

# Deep vein thrombosis of the lower limbs in injection drug users

Jędrzej Fischer<sup>1</sup> , Wiesława Kwiatkowska<sup>2</sup>, Wojciech Witkiewicz<sup>3</sup>

<sup>1</sup>Department of Angiology, Hypertension and Diabetology, Wrocław Medical University, Wrocław, Poland

<sup>2</sup>Department of Angiology and Diabetology, Regional Specialist Hospital in Wrocław, Research and Development Center in Wrocław, Poland

<sup>3</sup>Regional Specialist Hospital in Wrocław, Research and Development Center in Wrocław, Poland

## Abstract

*Venous thromboembolism is the third most common cardiovascular disease and is associated with a high risk of death or disability. One group of patients at particular risk of developing this disease are injection drug users. A series of five cases of patients addicted to narcotic drugs, hospitalized at the Department of Angiology for venous thromboembolism has been presented. The main risk factor was a venous or subcutaneous tissue injection of drugs. These cases show a complex clinical picture of venous thrombosis, difficulties in selecting and monitoring anticoagulant therapy, coexisting infections, as well as economic and psychosocial aspects.*

*Addiction to drugs administered by injection is a risk factor for venous thromboembolism, the clinical picture is complex, and treatment is a major challenge for vascular medicine and drug addiction therapy. Education and preventive measures within the communities of drug addicts could be the most important actions aimed at reducing the incidence of deep vein thrombosis.*

**Key words:** venous thromboembolism, deep vein thrombosis, injection drug users

Acta Angiol 2022; 28, 2: 56–62

## Introduction

Venous thromboembolism (VTE) is a serious public health problem. It occurs in 1–2 cases per 1000 people; in two-thirds of cases, it manifests as isolated deep vein thrombosis (DVT), and in one-third of cases as a pulmonary embolism (PE). There is a high risk of recurrence of the disease, development of post-thrombotic syndrome, and in the more severe cases chronic complications leading to permanent disability [1]. There are many risk factors for this disease, including old age, cancers, use of contraceptives, injuries, infections, and immobilization. One group of patients who are particularly predisposed to the development of DVT are injection drug users (IDUs). Below we report five

cases of patients diagnosed with VTE where the main risk factor was venous or subcutaneous tissue injection of drugs. All presented patients were diagnosed with viral infections that co-existed with drug addiction: either human immunodeficiency virus (HIV) or hepatitis B (HBV) or C viruses (HCV), or co-infections. The cases of these patients have been presented to share our observations on this specific disease course, which is slightly different from the classical one and to highlight the challenges associated with treating these particular patients. The authors would also like to attract the attention of communities that care for drug addicts, experts involved in the treatment of addictions, as well as experts dealing with VTE in order to convey the seriousness of this public health issue, which is marginally

**Address for correspondence:** Jędrzej Fischer, Department of Angiology, Hypertension and Diabetology, Wrocław Medical University, Wrocław, 213 Borowska Street, 50–556 Wrocław, Poland, e-mail: jedrzej.fischer@umw.edu.pl

or not at all addressed in most studies and guidelines. All patients presented here were hospitalized in the Department of Angiology of the Regional Specialist Hospital in Wrocław, Poland, in the years 2010-2016. Every year the unit admits approximately 800 patients, 10% of whom are VTE patients.

