

# Risk factors for deep venous thrombosis in patients undergoing orthopedic surgical procedures

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Factores de riesgo para trombosis venosa profunda en pacientes sometidos a procedimientos traumatológicos

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## Resumen

**D**eep venous thrombosis is (DVT) a particularly frequent complication of orthopedic surgery. Therefore, physicians need to identify all risk factors related to DVT to take preventive measures to decrease the overall chance of developing this complication. Several risk factors may be present in this context, including modifiable and non-modifiable risk factors, as well as those related to surgery in general, and to orthopedic procedures specifically. Abundant research has assessed the relative importance of these risk factors in the clinical setting, shaping the management of patients in practice. This review aims to analyze the various risk factors associated with DVT and their physiopathology in the particular context of patients submitted to orthopedic procedures.

**Keywords:** Deep venous thrombosis, orthopedic surgery, thrombogenesis, risk factors, prevention.

## Resumen

**L**a trombosis venosa profunda (TVP) es una complicación particularmente frecuente de la cirugía ortopédica. Por lo tanto, los médicos deben identificar todos los factores de riesgo relacionados con la TVP para tomar medidas preventivas a fin de disminuir la posibilidad general de desarrollar esta complicación. Varios factores de riesgo pueden estar presentes en este contexto, incluidos los factores de riesgo modificables y no modificables, así como los relacionados con la cirugía en general y los procedimientos ortopédicos en particular. Numerosas investigaciones han evaluado la importancia relativa de estos factores de riesgo en el entorno clínico, de cara al manejo de los pacientes en la práctica. Esta revisión tiene como objetivo analizar los diversos factores de riesgo asociados a la TVP y su fisiopatología en el contexto particular de los pacientes sometidos a procedimientos ortopédicos.

**Palabras clave:** Trombosis venosa profunda, cirugía ortopédica, trombogénesis, factores de riesgo, prevención.

**S**urgical procedures fulfill a role in treating a broad spectrum of pathologies at all ages, from neonates to the elderly. Surgical care has acquired many roles in the past decades to the point that economists and researchers consider it a fundamental component of healthcare and the overall socioeconomic development<sup>1</sup>. It was estimated that over 320 million surgical procedures would be needed to address the burden of surgical diseases in 2010. Moreover, rates of surgical needs varied across the continents, ranging from 3,000 procedures per 100,000 individuals in Latin America to over 6,000 procedures per 100,000 individuals in Western Sub-Saharan Africa. It is worth noting that unintentional injuries from accidents or trauma were the most common cause of requiring a surgery worldwide<sup>2</sup>.

Trauma is the leading cause of death and disability in the United States; therefore, proper management is required to minimize its fatality. Falls and car accidents remain the leading cause of traumatic injury, mainly producing head and neck injuries, followed by torso and extremities injuries<sup>3</sup>. Considering that 1 of every ten trauma patients has a fracture, these cases are common for orthopedic surgeons<sup>4</sup>. Like every surgical procedure, orthopedic procedures have inherent risks, such as wound infections, bleeding and improper union of the bone<sup>5</sup>. Nonetheless, more risks are particularly added to orthopedic procedures given that patients tend to be in bed for longer, and the immobility required for proper healing, both of which can lead to other types of complications, such as deep vein thrombosis (DVT)<sup>6</sup>.

The prevalence of DVT after orthopedic surgery is as high as 7%, among the highest rates when compared to other medical departments<sup>7</sup>. Likewise, patients exposed to traumatic injuries have a greater risk of developing DVT<sup>8</sup>. Moreover, surgical procedures increase the risk of DVT, especially orthopedic procedure<sup>7</sup>. Therefore, physicians need to identify all risk factors related to DVT to take preventive measures to decrease the overall chance of developing this complication<sup>9</sup>. This review aims to analyze the various risk factors associated with DVT and their physiopathology in the particular context of patients submitted to orthopedic procedures.

#### **Risk factors for deep vein thrombosis in orthopedic patients: from the basics to specifics**

Thrombus formation is part of the normal hemostasis mechanisms, along with coagulation and fibrinolysis. Nonetheless, pathologic conditions trigger abnormal pathways, resulting in exaggerated thrombogenesis. Despite the variety of conditions related to thrombus formation, the requirements for this phenomenon have been narrowed down to three variables, known as Virchow's triad<sup>10</sup>. This includes venous stasis, endothelial dysfunction and hypercoagu-

lability<sup>11</sup>. Although these three elements tend to appear separately in different conditions, specific pathologies may include all; significantly increasing the risk for thrombotic events such as DVT<sup>10</sup>. For example, evidence has demonstrated that traumatic injury is one condition that recruits all of the variables of the Virchow's triad<sup>12</sup>.

