COMMENTARIES Today and Every Day: Blood Clot Concerns Beyond COVID-19

Samantha M. Rizzo¹ ¹ Georgetown University School of Medicine Keywords: Venous thromboembolism (VTE), pulmonary embolism (PE), deep vein thrombosis (DVT) https://doi.org/10.52504/001c.29781

Georgetown Medical Review

Vol. 5, Issue 1, 2021

Introduction

Recently, the United States government resumed administration of the Johnson & Johnson COVID-19 vaccine after a temporary pause due to six cases of rare blood clots in women. Across several platforms, many shared the news about the vaccine and continue to have conversations about blood clots. The discussions surrounding cerebral sinus vein thrombosis, and blood clots in general, are encouraging, as blood clots impact the lives of countless patients and families. However, venous thromboembolism (VTE) should not be thought of solely as a rare side effect of a vaccine. Rather, VTE is a common phenomenon related to several aspects of daily lives: for example, oral contraceptive use among women, smoking, and obesity.¹

VTE, which encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE), might not generally be viewed as a serious public health issue. However, VTE is the third most common cardiovascular disorder, following heart attack and stroke.¹ In the United States, PE is a common in-hospital complication and the most preventable cause of death among hospitalized patients.¹ VTE should not be viewed as an isolated event as the rates of VTE recurrence are high, particularly in individuals who experience an unprovoked clotting event.¹

Inherited and Lifestyle Risk Factors for VTE

There are several inherited, lifestyle, and acquired risk factors that predispose individuals to experience a thrombotic event. Inherited risk factors, including a family history of VTE and inherited thrombophilias, increase the likelihood of developing a VTE.^{1,2} Individuals who are homozygous carriers for genetic mutations such as factor V Leiden or the prothrombin gene mutation are more likely to experience VTE than heterozygous carriers, though the risk is still heightened in individuals who are heterozygous for these thrombophilias.² A family history of VTE also increases an individual's likelihood of experiencing a VTE, even in the absence of a known thrombophilia.² Providers should encourage patients to learn of any clotting events or genetic conditions that run within their families so patients can better understand their inherited risk factors.

Lifestyle behaviors and environmental risk factors also impact an individual's chances of developing a thrombotic event. Individuals who are obese are at a heightened risk for VTE, and obesity may interact with other clotting risk factors, such as hospitalizations and inherited thrombophilias to further increase risk.^{3,4} Smoking has been reported as a risk factor for arterial and venous thromboembolism, and smoking status should be considered when determining an individual's risk for VTE.^{4,5} Diet, physical activity levels, and environmental factors like increased exposure to air pollution have also been investigated as risk factors for VTE, though the risks are not completely characterized.⁴ Unlike genetic composition, individuals can work with healthcare professionals to implement healthy lifestyle modifications to help mitigate VTE risk, particularly through smoking cessation and individualized diet and exercise plans.

Acquired VTE Risk Factors: An Emphasis on Women's Health

Acquired risk factors include older age, a prior history of VTE, recent hospitalization or surgery, and cancer.¹ Significantly, women face additional acquired risk factors in the settings of pregnancy, oral contraceptive use, and hormone replacement therapy. In the United States, PE remains a serious cause of morbidity and mortality among pregnant and post-partum women: reports indicate that 9-11% of pregnancy related deaths can be attributed to PE.⁶ Women should receive education about the signs and symptoms of DVT and PE so they can remain hypervigilant during pregnancy and the post-partum period.

Another particularly important acquired risk factor is the use of oral contraceptive pills and hormone replacement therapy. Oral contraceptives containing estrogen confer an increased risk of DVT and PE compared to other long-acting reversible contraceptive measures, and the risk is particularly elevated in women with a known thrombophilia or prior history of VTE.⁷ Similarly, hormonal replacement therapy is associated with a definitive increased risk of VTE.^{7,8} Physicians have an obligation to discuss these associations with all women who are considering starting oral contraceptives or hormonal replacement therapy. Prior to initiation of these therapies, patients and providers should familiarize themselves with the patient's existing VTE risk factors and assess whether the benefits outweigh the thrombotic risks associated with each treatment option.⁸

Blood Clot Concerns: COVID-19 and Beyond

COVID-19 has generated a great deal of discussion concerning VTE, as a complication associated with the virus and vaccine. High frequencies of major arterial or venous thromboembolic events, cardiovascular events, and symptomatic VTE have been reported in patients with COVID-19, particularly among those who are hospitalized and admitted to the ICU.⁹

Following the CDC and FDA's joint recommendation to halt and restart the administration of the Johnson & Johnson COVID-19 vaccine in the setting of six women experiencing cerebral sinus vein thrombosis, it seems that blood clots have become a relevant topic of discussion. However, today and every day, individuals should be aware of the risk factors for potentially life-threatening blood clots. VTE should not solely be viewed as an exceedingly rare complication of a vaccine. Rather, physicians and healthcare professionals must educate patients about the inherited, lifestyle, and acquired VTE risk factors, and encourage life-style modifications and behaviors that can mitigate the risk of experiencing a potentially life-threatening thrombotic event.

REFERENCES

Piazza G, Hohlfelder B, Goldhaber SZ. *Handbook for Venous Thromboembolism*. Springer; 2015.
Martinelli I, De Stefano V, Mannucci PM. Inherited risk factors for venous thromboembolism.

Nat Rev Cardiol. 2014;11(3):140-156. doi:10.1038/nrcardio.2013.211

3. Yang G, De Staercke C, Hooper WC. The effects of obesity on venous thromboembolism: A review. *Open J Prev Med.* 2012;2(4):499-509. doi:10.4236/ojpm.2012.24069

4. Crous-Bou M, Harrington L, Kabrhel C. Environmental and Genetic Risk Factors Associated with Venous Thromboembolism. *Semin Thromb Hemost*. 2016;42(8):808-820. <u>doi:10.1055/</u><u>s-0036-1592333</u>

5. Cheng YJ, Liu ZH, Yao FJ, et al. Current and former smoking and risk for venous thromboembolism: a systematic review and meta-analysis. *PLoS Med.* 2013;10(9):e1001515. doi:10.1371/journal.pmed.1001515

6. Abe K, Kuklina EV, Hooper WC, Callaghan WM. Venous thromboembolism as a cause of severe maternal morbidity and mortality in the United States. *Semin Perinatol*. 2019;43(4):200-204. doi:10.1053/j.semperi.2019.03.004

7. Gialeraki A, Valsami S, Pittaras T, Panayiotakopoulos G, Politou M. Oral Contraceptives and HRT Risk of Thrombosis. *Clin Appl Thromb Hemost*. 2018;24(2):217-225. <u>doi:10.1177/1076029616683802</u>

8. Eisenberger A, Westhoff C. Hormone replacement therapy and venous thromboembolism. *J* Steroid Biochem Mol Biol. 2014;142:76-82. doi:10.1016/j.jsbmb.2013.08.016

9. Piazza G, Campia U, Hurwitz S, et al. Registry of Arterial and Venous Thromboembolic Complications in Patients With COVID-19. *J Am Coll Cardiol*. 2020;76(18):2060-2072. doi:10.1016/j.jacc.2020.08.070