## Description of cases

### Case 1

A 39-year-old man was admitted to the accident and emergency department (A&E) with pain, swelling, and cyanosis of his right lower limb; he was diagnosed with proximal DVT based on the clinical picture and ultrasonography. Because the patient did not give consent for hospital treatment, low molecular weight heparin (LMWH) was prescribed for outpatient treatment. The patient returned to the A&E unit after a week. As it turned out, he did not follow the prescribed treatment, and the disease symptoms had intensified. This time he was admitted to the Angiology Department, a Doppler echocardiography was again performed, confirming the presence of thrombus with mixed echogenicity that had completely filled the distal part of the common femoral vein and the femoral and popliteal veins; no blood flow was detected. A medical history revealed infection with HIV and long-term active drug addiction by means of injections, with recent administration of ephedrine intravenously (mixing the popular tablets used for a runny nose with readily available chemicals) and previous use of the so-called "compote" (Polish heroin) which was injected into the vein or subcutaneous tissue, most often within the thigh area. Six months earlier, the patient had ceased treatment at the acquired immunodeficiency and drug rehabilitation clinics. Moreover, in recent months he had been treated for a right thigh abscess. In the physical examination the advanced features of lipoatrophy, especially to the face, buttocks, and limbs attracted particular attention. The abdominal palpation revealed an enlarged liver and spleen. Single crackles at the lung base were identified. Enlarged peripheral lymph nodes were also observed. The right lower limb was swollen and livid, with visible dilated superficial veins; there was increased consistency and soreness of the soft tissue. On the skin of both lower limbs, numerous discolorations were visible, i.e., along the saphenous vein (Fig. 1). Scars and minor ulcers covered with dry necrosis were located on the lower limb and along the saphenous vein (Fig. 2). Moreover, confluent subcutaneous hematoma and petechiae could be seen in the distal area of the right lower limb (Fig. 3).

Laboratory tests showed: high C-reactive protein level (CRP) — 185 mg/L, white blood cells count

(WBC) — 13.4 K/uL, low hemoglobin (Hb level 7.5 g/dL), elevated D-dimer level (4661  $\mu$ g/L), hypokalemia and hyponatremia, and positive serological tests for HCV. Hepatosplenomegaly was evident with abdominal ultrasound, and on the chest X-ray, micronodular lesions in the left apex and the sub-apical zone were observed, which had progressed compared with the X-ray performed a year earlier.

Anticoagulant therapy was initiated (enoxaparin — 1 mg/kg of body weight every 12 hours) in addition to the lower limb elevation and compression therapy. Metamizole and paracetamol were also administered due to fever (up to 40°C). The entire clinical picture suggested a diagnosis of acquired immunodeficiency syndrome (AIDS), which is associated with specific pulmonary lesions. The patient was referred to the Infectious Diseases Unit. It was recommended that class II compression stockings be used, as well as a minimum of three months of anticoagulation treatment with enoxaparinum 1.5 mg/kg of body weight, once a day. The information received from this Unit confirmed the diagnosis of pulmonary mycobacteriosis.

### Case 2

A 43-year-old male professional driver was admitted to the Department of Angiology on a scheduled basis for diagnostic purposes in connection with a history of DVT in the left lower extremity seven months prior. A medical history upon admission revealed intravenous drug dependence in the past (13 years earlier), presence of HCV infection, and current treatment with an anticoagulant (rivaroxaban). In the physical examination, skin lesions on the lower limbs were noted; on the left thigh, there was a scaly tattoo (Fig. 4), and on both extremities, numerous scars, small scattered ulcers covered with necrotic scabs with local skin/subcutaneous tissue infections around them, and irregular, spread discolorations within the calf area (Fig. 5). Lesions in the lower limbs suggested active injecting of narcotic drugs. During the few days of hospitalization, attempts were made to establish a reliable medical history of addiction. On the last day of hospitalization, the patient admitted he was still taking drugs by injection (amphetamines, ephedrine), even when the thrombosis had been diagnosed. He also reported that his attempt to disguise the problem was due to the fear of losing his family.

In the laboratory analyses, the serological tests for HCV infection were positive, and mild anemia was found (Hb 11.4 g/dL). Genetic studies for thrombophilia showed homozygous mutation of the homocysteine gene (MTHFR C677T) with normal homocysteine concentration. Ultrasound of the veins showed an obstruction in the distal part of the iliac vein, the common femoral vein (without recanalization characteristics);



