

Cite as: Deng X, Su Y, Fu YT, Zhang HC, Zhang YK, Wang HX. Advances in the pathogenesis and risk factors of deep vein thrombosis in lower extremity fractures [J]. Chin J Clin Res, 2025, 38(2):182-185.

DOI: 10.13429/j.cnki.cjcr.2025.02.005

Advances in the pathogenesis and risk factors of deep vein thrombosis in lower extremity fractures

DENG Xin, SU Yun, FU Yutian, ZHANG Haochun, ZHANG Yongkun, WANG Hongxun
*Department of Trauma Orthopedics, Affiliated Zhongshan Hospital of Dalian University, Dalian,
Liaoning 116000, China*

Corresponding author: WANG Hongxun, E-mail: 492705108@qq.com

Abstract: Lower extremity fractures is a common clinical condition that significantly affects patients' daily activities and work. These patients are often accompanied by major risk factors for deep vein thrombosis (DVT), such as venous wall injury, slow blood flow, and a hypercoagulable state. As a result, the incidence of DVT is high in this population. If prevention and intervention are not promptly implemented, DVT can lead to thromboembolism, which may travel to the pulmonary artery, resulting in pulmonary embolism and posing a serious threat to the patient's life. Therefore, it is crucial to gain a deeper understanding of the pathogenesis and risk factors of DVT. This review summarizes the mechanisms and risk factors of DVT. This review summarizes the mechanisms and risk factors associated with DVT in lower extremity fractures, aiming to provide a reference for clinicians in the early identification and management of DVT.

Keywords: Lower limb fracture; Deep vein thrombosis; Pathogenesis; Risk factor; Stasis; Vascular damage; Hypercoagulability; Anesthesia; Tourniquet

Lower extremity fracture is a common clinical disease that significantly affects patients' daily life and work. These patients often combine the Virchow's: endothelial damage, abnormal blood flow, and hypercoagulability, and thus have a high incidence of deep vein thrombosis (DVT) [1]. The development of DVT significantly affects the venous blood circulation in the lower extremity, and some patients suffer from distal ischemia and hypoxia due to the impaired blood flow in the affected limbs, which may lead to distal tissue necrosis or even amputation. If the thrombus is dislodged and travels with the blood flow to the right heart and pulmonary arterial system, it may cause fatal pulmonary embolism (PE) [2]. Previous literature has reported significant differences in the incidence of DVT at various sites of lower extremity fractures. Among them, the incidence of DVT in patients with pelvic acetabular fracture, hip fracture, femoral stem fracture, periprosthetic knee fracture, tibiofibular fracture, and ankle fracture was 3%-48%, 38.25%-56.83%, 40%-86%, 50.4%, 30%, and 18.97%, respectively [3-6]. The incidence of DVT has a significant impact on perioperative outcomes in patients with lower extremity fracture and prognosis, and during this period, DVT shows the characteristics of susceptibility, high disability rate and high mortality. Therefore, an in-depth discussion of the pathogenesis of DVT and its risk factors is necessary for patients with lower extremity fractures. Currently, there is a lack of systematic research on the

pathogenesis and risk factors of DVT in the clinic, and this article will comprehensively review these two aspects, with a view to providing further reference for the clinical prevention and treatment of DVT.

1 Pathogenesis of DVT

The main pathogenesis of DVT can be summarized as the three factors of thrombosis proposed by Virchow: endothelial damage, abnormal blood flow, and hypercoagulability. Venous stagnation caused by prolonged bed rest, hypercoagulable state after surgery, and vascular wall damage caused by trauma in patients with lower extremity fracture can all lead to DVT.

1.1 Endothelial damage

The vein wall consists of an outer layer, an intermediate layer and an inner layer. When the inner layer is damaged, the endothelial cells are defective or stripped, which can lead to localized blood cell aggregation in the body and adhesion to platelets, and ultimately the formation of blood clots. Damage to the vein wall can be categorized into three types: physical, chemical, and infectious injuries. Physical injury is usually caused by external trauma, such as local vascular tear or contusion, commonly seen in violent extrusion, repeated venepuncture, fracture block compression,

surgical operation injury, etc.; chemical injury mainly occurs in the injection of a variety of antibiotics, hypertonic solutions, and other irritating solutions; infectious injury can be directly caused by phlebitis, or may be indirectly induced by other foci of infection. The endothelium plays a pivotal role in the hemostatic response and is integral to the vascular reaction to injury that culminates in thrombosis. Endothelial damage significantly elevates the risk of DVT [7]. Studies have demonstrated a marked increase in the expression levels of interleukins, tumor necrosis factor- α , and fibrinogen in DVT patients, with a positive correlation between these levels and the extent of vascular damage [8]. This relationship is critical for the clinical assessment of DVT severity and the degree of associated vascular injury. Furthermore, a notably high incidence of DVT has been observed in patients with iliac and femoral vein injuries, likely attributable to venous vascular damage [9].

1.2 Abnormal blood flow

Patients with lower extremity fracture often suffer from pain, postoperative muscle relaxation, and the use of anesthesia drugs, resulting in a slowing of systemic peripheral venous blood circulation. In addition, prolonged bed rest and activity limitation can also further reduce the rate of venous blood flow in the lower extremities. Studies have demonstrated that prolonged bed rest significantly elevates the risk of DVT, primarily attributable to venous stasis resulting from reduced lower extremity mobility [10].

1.3 Hypercoagulable state

The hypercoagulable state of blood is caused by the interaction of vascular endothelial cells, platelets, thrombin, anticoagulant and fibrinolytic systems. When a hypercoagulable state of the blood occurs, clotting factors and platelets in the blood are more likely to aggregate together to form a thrombus. This thrombus may form in the deep veins of the lower extremities, leading to DVT [11]. Some studies have reported that the incidence of preoperative DVT in patients with fracture is about 18.4% due to the hypercoagulable state, and the incidence of DVT in patients with fractures of the lower extremities is 40%-60% [12]. Lin et al. [13] have shown that in the fracture state, reduced activity increases the risk of bleeding, blood viscosity, and infections, which leads to hypercoagulability of the blood; which, in turn, increases the chances of DVT. You et al. [14] used thromboelastography to detect coagulation status in 35 patients with hip fracture and found that 11 patients were in a hypercoagulable state at the time of admission. All patients showed evident hypercoagulability at 2 weeks and persisted up to 6 weeks. In addition, more than 50% of patients remaining hypercoagulable for 6 weeks after fracture, despite thromboprophylaxis.