Despite the relative simplicity behind the origin of traumatic injuries, it is worth stating that trauma involves a series of complex pathophysiologic events that can potentially lead to several complications<sup>13</sup>. Coagulopathy is a well-known condition that often appears in trauma patients, termed trauma-induced coagulopathy (TIC)<sup>14</sup>. In the early stages of trauma, TIC typically follows a hypocoagulable state resulting in bleeding; in later stages, TIC is characterized by a hypercoagulable state resulting in DVT and thromboembolism. Several theories have been exposed to explain the genesis of TIC, ranging from direct tissue damage due to trauma to detailed molecular mechanisms involving the immune system, endothelial damage and platelet activation<sup>15</sup>.

As a result, trauma is considered a risk factor for developing DVT. Several studies have demonstrated that severe trauma patients usually show increased procoagulants in the systemic circulation. It has been demonstrated that trauma patients tend to show an accelerated generation of thrombin<sup>16</sup>. Other studies have demonstrated in models of non-stimulated thrombin generation that trauma patients have spontaneous thrombin synthesis<sup>17</sup>. Moreover, several cell-derived microparticles have been identified in the acute phase of trauma, such as platelet, leukocyte and endothelial-derived microparticles, all of which actively participate as procoagulants<sup>18</sup>. These factors partially explain the pathophysiology underlying coagulation disorders in trauma patients and its role in DVT.

However, another vital variable to consider concerning trauma is its location. Although abdominal and chest trauma have a relation with DVT<sup>12</sup>, lower limb trauma has the strongest correlation with DVT<sup>19</sup>. Pop et al.<sup>20</sup> assessed over 170 patients with lower limb fractures who had a Doppler ultrasound exam performed. It was reported that nearly 30% of all the patients had DVT. Moreover, the authors stated that femoral fractures, including proximal, distal and diaphysis fractures, had the most significant risk for DVT when compared to fractures below the knee. Although other studies show incidence variations between 6% to 40%, certain factors have to be considered, such as geographical and age distribution, among others<sup>21</sup>. Nonetheless, evidence undeniably shows that DVT is a frequent complication in lower limb trauma; therefore, it is appropriate to classify trauma as an independent risk factor for DVT.

On the other hand, some unmodifiable risk factors come into play regarding DVT incidence. Firstly, age has been known to play a significant role in the incidence of DVT for a long time. For that matter, Bizien et al.<sup>22</sup> performed a prospective study with over 600 patients that had their

first episode of DVT. After multivariate analysis, it was concluded that the risk of DVT increased by 3% each year that the patients increased in age. Moreover, when segmented by quartiles, the odds ratio (OR) showed an upwards trend concerning age, with the highest OR being 3.1 (95% CI, 1.3-7.5) for the group aged 75-99 years. Older studies concur with these findings, showing that the incidence of DVT rises exponentially with age, from negligible rates among children under 15 to over 600 cases per 100,000 individuals per year at the age of 80<sup>23</sup>.

Sex is another unmodifiable risk factor that has been correlated with DVT. Although oral contraceptives and postmenopausal hormone replacement have been associated with DVT in women, when those factors are taken out of the equation, no consistent differences are found in the incidence of DVT between men and women<sup>23</sup>. Likewise, Anderson et al.<sup>24</sup> found that the incidence of DVT in both sexes was identical; however, Silverstein et al.<sup>25</sup> noted a slight skew towards younger women, as well as a greater risk among older men. Additionally, race and ethnicity allegedly play an essential role in DVT incidence. White et al.<sup>26</sup> studied the incidence among different ethnic groups in California, showing that DVT incidence was higher among Caucasians and African Americans; meanwhile, the incidence in Hispanics and Asians was significantly lower, suggesting that the latter two had a protective role against DVT.

On the other hand, some modifiable risk factors are strongly correlated with DVT. Obesity, defined as a body-mass index (BMI) above 30 kg/m<sup>2</sup>, has been associated with a higher incidence of DVT. Some studies suggest that obesity leads to a 2 to 3-fold higher risk for DVT in both genders<sup>27</sup>. The latter relationship is not mediated by differences in levels of fibrinogen, factor VIII, factor IX and D-dimer, according to one study<sup>28</sup>. It is hypothesized that body weight leads to impaired venous return and that some biochemical hallmarks of obesity, such as increased inflammation and endothelial dysfunction, may play a role in thrombogenesis<sup>29</sup>. Also, a history of smoking is mildly correlated with the incidence of DVT. A meta-analysis showed that the OR for current and former smokers was 1.23 and 1.10, respectively. Moreover, the risk tends to increase by 10.2% for every additional ten cigarettes per day smoked or by 6% for every additional ten pack-years<sup>30</sup>.