**Figure 1.** Discoloration and scarring along the saphenous vein; the so-called “track marks”

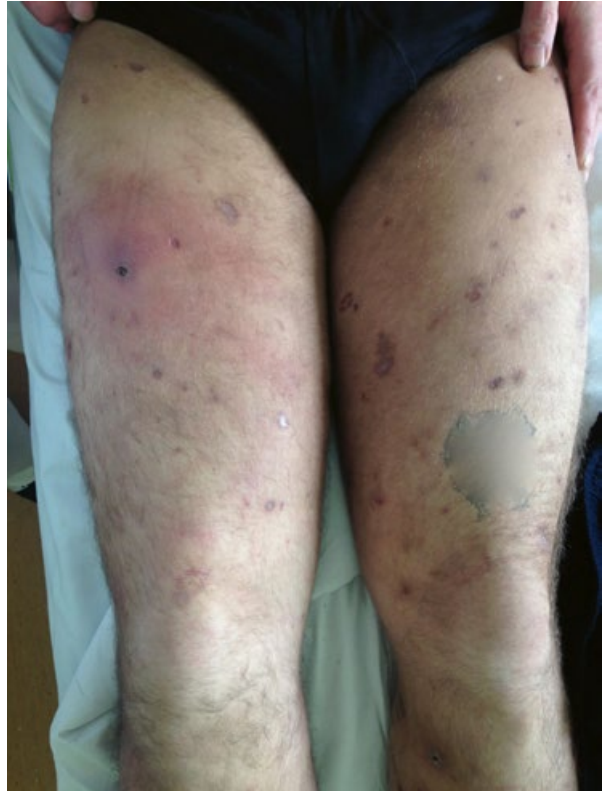


**Figure 2.** “Track marks” in addition to minor ulcers covered with dry necrosis are visible



**Figure 3.** Confluent subcutaneous hematoma and petechiae of the right lower limb

mural thrombi with mixed echogenicity were also observed in the femoral vein, popliteal, and saphenous veins (moderate recanalization).



**Figure 4.** Small, scattered ulcers covered with necrotic scabs, the so-called “skin popping”, are visible, with local skin/subcutaneous tissue infections around them. Tattoo on the left thigh (it has been blurred to prevent identification of the patient)



**Figure 5.** Numerous scars, as well as small, scattered ulcers covered with necrotic scabs (“skin popping”) are visible, with local skin/subcutaneous tissue infections around them

Considering the patient had received over six months of anticoagulant therapy and reported active injection of narcotic substances, anticoagulants were discontinued and the patient was advised to use class II compression stockings and to book into a drug rehabilitation center.

### Case 3

A 42-year-old man was brought by ambulance to the A&E department because of swelling and cyanosis of the right lower limb. A medical history revealed HIV and HCV infections. In the past, the patient had been addicted to intravenous drugs (heroin), and he was currently undergoing methadone treatment. The patient had experienced an episode of acute renal failure as a result of a drug overdose. A physical examination revealed right lower limb swelling, soreness and increased calf consistency, cyanosis of the skin, and widening of the superficial veins. In the area of the right groin, local skin and subcutaneous tissue thickening was visible, in addition to subcutaneous hemorrhage and scarring (Fig. 6). Ultrasound examination showed an occluding thrombosis of the common femoral vein, the femoral vein, and the popliteal vein. The vein lumen was filled with thrombotic material of mixed echogenicity, and was non-collapsible in the transverse compression testing, with no signs of blood flow. Additionally, we observed the presence of a tumor with mixed echogenicity compressing the femoral veins at the site where they join, suggesting local inflammation/hematoma.

The patient denied active intravenous use of narcotic drugs. However, he was behaving peculiarly and repeatedly changed the information he was providing. He tried to explain the “thickening” as a groin injury or wrong body positioning during sleep. At the end of the hospitalization, he confessed to returning to drug use and to administering heroin multiple times in the same location (common femoral vein).

Laboratory tests for D-dimer (1611 ug/L) and CRP (15.9 mg/L) were performed. There were no significant changes found in the chest X-ray. Abdominal ultrasound showed an enlarged liver with a homogeneous, slightly increased echo texture.



**Figure 6.** Subcutaneous hematoma in the right groin (location of administration of heroin, at the location of the common femoral vein); a “blown vein”

Treatment with anticoagulants (enoxaparinum 1 mg/kg of body weight every 12 hours), compression therapy, and lower leg elevation were initiated, as well as empirical antibiotic therapy (amoxicillin with clavulanic acid). The patient was discharged with instructions to take enoxaparin 120 mg every 24 hours for 12 weeks, as well as to use class II compression stockings, and to book into a local drug rehabilitation clinic. A follow-up visit to the Angiology Clinic was scheduled after three months, which the patient did not attend.