2 Risk factors for DVT

Combined with the disease characteristics of patients with lower extremity fractures, the risk factors for DVT of lower extremity fractures can be summarized as gender, age, body mass index (BMI), underlying disease, surgical method, surgical time, surgical site, anesthesia method, endograft use, and tourniquet use.

2.1 Gender

Ling et al. [15] analyzed the clinical data of 307 hospitalized patients with lower extremity fractures complicated by venous thrombophilia (VTE), and found that there were 202 male patients, of which 31 cases were complicated by VTE, with a VTE incidence rate of 15.3%. There were 105 female patients, of which 23 cases were complicated by VTE; the difference between males and females was statistically significant in terms of DVT and the incidence rate was higher in females. In terms of DVT, the difference between men and women is statistically significant, and the incidence rate of women is higher. A foreign study found that the overall incidence of DVT was higher in women than in men, but the incidence of proximal DVT was higher in men than in women [16]. According to the literature review, the incidence of DVT is significantly higher in female patients. Therefore, more attention should be paid to DVT prophylaxis in female patients in clinical practice. Meanwhile, close monitoring and effective measures to reduce the risk of DVT are needed in special circumstances such as pregnancy, postpartum, and when receiving estrogen replacement therapy.

2.2 Age

Age is an independent risk factor for DVT [17-18]. Cao et al. [19] found that age was an independent risk factor for DVT in elderly patients with intertrochanteric femoral fractures. Age ≥ 45 was reported to be one of the major risk factors for DVT [20]. Sloan et al. [21] found that age ≥ 45 influenced the risk factors for DVT. Li et al. [22] noted that the risk of DVT in hip fracture patients in the age groups of 45-59, 60-74, and ≥ 75 years was 3.12, 3.20, and 6.45 times higher than that in patients < 45 years, respectively. Despite the different views on age as a factor, it is now established as an important preventive factor in current clinical guidelines. Therefore, it is important to take age as a key factor into account when developing preventive measures and therapeutic regimens, and to adopt targeted measures.

2.3 BMI

Overweight or obese patients are more likely to develop DVT compared to those with normal weight [23]. Yang et al. [24] collected clinical data from 136 orthopedic patients who underwent surgical treatment, and after the study, BMI ≥ 24 kg/m² was found to be an independent risk factor for the development of lower

extremity DVT in orthopedic patients after surgery. Tang [25] found that the risk factors for postoperative DVT in patients undergoing major lower extremity orthopedic surgery included increased age, higher BMI, higher cholesterol and triacylglycerol, and increased intraoperative bleeding. Su [26] analyzed the statistical data of 400 patients undergoing lower extremity fracture surgery using univariate and logistics regression, and the results showed that obesity is a high-risk factor for postoperative complications of DVT. Numerous studies have shown that overweight or obesity significantly increases the incidence of postoperative DVT in lower extremity fracture surgery, and the mechanism may be related to chronic elevated intra-abdominal pressure and slow blood flow in obese patients. In addition, decreased antioxidant capacity of vascular endothelial cells and dysregulated adipocyte metabolism in obese individuals may also be important factors [27]. Other studies have shown that the level of platelet-derived microparticles (pDMP) is significantly higher in obese patients than in normal individuals, and the level is positively correlated with BMI and body fat, so that obese individuals are often in a state of platelet activation [28].

2.4 Underlying Diseases

Elderly patients have low vascular elasticity and are also comorbid with a variety of underlying diseases, such as hypertension, and coronary artery disease, which greatly exacerbate vascular injury and increase the risk of DVT. Literature reports confirm that underlying diseases such as hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease, and pulmonary disease are closely related to the development of DVT in patients with lower extremity fractures, and that these underlying diseases lead to poor blood circulation and increase the risk of DVT in patients with lower extremity fractures [29]. Therefore, patients should be thoroughly evaluated before and after surgery, and appropriate measures should be taken to prevent and minimize the development of DVT.

2.5 Duration of surgery

Prolonged duration of surgery increases the chance of postoperative complications of DVT in patients. Dong et al. [30] showed that the duration of surgery ≥ 2 h increases the development of postoperative DVT and PE. In patients with elderly hip fracture, prolonged operative time greatly increases the risk of postoperative complication of DVT, and Bai et al. [31] found that an operative duration of >2 h was an independent risk factor for perioperative DVT in elderly hip fracture patients. Another study concluded that operation time >1 h was a risk factor for postoperative DVT formation in femoral neck fracture [32]. For patients with femoral neck fracture with diabetes mellitus. Liu et al. [33] concluded that an operation time of >2 h increased the risk of postoperative complication of DVT. In addition to elderly hip fractures,

other types of lower extremity fractures such as fractures in the foot and ankle, around the knee and other locations of postoperative complication of DVT have a close relationship with the length of the operation time, which has been reported by different scholars, but the vast majority of them are that the operation time of >1 h and >2 h is closely related to the formation of DVT. Therefore, it is necessary to carry out a scientific and rational assessment of the operation time when choosing the surgical method in order to minimize the development of DVT.

2.6 Anesthesia

Most of the literature has shown that general anesthesia has a high incidence of postoperative DVT compared to intrathecal anesthesia [34-35]. Xu et al. [36] grouped 90 elderly patients with lower extremity fractures into a control group (general anesthesia) and an observation group (intrathecal anesthesia) by a randomized numerical table, and performed a postoperative lower extremity vascular ultrasound review, which showed that six cases of DVT occurred in the control group, whereas the observation group did not have the complication; the results of the study showed that the use of intrathecal anesthesia can effectively reduce the incidence of postoperative DVT compared to general anesthesia in elderly patients with lower extremity fractures. The results of this study suggest that the use of intrathecal anesthesia can effectively reduce the incidence of postoperative DVT compared with general anesthesia in elderly patients with lower extremity fractures. Zeng et al. [37] used the same method to compare the incidence of postoperative DVT under different anesthesia methods in patients with intertrochanteric fractures, and found that intrathecal anesthesia could reduce the incidence of postoperative DVT in the lower extremity of elderly patients with intertrochanteric femur fractures. At present, general anesthesia or intralesional anesthesia is usually chosen as the commonly used methods for patients with lower extremity fractures, and other types of anesthesia are less commonly used. Avoiding general anesthesia is a viable option for patients who are more suitable for intrathecal anesthesia and hope to reduce the risk of postoperative DVT complications.