Limb fractures are the most common cause of admission to the orthopedic department; tibia and femur fractures are the most frequent fractures. Proper management of fractures requires the usage of casts until surgical intervention, which is needed in as often as 80% of the cases, only to use another type of immobilization after the surgery<sup>31</sup>. In light of the above, orthopedic patients, especially those with lower limb fractures, tend to have long bedrest periods with little to no mobilization. Immobility is a well-recognized risk factor for DVT in surgical patients, and in the case of orthopedic patients, it is almost obligatory, given that proper bone healing requires immobilization of the damaged limb<sup>32</sup>.

Sartori et al.<sup>33</sup> assessed the correlation between DVT and immobility by studying a population segmented into two groups divided by the presence or absence of immobility. The study's endpoint was the detection of proximal DVT or isolated distal DVT. According to the results, the immobility group had a 3.59 OR (95% CI: 1.78-7.23) compared to the control group; nonetheless, the risk for isolated distal DVT was similar between the two groups. Moreover, the authors stated that the incidence of DVT during the first three days was similar between the two groups; however, after four days, the immobility group outperformed the control group as the days passed. In conclusion, the authors suggested that immobility for longer than three days is an independent risk factor for DVT.

Another aspect to consider regarding orthopedic patients is ankle dorsiflexion (AD), which tends to be restricted in lower limb fractures due to cast immobilization. The relevance of this relies upon the fact that AD promotes venous return because of the contraction of the gastrocnemius muscle, which stimulates venous blood flow<sup>34</sup>. Likewise, it was demonstrated that a 30° dorsiflexion movement guided by inspiration effectively promotes venous return from the lower limb, working as a method to prevent DVT<sup>35</sup>. Another study analyzed 124 patients with cast leg immobilization after surgical repair of Achilles tendon rupture. After two weeks postoperatively, the incidence of DVT was assessed by duplex ultrasound, and it was correlated with the presence or absence of AD. Patients with poor AD had over 40% incidence of DVT; meanwhile, those with good AD had an incidence of 23%. For this reason, poor AD is considered a risk factor for DVT in orthopedic patients<sup>36</sup>.

Lastly, nearly 80% of the patients admitted to the orthopedic department need surgical management. The surgery itself is considered a risk factor for DVT<sup>9</sup>, which seems to be especially true in orthopedic cases. The incidence of DVT after orthopedic surgery is slightly over 7%, and it tends to increase when the surgical time goes above 120 minutes<sup>7</sup>. Another study assessed the incidence of DVT in a large population that underwent hip replacement arthroplasty (HRA), knee replacement arthroplasty (KRA) and hip fracture surgery (HFS). The study reported the relative risks (RR) for the group over 70 years as follows: 2.8 for HFS, 1.56 for KRA and 1.24 for HRA. In conclusion, some types of surgery confer more significant risk for DVT than others; however, almost every lower limb surgery significantly increases the risk of DVT<sup>37,38</sup>.

DVT is a relevant condition to consider in every hospitalized patient, especially in the context of surgical patients. Moreover, DVT is particularly relevant in orthopedic patients, primarily those with lower limb compromise. Given the high incidence of DVT in these patients, the physician must establish the risk factors of every patient individually in order to provide preventive measures if needed. Age, sex and ethnicity are some of the unmodifiable risk factors that are correlated with the incidence of DVT. On the other hand, non-modifiable risk factors such as smoking and obesity also play a part in DVT incidence. Some risk factors are specific for orthopedic patients; for example, immobility due to cast strongly correlates with DVT. In addition, a low range of motion for AD has also been associated with DVT. Finally, the surgery itself increases the risk of DVT in these patients. Therefore, risk assessment should be mandatory on admission in order to consider DVT prophylaxis.

