a single healthcare system experience. 2021. Presented at LHSU Research Day, 2021.

14. Li A, Kuderer NM, Warner J et al : Incidence of and Risk Factors for Venous Thromboembolism Among Hospitalized Patients with Cancer and COVID-19: Report from the COVID-19 and Cancer Consortium (CCC19) Registry. 2020 ASH Annual Meeting & Exposition. Abstract 13. Presented December 5, 2020.
15. Patell R, Bogue T, Bindal P, et al. Incidence of thrombosis and hemorrhage in hospitalized cancer patients with COVID-19. *J Thromb Haemost.* 2020.
16. Patell R, Midha S, Kimani S, et al. Variability in Institutional Guidance for COVID-19-Associated Coagulopathy in the United States. *Thrombosis and haemostasis.* 2020.
17. Barnes GD. Anticoagulation to Prevent VTE in COVID-19: Interim Analysis. 2020; https://www.acc.org/latest-in-cardiology/journal-scans/2021/02/04/04/04/attach-activ4a-and-remap-cap?utm_source=journalscan&utm_medium=email_newsletter&utm_campaign=journalscan&utm_content=20210211. Accessed 3/3/21, 2021.
18. Roberts LN, Whyte MB, Georgiou L, et al. Post-discharge venous thromboembolism following hospital admission with COVID-19. *Blood.* 2020.
19. Patell R, Bogue T, Koshy AG, et al. Post-discharge thrombosis and hemorrhage in patients with COVID-19. *Blood.* 2020.
20. Lyman GH, Carrier M, Ay C, et al. American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer. *Blood Adv.* 2021;5(4):927-974.



Alok Khorana



Rushad Patell

21 March 2021

collaps the text ^



Scientific and Web contents by Polistudium s.r.l.

Via Anfossi 36, 20135 Milan, Italy

info@polistudium.it

© COPYRIGHT 2019 ICTHIC Magazine