2.7 Endoprosthesis use

Commonly used endoprostheses for lower extremity fractures include plates, screws, intramedullary pins, artificial bone, and artificial joints. Endoprostheses cause adverse reactions such as allergic reactions and thermal polymerization reactions that may damage the vascular lining or activate the coagulation system causing DVT [38].

2.8 Tourniquet use

Tourniquets are widely used in lower extremity fracture surgery for their ability to provide a clear surgical field of view; however, according to the Chinese Guidelines for Prevention of Venous Thromboembolism in Major Orthopedic Surgery, the use of tourniquets is a high-risk factor for the development of DVT after fracture surgery [39]. Intraoperative use of tourniquet blocks blood return to the distal limb, which tends to lead to venous blood stasis, which is more likely to form DVT [40]. According to the results of a foreign study, in anterior cruciate ligament reconstruction, compared with the use of a tourniquet, the absence of a tourniquet significantly reduces the incidence of postoperative DVT, and also significantly reduces the amount of drainage and the amount of blood loss [41]. Therefore, avoiding the use of a blood band can help reduce the risk of DVT when visibility of the surgical area is adequate.

3 Summary

DVT is a common and serious complication in patients with lower extremity fractures, which has a significant impact on both recovery and life. This article summarizes recent studies on the risk factors and pathogenesis of DVT in patients with lower extremity fractures. In terms of pathogenesis, the main mechanisms of DVT in patients with lower extremity fractures include venous injury, hypercoagulability, and slow venous blood flow, which together promote the development of DVT. In terms of risk factors, female patients, advanced age, overweight or obesity, prolonged operation time, general anesthesia, use of endografts, and use of intraoperative tourniquets are all risk factors for DVT. The prevention of DVT should be emphasized in patients with such risk factors. In conclusion, the pathogenesis and risk factors of DVT in patients with lower extremity fractures are complex and diverse, and should be fully emphasized in clinical practice, and corresponding measures should be taken to reduce the development of DVT.

Conflict of interest None

Reference

- [1] Ruan YL, Wang FT, Du XQ, et al. Rehabilitation nursing after lower limb fracture: preventing deep vein thrombosis and enhancing quality of life[J]. *Medicine*, 2023, 102(47): e36180.
- [2] Wenger N, Sebastian T, Engelberger RP, et al. Pulmonary embolism and deep vein thrombosis: similar but different[J]. *Thromb Res*, 2021, 206:88-98.
- [3] Schellenberg M, Benjamin E, Inaba K, et al. When is it safe to start pharmacologic venous thromboembolism prophylaxis after pelvic fractures? a prospective study from a level I trauma center[J]. *J Surg Res*, 2021, 258: 272-277.
- [4] Yang H, Yang JF, Cui WJ, et al. Analysis of occurrence regularity and risk factors of deep venous thrombosis in elderly patients with hip fracture during perioperative period[J]. *Chin J Bone Jt Inj*, 2019, 34(6): 599-601. [In Chinese]
- [5] Wu JT. Risk factors of postoperative incidence of LEDVT in patients with ankle fracture and the guiding significance of dynamic monitoring of serum D-D level[J]. *J Med Forum*, 2022, 43(2): 81-84. [In Chinese]
- [6] Ren X, Zhang JY, Liu YM, et al. Meta-analysis of the incidence of perioperative deep vein thrombosis in elderly hip fracture patients[J]. *China Medicine Herald*, 2023, 20(24): 85-88. [In Chinese]
- [7] Bochenek ML, Schäfer K. Role of endothelial cells in acute and chronic thrombosis. *hamostaseologie*[J]. 2019, 39(2): 128-139.
- [8] Sun H, Chen H. Study on characteristics of IL, TNF- α and FIB expression in patients with deep vein thrombosis and their correlation with vascular injury[J]. *Chin J Mod Drug Appl*, 2022, 16(24): 75-78. [In Chinese]
- [9] Falcon AK, Caballero LM, Filiberto DM, et al. Risk factors for venous thromboembolism and eventual amputation in traumatic femoral and iliac vein injuries: a trauma quality improvement program analysis[J]. *Am Surg*, 2024, 90(7): 1879-1885.
- [10] Brill A. Multiple facets of venous thrombosis[J]. *Int J Mol Sci*, 2021, 22(8): 3853.
- [11] Li YX, Jiang JM, Shi DC, et al. A prognostic nomogram model to predict deep vein thrombosis in preoperative pelvic fracture patients[J]. *J Pract Orthop*, 2024, 30(3): 217-221. [In Chinese]
- [12] Xiao S, Wang FX, Chen YH, et al. Factors affecting the occurrence of phlebotrombosis in the veins of lower extremity in patients with foot and ankle fracture[J]. *Guide China Med*, 2021, 19(33): 43-45. [In Chinese]
- [13] Lin CH, Chen YF, Chen B, et al. D-dimer combined with fibrinogen predicts the risk of venous thrombosis in fracture patients[J]. *Emerg Med Int*, 2020, 2020: 1930405.
- [14] You D, Skeith L, Korley R, et al. Identification of hypercoagulability with thrombelastography in patients with hip fracture receiving thromboprophylaxis[J]. *Can J Surg*, 2021, 64(3): E324-E329.
- [15] Ling K, Pang L, Chen ZR, et al. Clinical analysis of patients with lower limb fractures accomplished with venous thromboembolism[J]. *Chin J Bone Jt Inj*, 2013, 28(10): 941-943. [In Chinese]
- [16] Cosmi B, Borgese L, Legnani C, et al. Sex differences in clinical presentation of lower extremity deep vein thrombosis[J]. *J Womens Health*, 2024, 33(6): 758-764.
- [17] Sartori M, Borgese L, Favaretto E, et al. Age-adjusted D-dimer, clinical pre-test probability-adjusted D-dimer, and whole leg ultrasound in ruling out suspected proximal and calf deep venous thrombosis[J]. *Am J Hematol*, 2023, 98(11): 1772-1779.
- [18] Zhang LL, Shang JY, Liu YL, et al. Factors affecting the short-term progression of lower extremity distal deep vein thrombosis[J]. *Journal of Chinese Practical Diagnosis and Therapy*, 2024, 38(1): 62-65. [In Chinese]
- [19] Cao PK, Zhu TY, Wang FK, et al. Clinical value of age-adjusted D-dimer level in predicting lower extremity deep vein thrombosis before intertrochanteric fracture surgery in elderly patients[J]. *J Vasc Endovasc Surg*, 2023, 9(6): 663-668. [In Chinese]
- [20] Zeng BY, Wang BQ, Zuo JW. Risk factors analysis of patients with lower extremity deep vein thrombosis of different ages and genders[J]. *Mod Med J China*, 2020, 22(8): 12-18. [In Chinese]
- [21] Sloan M, Sheth N, Lee GC. Is obesity associated with increased risk of deep vein thrombosis or pulmonary embolism after hip and knee arthroplasty? A large database study[J]. *Clin Orthop Relat Res*, 2019, 477(3): 523-532.
- [22] Li SH, Zhang K, Feng DX, et al. Occurrence of deep venous thrombosis in lower extremities within 24h after hip fracture and change in incidence of thrombosis after delayed admission[J]. *Orthopaedics*, 2019, 10(4): 307-313. [In Chinese]
- [23] Tang OL, Li HY, Du YF, et al. Risk factors for lower extremity deep vein thrombosis in patients with acute pancreatitis[J]. *J Vasc Endovasc Surg*, 2023, 9(6): 669-672. [In Chinese]
- [24] Yang C, Govur Imar, Anar, et al. Intraoperative risk factors of postoperative deep venous thrombosis of the lower extremity in orthopedic patients[J]. *J Vasc Endovasc Surg*, 2022, 8(9): 1043-1048. [In Chinese]
- [25] Tang XW. Analysis of risk factors and establishment of prediction model for postoperative deep venous thrombosis in patients undergoing major orthopedic surgery[D]. Nanchong: North Sichuan Medical College, 2023. [In Chinese]
- [26] Su Q. Study on related factors of deep venous thrombosis after lower limb fracture surgery[D]. Lanzhou: Gansu University of Chinese Medicine, 2021. [In Chinese]