## References

1. Meara JG, Leather AJM, Hagander L, Alkire BC, Alonso N, Ameh EA, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Am J Obstet Gynecol*. 2015 Sep;213(3):338–40.
2. Rose J, Weiser TG, Hider P, Wilson L, Gruen R, Bickler SW. Estimated need for surgery worldwide based on prevalence of diseases: implications for public health planning of surgical services. *Lancet Glob Health*. 2015 Apr 27;3(Suppl 2):S13–20.
3. DiMaggio C, Ayoung-Chee P, Shinseki M, Wilson C, Marshall G, Lee DC, et al. Traumatic Injury in the United States: In-Patient Epidemiology 2000–2011. *Injury*. 2016 Jul;47(7):1393–403.
4. Alhadhoud MA, Alsiri NF. The epidemiology of traumatic musculoskeletal injuries in Kuwait: Prevalence and associated risk factors. *J Taibah Univ Med Sci [Internet]*. 2022 Feb 5 [cited 2022 Jun 16]; Available from: <https://www.sciencedirect.com/science/article/pii/S1658361222000300>
5. Ricketts D, Rogers R, Roper T, Ge X. Recognising and dealing with complications in orthopaedic surgery. *Ann R Coll Surg Engl*. 2017 Mar;99(3):185–8.
6. Scherptong-Engbers M, Blom J, Cushman M, Rosendaal F, Vlieg A. The contribution of immobility risk factors to the incidence of venous thrombosis in an older population. *J Thromb Haemost JTH*. 2013 Dec 11;12.
7. Bui MH, Hung DD, Vinh PQ, Hiep NH, Anh LL, Dinh TC. Frequency and Risk Factor of Lower-limb Deep Vein Thrombosis after Major Orthopedic Surgery in Vietnamese Patients. *Open Access Maced J Med Sci*. 2019 Dec 20;7(24):4250–4.
8. Nielsen S, O'Connor D, Kaul S, Sharma J, Napolitano M, Simonian G, et al. Early Detection of Deep Venous Thrombosis in Trauma Patients. *Cureus*. 12(7):e9370.
9. Cushman M. Epidemiology and Risk Factors for Venous Thrombosis. *Semin Hematol*. 2007 Apr;44(2):62–9.
10. Kushner A, West WP, Pillarisetty LS. Virchow Triad. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2021 [cited 2021 Nov 13]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK539697/>
11. Kumar DR, Hanlin E, Glurich I, Mazza JJ, Yale SH. Virchow's Contribution to the Understanding of Thrombosis and Cellular Biology. *Clin Med Res*. 2010 Dec;8(3–4):168–72.
12. Nielsen S, O'Connor D, Kaul S, Sharma J, Napolitano M, Simonian G, et al. Early Detection of Deep Venous Thrombosis in Trauma Patients. *Cureus*. 12(7):e9370.
13. Keel M, Trentz O. Pathophysiology of polytrauma. *Injury*. 2005 Jun;36(6):691–709.
14. Moore EE, Moore HB, Kornblith LZ, Neal MD, Hoffman M, Mutch NJ, et al. Trauma-induced coagulopathy. *Nat Rev Dis Primer*. 2021 Apr 29;7(1):1–23.
15. Hayakawa M. Pathophysiology of trauma-induced coagulopathy: disseminated intravascular coagulation with the fibrinolytic phenotype. *J Intensive Care*. 2017 Jan 31;5(1):14.
16. Hayakawa M, Sawamura A, Gando S, Kubota N, Uegaki S, Shimojima H, et al. Disseminated intravascular coagulation at an early phase of trauma is associated with consumption coagulopathy and excessive fibrinolysis both by plasmin and neutrophil elastase. *Surgery*. 2011 Feb 1;149(2):221–30.
17. Hayakawa M, Gando S, Ono Y, Wada T, Yanagida Y, Sawamura A, et al. Noble-Collip Drum Trauma Induces Disseminated Intravascular Coagulation But Not Acute Coagulopathy of Trauma. *Shock*. 2015 Mar;43(3):261–7.
18. Matijevic N, Wang YWW, Wade CE, Holcomb JB, Cotton BA, Schreiber MA, et al. Cellular microparticle and thrombogram phenotypes in the Prospective Observational Multicenter Major Trauma Transfusion (PROMMTT) Study: Correlation with coagulopathy. *Thromb Res*. 2014 Sep 1;134(3):652–8.
19. Abelseh G, Buckley RE, Pineo GE, Hull R, Rose MS. Incidence of deep-vein thrombosis in patients with fractures of the lower extremity distal to the hip. *J Orthop Trauma*. 1996;10(4):230–5.
20. Pop D, Dis M, Apostu D, Oltean-Dan D, Gabri Z, Lucaciu O, et al. Incidence of deep vein thrombosis in lower limb fractured patients. *Hum Vet Med*. 2020 Feb 23;12:17–21.
21. Kapoor CS, Mehta AK, Patel K, Golwala PP. Prevalence of deep vein thrombosis in patients with lower limb trauma. *J Clin Orthop Trauma*. 2016;7(Suppl 2):220–4.
22. Bizien N, Noel-Savina E, Tromeur C, Delluc A, Mottier D, Leroyer C, et al. Age is a major risk factor of venous thromboembolism (VTE). *Eur Respir J [Internet]*. 2011 Sep 1 [cited 2022 Apr 15];38(Suppl 55). Available from: [https://erj.ersjournals.com/content/38/Suppl\\_55/p3936](https://erj.ersjournals.com/content/38/Suppl_55/p3936)
23. White RH. The Epidemiology of Venous Thromboembolism. *Circulation*. 2003 Jun 17;107(23\_suppl\_1):I–4.
24. Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Patwardhan NA, Jovanovic B, et al. A Population-Based Perspective of the Hospital Incidence and Case-Fatality Rates of Deep Vein Thrombosis and Pulmonary Embolism: The Worcester DVT Study. *Arch Intern Med*. 1991 May 1;151(5):933–8.
25. Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ III. Trends in the Incidence of Deep Vein Thrombosis and Pulmonary Embolism: A 25-Year Population-Based Study. *Arch Intern Med*. 1998 Mar 23;158(6):585–93.
26. White RH, Zhou H, Romano PS. Incidence of Idiopathic Deep Venous Thrombosis and Secondary Thromboembolism among Ethnic Groups