### Case 4

A 29-year-old man came to the hospital emergency unit with increasing swelling, and pain in the left lower limb. At the time of admission to the Department of Angiology, the patient experienced respiratory dyspnea at rest. Ultrasound showed an occluding thrombosis of the following veins: popliteal, femoral, and common femoral with a clot tail in the external iliac vein. In the past, the patient had been treated for external left iliac artery pseudoaneurysm. The medical history revealed a five-year addiction to intravenous psychoactive substances (specifically, heroin). In the physical examination, swelling of the right lower limb, cyanosis, and numerous enlarged and tender lymph nodes in the groins were noted. Furthermore, in the region of the greater saphenous veins, numerous skin indurations were observed (lesions from injections), as well as scarring and inflammatory changes in the lower leg and in both groins. During the patient’s stay on the ward, he ran a fever. The laboratory tests revealed high markers of inflammation — CRP 242 mg/L, WBC 26 K/L, elevated D-dimer level 1889 ug/L, mild anemia (Hb 11.2 g/dL), hyponatremia, and positive serological tests for HCV infection.

Based on a computed tomography angiography (CTA) of the lungs, PE was excluded. Treatment with anticoagulants was initiated (initially intravenous unfractionated heparin was administered, controlled by activated partial thromboplastin time; then, enoxaparin, 1 mg/kg of body weight every 12 hours), as well as compression therapy and limb elevation. Empirical antibiotic therapy was also administered. Inflammatory lesions on both lower limbs transformed causing abscesses (with ulceration on the left side, debridement of which resulted in evacuation of bloody-purulent content). The patient’s condition improved, and the fever subsided. The patient was discharged, with instructions to take classic heparin subcutaneously 2 x 5000 IU/0.2 ml (due to lack of medical insurance, this treatment was the most appropriate due to the costs). Class II compression stockings or flexible bandages were also recommended. The patient was referred to a local substance abuse treatment center.

### Case 5

A 28-year-old woman, hospitalized twice in the Department of Angiology, reported a total of three episodes of thrombosis in an 18-month period. During her first stay in the hospital, ultrasonography revealed an occluding external iliac vein and a femoral vein thrombosis, all on the right side. Subsequent incidents involved the left lower limb; the femoral, popliteal, and deep thigh veins. The medical history revealed a 10-year addiction to intravenous psychoactive drugs, mostly heroin, in addition to HIV and HCV infections. Further, a healed suppurating right groin fistula (Fig. 7) and a chronic suppurating right foot ulcer (Fig. 8) were reported.

Anticoagulant therapy (enoxaparin, 1 mg/kg of body weight every 12 hours), compression therapy, and lower limb elevation were used, as well as empirical antibiotic therapy (ciprofloxacin during one stay; amoxicillin with clavulanic acid during the subsequent visit). Ulcers were debrided and bandaged. The recommendations following hospital discharge on each occasion did not differ and included anticoagulant treatment (enoxaparin, 1.5/kg of body weight, one abdominal injection daily), class II compression stockings, and bandages for skin lesions. The female patient was booked in for a thrombophilia test, which she did not attend.

### Discussion

Drug addiction has been a major global social issue for many years. Based on data from 2015 [2, 3], it is estimated that there are 10.2 to 23.7 million IDUs aged 15–64 years in the world; these are people who are addicted to psychoactive substances. Among many complications, one issue that continuously poses not only a diagnostic but also a therapeutic challenge is lower limb DVT. The lack of clear guidelines for anticoagulation therapy in this group of patients, who are at high risk of bleeding, as well as their psychosocial problems, prove extremely challenging. The complex psyche of these patients, and their sense of social exclusion, brings about a negative attitude toward medical care and treatment. As such, this results in a late diagnosis of the disease, as well as a lack of cooperation between the patient and the doctor. The proportion of IDU patients without health insurance ranges from 50% to even 70% [4, 5], and one of the most common explanations for “not seeking” medical attention is financial problems. Among the cases described here, only the first patient admitted openly active drug addiction. In all other cases, it was the frequent conversations of doctors with the patients that helped to determine the real cause of current DVT. At this point, it is worth mentioning that a thorough physical examination and knowledge of



Figure 7. A healed right groin fistula



Figure 8. Oval, suppurating ulcer of the right foot dorsum

characteristics of the clinical course can lead clinicians to a correct diagnosis. Publicly available information shows that DVT in IDUs is more common among:

- young or middle-aged people, usually under the age of 40 years [6]
- men; depending on the source, the male: female ratio is reported to be 11.5:1, 7:1 and 2.8:1 [7–9]
- patients with a previous episode of DVT, especially if relapse occurred within the first six months [10].