- [27] Pang C, Jia WP. Current research on adipose tissue hypoxia and obesity-related inflammation[J]. Natl Med J China, 2008, 88(36): 2588-2591. **[In Chinese]**
- [28] Signorelli SS, Oliveri Conti G, Fiore M, et al. Platelet-derived microparticles (MPs) and thrombin generation velocity in deep vein thrombosis (DVT): results of a case-control study[J]. Vasc Health Risk Manag, 2020, 16: 489-495.
- [29] Gui HZ, Wang L, Gao CG, et al. Analysis of influencing factors for deep vein thrombosis after lower extremity fracture surgery[J]. J Vasc Endovasc Surg, 2023, 9(6): 726-730. **[In Chinese]**
- [30] Dong YJ, Zhang TH, Zhong S, et al. Analysis on risk factors for deep vein thrombosis in patients with traumatic fractures[J]. Chin J Orthop, 2015, 35(11): 1077-1083. **[In Chinese]**
- [31] Bai YP, Qiu YM, Ding JH, et al. Risk factors of deep vein thrombosis during perioperative time in geriatric patients with hip fractures[J]. Orthop Biomech Mater Clin Study, 2022, 19(4): 21-25. **[In Chinese]**
- [32] Huang M. Risk factors of deep venous thrombosis formation after operation of femoral neck fracture[J]. Med Innov China, 2022, 19(20): 80-83. **[In Chinese]**
- [33] Liu BB, Ge X. Risk factors for postoperative deep vein thrombosis of the lower extremity in elderly patients with diabetes mellitus combined with femoral neck fracture and countermeasures for protection[J]. General Practice Nursing, 2022, 20(14): 1994-1996. **[In Chinese]**
- [34] Yao J, Meng JH, Wang WJ, et al. Effect of different anesthesia on deep venous thrombosis after orthopedic surgery[J]. J Ningxia Med Univ, 2013, 35(1): 29-31, 36. **[In Chinese]**
- [35] Xiao X, Li GC, Duan YB, et al. Effects of different anesthesia methods on deep vein thrombosis of lower extremity after total knee arthroplasty[J]. J Anhui Med Coll, 2022, 21(3): 22-23, 26. **[In Chinese]**
- [36] Xu Z, Li C. Comparison of incidence of LDVT in elderly patients with lower extremity fracture under intraspinal anesthesia and general anesthesia[J]. Shenzhen J Integr Tradit Chin West Med, 2024, 34(1): 26-29. **[In Chinese]**
- [37] Zeng YL, Xiao R, Tian X, et al. Effect of neuraxial anesthesia on postoperative recovery and deep vein thrombosis formation of lower extremity in elderly patients with femoral intertrochanteric fracture[J]. J Vasc Endovasc Surg, 2023, 9(11): 1186-1190. **[In Chinese]**
- [38] Yi WL, Liang B. Advances in risk factors and prevention of deep venous thrombosis after spine surgery[J]. Med Recapitul, 2016, 22(23): 4641-4645. **[In Chinese]**
- [39] Qiu GX. Guidelines for prevention of venous thromboembolism in orthopedic surgery in China[J/OL]. Chin J Jt Surg Electron Ed, 2009, 3(3): 380-383. **[In Chinese]**
- [40] Zhang HG, Liu H, Wang ZB, et al. Analysis of high-risk factors for lower limb venous thrombosis during perioperative period of bone and joint surgery[J]. Health Vocat Educ, 2023, 41(23): 144-147. **[In Chinese]**
- [41] Nagashima M, Takeshima K, Origuchi N, et al. Not using a tourniquet may reduce the incidence of asymptomatic deep venous thrombosis after ACL reconstruction: an observational study[J]. Orthop J Sports Med, 2021, 9(12): 23259671211056677.