in California. *Ann Intern Med.* 1998 May;128(9):737–40.

27. Stein PD, Beemath A, Olson RE. Obesity as a risk factor in venous thromboembolism. *Am J Med.* 2005 Sep;118(9):978–80.
28. Abdollahi M, Cushman M, Rosendaal FR. Obesity: risk of venous thrombosis and the interaction with coagulation factor levels and oral contraceptive use. *Thromb Haemost.* 2003 Mar;89(3):493–8.
29. Blokhin IO, Lentz SR. Mechanisms of thrombosis in obesity. *Curr Opin Hematol.* 2013 Sep;20(5):437–44.
30. Cheng YJ, Liu ZH, Yao FJ, Zeng WT, Zheng DD, Dong YG, et al. Current and Former Smoking and Risk for Venous Thromboembolism: A Systematic Review and Meta-Analysis. *PLoS Med.* 2013 Sep 17;10(9):e1001515.
31. Omoke NI, Ekumankama FO. Incidence and Pattern of Extremity Fractures seen in Accident and Emergency Department of a Nigerian Teaching Hospital. *Niger J Surg Off Publ Niger Surg Res Soc.* 2020;26(1):28–34.
32. Jain AK. The rational treatment of fractures: Use the evidence with caution. *Indian J Orthop.* 2011;45(2):101–2.
33. Sartori M, Favaretto E, Cosmi B. Relevance of immobility as a risk factor for symptomatic proximal and isolated distal deep vein thrombosis in acutely ill medical inpatients. *Vasc Med Lond Engl.* 2021 Oct;26(5):542–8.
34. Uhl JF, Gillot C. Anatomy of the veno-muscular pumps of the lower limb. *Phlebology.* 2015 Apr;30(3):180–93.
35. Pi H, Ku H, Zhao T, Wang J, Fu Y. Influence of Ankle Active Dorsiflexion Movement Guided by Inspiration on the Venous Return from the Lower Limbs: A Prospective Study. *J Nurs Res JNR.* 2018 Apr;26(2):123–9.
36. Aufwerber S, Praxitelous P, Edman G, Silbernagel KG, Ackermann PW. Increased risk of deep venous thrombosis in patients with poor ankle dorsiflexion after lower limb immobilization. *OTA Int.* 2019 Jun;2(2):e038.
37. Lee SY, Ro DH, Chung CY, Lee KM, Kwon SS, Sung KH, et al. Incidence of Deep Vein Thrombosis after Major Lower Limb Orthopedic Surgery: Analysis of a Nationwide Claim Registry. *Yonsei Med J.* 2015 Jan 1;56(1):139–45.
38. M Rivera, F Contreras, M de la Parte, O Méndez, Y Colmenares, M Velasco. Aspectos clínicos y terapéuticos de las Trombosis Venosas y Arteriales. *Revista Archivos Venezolanos de Farmacología y Terapéutica.* 2000; 19 (2): 71-81