In the physical examination, the following symptoms should raise suspicion:

- lesions in the form of tumors, abscesses, or groin fistulas that are leaking or bleeding
- linear, discolored indurations and scarring along the veins, so-called “track marks”
- purulent infections of superficial veins
- scattered scars on the skin and subcutaneous tissue, with necrotic foci; so-called “skin popping”
- skin and subcutaneous tissue inflammation
- accompanying fever.

The clinical picture often does not resemble the typical course of DVT, and it is common to identify a septic type DVT. This requires administration of empirical antibiotic therapy as soon as possible while the purulent lesions often require surgery. The infections are usually caused by Gram-positive bacteria, most often the staphylococcus aureus.

Injection drug use is responsible for a growing number of HIV infections. The percentage of IDUs infected with HIV exceeds 40% in some countries [2, 11]. On the other hand, HIV infection is considered a risk factor for venous thromboembolism, and it is estimated that HIV-positive people carry a 2–10 times higher risk of DVT than the general population [12]. Globally, it is estimated that 52.3% of IDUs are HCV-antibody positive, and 9.1% are HBV surface antigen positive [2].

An important problem that remains unresolved is the choice of appropriate treatment for DVT among IDUs. When introducing a therapy, we need to bear in mind the presence of active drug dependence, and thus, an increased risk of hemorrhagic complications. The choice is usually between LMWH and oral anticoagulants; the former is usually favored. This choice has been confirmed by the opinions of experts [13]. Apart from the risks of bleeding disorders, which are difficult to manage, oral medications can also interact with narcotic drugs, and thus, there is a need for regular and appropriate monitoring. According to the general guidelines, the therapy should last up to 12 weeks [14]. Compression therapy should also be recommended to patients, with graduated compression stockings or elastic bandages, as well as a referral to a drug rehabilitation center. The patients described here were scheduled for a follow-up visit at the Angiology Outpatient Unit, which they did not attend. Therefore, it is difficult to determine how long, if at all, these patients adhered to the recommended treatment after leaving the hospital. IDUs have been found to have three times more frequent recurrence of thrombosis in the first six months after an episode in comparison to the general population [10, 15]. This suggests that IDUs tend to deny the problem, and therefore, discontinue therapy early. This leads to the risk of further complications, including frequent,

severe post-thrombotic syndromes, and formation of hard-to-heal wounds.

In conclusion, it should be emphasized that the problem of DVT in intravenous drug users requires special investigation, as well as a holistic approach. Each patient should be treated individually, taking into account all aspects of the disease, including thrombosis, frequent co-existing characteristics of bacterial infection, accompanying viral diseases and their treatment, drug dependence, and their complex psychosocial problems.

## Conflict of interest

None.