Submission received: 2024-11-15

· 研究进展 ·

下肢骨折深静脉血栓形成的发病机制 和危险因素研究进展

邓鑫, 苏云, 富雨田, 张浩淳, 张永昆, 王洪勋

大连大学附属中山医院创伤骨科, 辽宁 大连 116000

摘要: 下肢骨折是一种常见的临床病症, 显著影响患者的日常生活和工作。这类患者通常伴随静脉壁损伤、血流缓慢及血液高凝状态等深静脉血栓形成(DVT)的主要危险因素, 因此, DVT 的发生率较高。如果未能及时进行预防和干预, DVT 可能导致血栓脱落并进入肺动脉, 从而引发肺栓塞, 对患者生命构成严重威胁。因此深入了解 DVT 的发病机制及其危险因素至关重要。基于上述情况, 本文综述了下肢骨折相关 DVT 的发病机制与危险因素, 以期为临床医生在早期识别及治疗 DVT 提供参考。

关键词: 下肢骨折; 深静脉血栓形成; 发病机制; 危险因素; 血液淤滞; 静脉损伤; 高凝状态; 麻醉; 止血带

中图分类号: R687.3 **文献标识码:** A **文章编号:** 1674-8182(2025)02-0182-04

Advances in the pathogenesis and risk factors of deep vein thrombosis in lower extremity fractures

DENG Xin, SU Yun, FU Yutian, ZHANG Haochun, ZHANG Yongkun, WANG Hongxun

Department of Trauma Orthopedics, Affiliated Zhongshan Hospital of Dalian University, Dalian, Liaoning 116000, China

Corresponding author: WANG Hongxun, E-mail: 492705108@qq.com

Abstract: Lower extremity fracture is a common clinical condition that significantly affects patients' daily activities and work. These patients are often accompanied by major risk factors for deep vein thrombosis (DVT), such as venous wall injury, slow blood flow, and a hypercoagulable state. As a result, the incidence of DVT is high in this population. If prevention and intervention are not promptly implemented, DVT can lead to thromboembolism, which may travel to the pulmonary artery, resulting in pulmonary embolism and posing a serious threat to the patient's life. Therefore, it is crucial to gain a deeper understanding of the pathogenesis and risk factors of DVT. This review summarizes the mechanisms and risk factors associated with DVT in lower extremity fractures, aiming to provide reference for clinicians in the early identification and management of DVT.

Keywords: Lower limb fracture; Deep vein thrombosis; Pathogenesis; Risk factor; Stasis; Vascular damage; Hypercoagulability; Anesthesia; Tourniquet

下肢骨折是一种常见的临床疾病, 对患者的日常生活和工作产生明显影响。下肢骨折患者常同时合并血栓形成的 Virchow 三要素, 即静脉壁损伤、血流缓慢和血液高凝状态, 因此深静脉血栓形成(deep vein thrombosis, DVT)的发生率较高^[1]。DVT 的发生显著影响下肢静脉血液循环, 部分患者因患肢血流障碍而出现远端缺血和缺氧, 这可能导致远端组织坏死甚至需要截肢; 若血栓脱落并随血液流动至右心及肺动脉系统, 则可引发致命性肺栓塞(PE)^[2]。既往文献报道, 下肢骨折各部位 DVT 的发生率存在显著差异。其中, 骨盆髋臼

骨折、髌骨骨折、股骨干骨折、膝关节周围骨折、胫腓骨骨折及踝关节骨折患者的 DVT 发生率分别为 3%~48%、38.25%~56.83%、40%~86%、50.4%、30% 和 18.97%^[3-6]。DVT 的发生对下肢骨折患者的围手术期疗效和预后具有显著影响, 且在此期间, DVT 表现出易发性、高致残率及高致死率等特点。因此, 对于下肢骨折患者而言, 深入探讨 DVT 的发病机制及其危险因素是十分必要的。目前, 临床上对 DVT 的发病机制和危险因素缺乏系统性的研究, 本文将从这两个方面进行全面综述, 以期为临床防治 DVT 提供进一步参考。

DOI: 10.13429/j.cnki.cjcr.2025.02.005

通信作者: 王洪勋, E-mail: 492705108@qq.com

出版日期: 2025-02-20



QR code for English version

1 DVT 的发病机制

DVT 的主要发病机制可归纳为德国学者 Virchow 提出的血栓形成三因素:静脉壁损伤、血流缓慢及高凝状态。下肢骨折患者因长期卧床导致的血液淤滞、手术后出现的血液高凝状态以及创伤引起的血管壁损伤均可导致 DVT。

1.1 静脉壁损伤 静脉壁由外层、中间层和内层组成。当内层受损时,内皮细胞发生缺陷或剥离,这会导致机体局部血细胞聚集并与血小板粘连,最终形成血栓。静脉壁的损伤可以分为物理性、化学性和感染性三种类型。物理性损伤通常是由外部创伤引起的,如局部血管撕裂或挫伤,常见于暴力挤压、反复静脉穿刺、骨折块压迫、手术操作损伤等;化学性损伤则主要发生在注射各种抗生素、高渗溶液以及其他刺激性溶液时;感染性损伤可直接由静脉炎引起,也可能通过其他感染灶间接诱发。内皮细胞在止血反应过程中扮演着至关重要的角色,是血管对于导致血栓形成损伤反应的组成部分。当内皮受损时,将显著增加 DVT 发生率^[7]。研究发现 DVT 患者白细胞介素、肿瘤坏死因子 α 和纤维蛋白原的表达水平显著增加,并且这种增加与血管损伤程度之间存在正相关关系^[8]。这为临床根据其表达情况来评估 DVT 及其引起的血管损伤程度至关重要。此外有报道称髂静脉和股静脉损伤的患者 DVT 发生率极高,这可能与静脉血管损伤有关^[9]。

1.2 血流缓慢 下肢骨折患者常因疼痛、术后肌肉松弛、麻醉药物的使用等导致全身周围静脉血液循环减缓;其次长期卧床和活动受限也会使下肢静脉血流速度进一步降低。研究表明,患者卧床时间增加会使 DVT 风险增加,这主要是肢体活动减少导致血液淤滞引起^[10]。

1.3 高凝状态 血液高凝状态是由血管内皮细胞、血小板、凝血酶、抗凝和纤溶系统等相互影响所引起的一种血液易凝状态。当血液高凝状态发生时,血液中的凝血因子和血小板会更容易聚集在一起形成血栓;这种血栓可能会在下肢深静脉中形成,导致 DVT^[11]。有研究报道,骨折患者由于其血液的高凝状态,术前 DVT 发生率约为 18.4%,下肢骨折患者 DVT 发生率为 40%~60%^[12]。Lin 等^[13] 研究指出,在骨折状态下,活动减少会增加出血、血液黏度和感染的风险,导致血液高凝,进而增加 DVT 的发生概率。You 等^[14] 在 35 例髋部骨折患者中使用血栓弹力图检测凝血状态,发现入院时有 11 例处于高凝状态;所有患者在 2 周时明显出现高凝情况,并且持续至 6 周,呈现持续高凝趋势尽管进行了血栓预防措施,超过 50% 的患者在骨折后 6 周仍保持高凝状态。

2 DVT 的危险因素

结合下肢骨折患者的疾病特点,可将下肢骨折 DVT 的危险因素总结为性别、年龄、身体质量指数(BMI)、基础疾病、手术方式、手术时间、手术部位、麻醉方式、内植物使用以及止血带使用等。现将其归纳如下。

2.1 性别 凌坤等^[15] 对 307 例下肢骨折的患者进行回顾性分析,发现围术期女性静脉血栓性疾病(VTE)的发生率高于

男性(21.9% vs 15.3%)。一项国外的研究发现,女性 DVT 的整体发病率较男性更高,但男性中近端 DVT 的发病率却高于女性^[16]。因此在临床中应更加重视女性患者的 DVT 预防措施。同时,在特殊情况下如孕期、产后以及接受雌激素替代治疗时,需要密切监测并采取有效措施来降低 DVT 风险。

2.2 年龄 年龄是 DVT 的一个独立危险因素^[17-18]。曹彭凯等^[19] 研究发现,在老年股骨粗隆间骨折患者中,年龄是 DVT 独立危险因素。有报道称,年龄 ≥ 45 岁是导致 DVT 主要危险因素之一^[20]。Sloan 等^[21] 研究发现,年龄 ≥ 45 岁是影响 DVT 的危险因素。李树灏等^[22] 研究指出,髋部骨折患者在 45~59 岁、60~74 岁及 ≥ 75 岁年龄段中,其发生 DVT 的风险分别是 < 45 岁患者的 3.12 倍、3.20 倍和 6.45 倍。尽管对年龄这一因素存在不同观点,但目前临床指南已将其确立为重要的预防因素。因此,在制定预防措施和治疗方案时,必须充分考虑年龄这一关键因素,并采取针对性措施。

2.3 BMI 相较于体重正常者,超重或肥胖患者更容易发生 DVT^[23]。杨晨等^[24] 收集了 136 例接受手术治疗的骨科患者的临床资料,经过研究发现 BMI ≥ 24 kg/m² 为骨科患者术后发生下肢 DVT 的独立危险因素。唐小王^[25] 研究发现下肢骨科大手术的患者术后 DVT 的高危因素包括年龄增加、BMI 较高、胆固醇及三酰甘油较高、术中出血量增多等。苏奇^[26] 对 400 例下肢骨折手术患者采用单因素及 logistic 回归进行资料的统计分析,结果显示肥胖是术后并发 DVT 的高危因素。大量研究已表明,超重或肥胖显著增加下肢骨折术后 DVT 的发生率,其机制可能与肥胖患者慢性腹内压升高及血流缓慢有关。此外,肥胖个体的血管内皮细胞抗氧化能力下降和脂肪细胞代谢失调也可能是重要因素^[27]。另有研究表明,肥胖患者体内血小板源性微颗粒(pDMP)的含量显著高于正常人,并且该含量与 BMI 及机体脂肪呈正相关,因此肥胖个体常处于血小板激活状态^[28]。

2.4 基础疾病 老年患者血管弹性低,同时合并多种基础疾病,如高血压、糖尿病、肺心病、冠状动脉粥样硬化性心脏病(冠心病)等,这大大加剧了血管损伤,增加了 DVT 的风险。文献报道证实,高血压、高脂血症、糖尿病、冠心病、肺部疾病等基础疾病与下肢骨折患者 DVT 的发生密切相关,这些基础疾病会导致血液循环不畅,增加了下肢骨折患者出现 DVT 的风险^[29]。因此,在手术前和手术后应该对患者进行全面评估,并采取相应措施预防和减少 DVT 的发生。

2.5 手术时间 手术时间延长会增加患者术后并发 DVT 的发生概率。董玉金等^[30] 研究显示,手术持续时间 ≥ 2 h 会增加术后 DVT 的发生以及 PE 的发生。对于老年髋部骨折患者,手术时间过长会极大增加术后并发 DVT 的风险,白云鹏等^[31] 研究发现手术时间 > 2 h 是老年髋部骨折患者围手术期 DVT 的独立危险因素。另一项研究则认为手术时间 > 1 h 是股骨颈骨折术后 DVT 发生的危险因素^[32];对于合并糖尿病的股骨颈骨折患者,刘蓓蓓等^[33] 则认为手术时间 > 2 h 会增加术后并发 DVT 的风险。除老年髋部骨折以外,其他类型的下肢骨折如足踝部、膝关节周围等位置的骨折术后并发 DVT 都

与手术时间的长度有着密切的关系,不同学者报道的时间各有差异,但绝大多数都是手术时间>1 h、>2 h 对 DVT 的形成密切相关。因此,在选择手术方式,需要进行科学合理性评估手术时间,以最大程度地减少 DVT 的发生。

2.6 麻醉方式 多数文献表明全身麻醉较椎管内麻醉相比,术后 DVT 的发生率高^[34-35]。许哲等^[36]经随机数字表分组,将 90 例下肢骨折老年患者均分为对照组(全身麻醉)与观察组(椎管内麻醉),术后进行下肢血管彩超复查,结果显示对照组有 6 例发生 DVT,而观察组未出现该并发症;研究结果表明,在下肢骨折的老年患者中,相较于全身麻醉,采用椎管内麻醉能够有效降低术后 DVT 发生率。曾艳利等^[37]利用相同的方法比较了股骨粗隆间骨折患者的不同麻醉方法术后 DVT 的发生率,结果发现椎管内麻醉可降低老年股骨粗隆间骨折术后下肢 DVT 的发生率。目前下肢骨折患者通常选择全身麻醉或椎管内麻醉作为普遍使用的方法,其他类型的麻醉方式较少采用,因此不予讨论。对于适合进行椎管内麻醉的患者来说,为了减少术后 DVT 并发症风险,避免使用全身麻醉是一个可行选择。