## References:

1. Braekkan SK, Grosse SD, Okoroh EM, et al. Venous thromboembolism and subsequent permanent work-related disability. *J Thromb Haemost.* 2016; 14(10): 1978–1987, doi: [10.1111/jth.13411](https://doi.org/10.1111/jth.13411), indexed in Pubmed: [27411161](https://pubmed.ncbi.nlm.nih.gov/27411161/).
2. Degenhardt L, Peacock A, Colledge S, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *The Lancet Global Health.* 2017; 5(12): e1192–e1207, doi: [10.1016/s2214-109x\(17\)30375-3](https://doi.org/10.1016/s2214-109x(17)30375-3).
3. Larney S, Peacock A, Mathers BM, et al. 2007 Reference Group to the UN on HIV and Injecting Drug Use. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. *Lancet.* 2008; 372(9651): 1733–1745, doi: [10.1016/S0140-6736\(08\)61311-2](https://doi.org/10.1016/S0140-6736(08)61311-2), indexed in Pubmed: [18817968](https://pubmed.ncbi.nlm.nih.gov/18817968/).
4. Riley ED, Wu AW, Junge B, et al. Health services utilization by injection drug users participating in a needle exchange program. *Am J Drug Alcohol Abuse.* 2002; 28(3): 497–511, doi: [10.1081/ada-120006738](https://doi.org/10.1081/ada-120006738), indexed in Pubmed: [12211362](https://pubmed.ncbi.nlm.nih.gov/12211362/).
5. Cronquist A, Edwards V, Galea S, et al. Health care utilization among young adult injection drug users in Harlem, New York. *J Subst Abuse.* 2001; 13(1-2): 17–27, doi: [10.1016/s0899-3289\(01\)00073-6](https://doi.org/10.1016/s0899-3289(01)00073-6), indexed in Pubmed: [11547618](https://pubmed.ncbi.nlm.nih.gov/11547618/).
6. White RH. The epidemiology of venous thromboembolism. *Circulation.* 2003; 107(23 Suppl 1): I4–I8, doi: [10.1161/01.CIR.0000078468.11849.66](https://doi.org/10.1161/01.CIR.0000078468.11849.66), indexed in Pubmed: [12814979](https://pubmed.ncbi.nlm.nih.gov/12814979/).
7. Liu HSY, Kho BCS, Chan JCW, et al. Venous thromboembolism in the Chinese population – experience in a regional hospital in Hong Kong. *Hong Kong Med J.* 2002; 8: 400–405.
8. Mohammadzadeh MA, Hossain-Akbar M, Ejtemaee-Mehr S. Vascular lesions in intravascular drug abusers in Guilan, north of Iran. *Arch Iran Med.* 2007; 10(4): 522–524, doi: [07104/AIM.0018](https://doi.org/07104/AIM.0018), indexed in Pubmed: [17903060](https://pubmed.ncbi.nlm.nih.gov/17903060/).
9. Czarnecki M, Knysz B, Kwiatkowska W, et al. Venous Diseases in Injecting Drug Users. 19th European Chapter Meeting of the

- International Union of Angiology, 24-26 Sept. 2010. Abstr. Final program and Abstract Book. 2010; 81.
10. Syed FF, Beeching NJ. Lower-limb deep-vein thrombosis in a general hospital: risk factors, outcomes and the contribution of intravenous drug use. *QJM*. 2005; 98(2): 139–145, doi: [10.1093/qjmed/hci020](https://doi.org/10.1093/qjmed/hci020), indexed in Pubmed: [15655094](https://pubmed.ncbi.nlm.nih.gov/15655094/).
  11. Strathdee SA, Stockman JK. Epidemiology of HIV among injecting and non-injecting drug users: current trends and implications for interventions. *Curr HIV/AIDS Rep*. 2010; 7(2): 99–106, doi: [10.1007/s11904-010-0043-7](https://doi.org/10.1007/s11904-010-0043-7), indexed in Pubmed: [20425564](https://pubmed.ncbi.nlm.nih.gov/20425564/).
  12. Klein SK, Slim EJ, de Kr, et al. Is chronic HIV infection associated with venous thrombotic disease? A systemic review. *J Med*. 2005; 63: 129–136.
  13. Mackenzie AR, Laing RB, Douglas JG, et al. High prevalence of iliofemoral venous thrombosis with severe groin infection among injecting drug users in North East Scotland: successful use of low molecular weight heparin with antibiotics. *Postgrad Med J*. 2000; 76(899): 561–565, doi: [10.1136/pmj.76.899.561](https://doi.org/10.1136/pmj.76.899.561), indexed in Pubmed: [10964121](https://pubmed.ncbi.nlm.nih.gov/10964121/).
  14. Tomkowski W, Kuca P, Urbanek T, et al. Żyłna choroba zakrzepowo-zatorowa – wytyczne profilaktyki, diagnostyki i terapii. Konsensus Polski 2017. *Acta Angiol*. 2017(2): 35–71, doi: [10.5603/AA.2017.0008](https://doi.org/10.5603/AA.2017.0008).
  15. Kwiatkowska W, Knysz B, Gąsiorowski J, et al. Deep vein thrombosis of the lower limbs in intravenous drug users. *Postepy Hig Med Dosw (Online)*. 2015; 69: 510–520, doi: [10.5604/17322693.1150215](https://doi.org/10.5604/17322693.1150215), indexed in Pubmed: [25983290](https://pubmed.ncbi.nlm.nih.gov/25983290/).