2.7 内植物使用 下肢骨折常用的内植物包括钢板、螺钉、髓内针、人工骨、人工关节等。内植物引起的过敏反应、热聚合反应等不良反应可能损伤血管内膜或激活凝血系统引起 DVT^[38]。

2.8 止血带使用 止血带在下肢骨折手术中被广泛应用,因其能够提供清晰的手术视野;然而根据《中国骨科大手术静脉血栓栓塞症预防指南》,止血带的使用是导致骨折术后发生 DVT 的一个高危因素^[39]。术中使用止血带阻滞了肢体远端血液回流,容易导致静脉血瘀滞,这更加容易形成 DVT^[40]。根据一项国外研究结果显示,在前交叉韧带重建术中,相较于使用止血带,不使用止血带能够显著降低术后 DVT 的发生率,并且还能明显减少引流量和失血量^[41]。因此,在手术区域可见度足够的情况下,避免使用止血带有助于降低 DVT 的发生风险。

3 小结

DVT 是下肢骨折患者常见且严重的并发症,对患者的康复和生命都具有重大影响。本文综述了近年来关于下肢骨折患者 DVT 危险因素和发病机制方面的研究。在发病机制方面,下肢骨折患者 DVT 主要形成机制包括静脉损伤、血液高凝状态以及静脉血流缓慢,三者相互作用,共同促进了 DVT 的发生。在危险因素方面,女性患者、高龄、超重或肥胖、手术时间过长、全身麻醉、内植物使用以及术中止血带使用均为 DVT 的危险因素。临床遇到合并此类危险因素的患者应更加重视 DVT 的预防。综上所述,下肢骨折患者 DVT 的发病机制和危险因素复杂多样,在临床实践中应给予充分重视,并采取相应措施以减少 DVT 的发生。

利益冲突 无

参考文献

[1] Ruan YL, Wang FT, Du XQ, et al. Rehabilitation nursing after

lower limb fracture: preventing deep vein thrombosis and enhancing quality of life[J]. *Medicine*, 2023, 102(47): e36180.

- [2] Wenger N, Sebastian T, Engelberger RP, et al. Pulmonary embolism and deep vein thrombosis: Similar but different [J]. *Thromb Res*, 2021, 206:88-98.
- [3] Schellenberg M, Benjamin E, Inaba K, et al. When is it safe to start pharmacologic venous thromboembolism prophylaxis after pelvic fractures? A prospective study from a level I trauma center [J]. *J Surg Res*, 2021, 258: 272-277.
- [4] 杨辉,杨金峰,崔文军,等.老年髋部骨折患者围手术期深静脉血栓形成的发生规律及危险因素分析[J]. *中国骨与关节损伤杂志*, 2019, 34(6):599-601.
- [5] 吴江涛.踝关节骨折患者术后 LEDVT 发生率的危险因素及血清 D-D 水平动态监测指导意义[J]. *医药论坛杂志*, 2022, 43(2): 81-84.
- [6] 任鑫,张佳宇,刘艳梅,等.老年髋部骨折患者围手术期深静脉血栓发生率的 meta 分析[J]. *中国医药导报*, 2023, 20(24): 85-88.
- [7] Bochenek ML, Schäfer K. Role of endothelial cells in acute and chronic thrombosis[J]. *Hamostaseologie*, 2019, 39(2):128-139.
- [8] 孙会,陈卉.深静脉血栓患者 IL、TNF- α 、FIB 表达特征及其与血管损伤情况的关联性研究[J]. *中国现代药物应用*, 2022, 16(24):75-78.
- [9] Falcon AK, Caballero LM, Filiberto DM, et al. Risk factors for venous thromboembolism and eventual amputation in traumatic femoral and iliac vein injuries: a trauma quality improvement program analysis[J]. *Am Surg*, 2024, 90(7): 1879-1885.
- [10] Brill A. Multiple facets of venous thrombosis[J]. *Int J Mol Sci*, 2021, 22(8): 3853.
- [11] 李永霞,姜家梅,侍冬成,等.骨盆骨折术后前下肢深静脉血栓形成预测模型探讨[J]. *实用骨科杂志*, 2024, 30(3):217-221.
- [12] 肖松,王凤雄,陈耀辉,等.足踝部骨折手术患者下肢静脉血栓发生影响因素[J]. *中国医药指南*, 2021, 19(33):43-45.
- [13] Lin CH, Chen YF, Chen B, et al. D-dimer combined with fibrinogen predicts the risk of venous thrombosis in fracture patients [J]. *Emerg Med Int*, 2020, 2020: 1930405.
- [14] You D, Skeith L, Korley R, et al. Identification of hypercoagulability with thrombelastography in patients with hip fracture receiving thromboprophylaxis[J]. *Can J Surg*, 2021, 64(3): E324-E329.
- [15] 凌坤,庞龙,陈志荣,等.下肢骨折并发静脉血栓性疾病男女性发病差异临床分析[J]. *中国骨与关节损伤杂志*, 2013, 28(10): 941-943.
- [16] Cosmi B, Borgese L, Legnani C, et al. Sex differences in clinical presentation of lower extremity deep vein thrombosis[J]. *J Womens Health*, 2024, 33(6): 758-764.
- [17] Sartori M, Borgese L, Favaretto E, et al. Age-adjusted D-dimer, clinical pre-test probability-adjusted D-dimer, and whole leg ultrasound in ruling out suspected proximal and calf deep venous thrombosis[J]. *Am J Hematol*, 2023, 98(11): 1772-1779.
- [18] 张莉莉,尚俊依,刘英丽,等.下肢远端深静脉血栓短期进展的影响因素[J]. *中华实用诊断与治疗杂志*, 2024, 38(1):62-65.
- [19] 曹彭凯,朱恬仪,王凤凯,等.年龄调整 D-二聚体水平在预测老

- 年股骨粗隆间骨折术前下肢深静脉血栓中的临床价值[J].血管与腔内血管外科杂志,2023,9(6):663-668.
- [20] 曾保尧,王斌强,左江伟.不同年龄和性别下肢深静脉血栓形成危险因素分析[J].中国现代医药杂志,2020,22(8):12-18.
- [21] Sloan M, Sheth N, Lee GC. Is obesity associated with increased risk of deep vein thrombosis or pulmonary embolism after hip and knee arthroplasty? A large database study[J]. Clin Orthop Relat Res, 2019,477(3):523-532.
- [22] 李树灏,张望,冯东旭,等.髌骨骨折 24 小时内及延迟入院的下肢深静脉血栓发生情况分析[J].骨科,2019,10(4):307-313.
- [23] 唐鸥鹭,李海燕,杜燕飞,等.急性胰腺炎患者发生下肢深静脉血栓的危险因素[J].血管与腔内血管外科杂志,2023,9(6):669-672.
- [24] 杨晨,吾甫尔·依马尔,阿娜尔,等.骨科患者术后发生下肢深静脉血栓的术中影响因素[J].血管与腔内血管外科杂志,2022,8(9):1043-1048.
- [25] 唐小王.骨科大手术患者术后深静脉血栓形成的危险因素分析及预测模型的建立[D].南充:川北医学院,2023.
- [26] 苏奇.下肢骨折术后形成深静脉血栓的相关因素研究[D].兰州:甘肃中医药大学,2021.
- [27] 庞臻,贾伟平.脂肪组织缺氧与肥胖相关性炎症的研究现状[J].中华医学杂志,2008,88(36):2588-2591.
- [28] Signorelli SS, Oliveri Conti G, Fiore M, et al. Platelet-derived microparticles (MPs) and thrombin generation velocity in deep vein thrombosis (DVT): results of a case-control study[J]. Vasc Health Risk Manag, 2020, 16: 489-495.
- [29] 桂海枝,王莉,高成钢,等.下肢骨折术后深静脉血栓形成的影响因素分析[J].血管与腔内血管外科杂志,2023,9(6):726-730.
- [30] 董玉金,张铁慧,钟声,等.创伤骨折患者深静脉血栓形成的危险因素分析[J].中华骨科杂志,2015,35(11):1077-1083.
- [31] 白云鹏,邱永敏,丁菊红,等.老年髌骨骨折围手术期深静脉血栓形成的危险因素分析[J].生物骨科材料与临床研究,2022,19(4):21-25.
- [32] 黄森.股骨颈骨折术后深静脉血栓形成的危险因素分析[J].中国医学创新,2022,19(20):80-83.
- [33] 刘蓓蓓,葛雪.老年股骨颈骨折合并糖尿病病人术后下肢深静脉血栓形成危险因素及防护对策[J].全科护理,2022,20(14):1994-1996.
- [34] 姚杰,孟尽海,王文娟,等.不同麻醉方法对骨科手术患者深静脉血栓形成的影响[J].宁夏医科大学学报,2013,35(1):29-31,36.
- [35] 肖旭,李光才,段玉屏,等.不同麻醉方法对行全膝关节置换术后下肢深静脉血栓形成的影响[J].安徽医学,2022,21(3):22-23,26.
- [36] 许哲,李灿.椎管内麻醉与全身麻醉下手术的下肢骨折老年患者 LDVT 发生率比较[J].深圳中西医结合杂志,2024,34(1):26-29.
- [37] 曾艳利,肖蕊,田轩,等.椎管内麻醉对老年股骨粗隆间骨折术后恢复及下肢深静脉血栓形成的影响[J].血管与腔内血管外科杂志,2023,9(11):1186-1190.
- [38] 易伟林,梁斌.脊柱手术后深静脉血栓形成的危险因素及预防的研究进展[J].医学综述,2016,22(23):4641-4645.
- [39] 邱贵兴.中国骨科大手术静脉血栓栓塞症预防指南[J].中华关节外科杂志(电子版),2009,3(3):380-383.
- [40] 张宏刚,刘辉,王志彬,等.骨关节围手术期下肢静脉血栓的高危因素分析[J].卫生职业教育,2023,41(23):144-147.
- [41] Nagashima M, Takeshima K, Origuchi N, et al. Not using a tourniquet may reduce the incidence of asymptomatic deep venous thrombosis after ACL reconstruction: an observational study[J]. Orthop J Sports Med, 2021, 9(12): 23259671211056677.

收稿日期:2024-11-15 编辑:王海琴

(上接第 172 页)

- [34] Ende-Verhaar YM, Meijboom LJ, Kroft LJM, et al. Usefulness of standard computed tomography pulmonary angiography performed for acute pulmonary embolism for identification of chronic thromboembolic pulmonary hypertension: results of the InShape III study[J]. J Heart Lung Transplant, 2019, 38(7): 731-738.
- [35] Avgerinos ED, Abou Ali AN, Liang NL, et al. Catheter-directed interventions compared with systemic thrombolysis achieve improved ventricular function recovery at a potentially lower complication rate for acute pulmonary embolism[J]. J Vasc Surg Venous Lymphat Disord, 2018, 6(4): 425-432.
- [36] Bloomer TL, El-Hayek GE, McDaniel MC, et al. Safety of catheter-directed thrombolysis for massive and submassive pulmonary embolism: results of a multicenter registry and meta-analysis[J]. Catheter Cardiovasc Interv, 2017, 89(4): 754-760.
- [37] Beyer SE, Shanafelt C, Pinto DS, et al. Utilization and outcomes of thrombolytic therapy for acute pulmonary embolism: a nationwide cohort study[J]. Chest, 2020, 157(3): 645-653.
- [38] Tak T, Karturi S, Sharma U, et al. Acute pulmonary embolism: contemporary approach to diagnosis, risk-stratification, and management[J]. Int J Angiol, 2019, 28(2): 100-111.
- [39] van Matre ET, Reynolds PM, MacLaren R, et al. Evaluation of unfractionated heparin versus low-molecular-weight heparin and fondaparinux for pharmacologic venous thromboembolic prophylaxis in critically ill patients with cancer[J]. J Thromb Haemost, 2018, 16(12): 2492-2500.

收稿日期:2024-11-13 编辑:叶小舟