IR for DVT

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Background

Deep venous thrombosis (DVT) may cause significant clinical complications including pulmonary thromboembolism (PE), phlegmasia cerulea dolens (PCD) leading to limb-threatening venous gangrene and severe morbidity secondary to chronic venous hypertension and post-thrombotic syndrome (PTS). Venous thromboembolism (VTE), which includes DVT and PE, occurs for the first time in about 1 in 1000 persons each year, and the incidence rises with age to at least 5 in 1000 persons in those over the age of 80 years[1,2)]. PE is present in approximately 70% of DVT cases, and DVT is present in >30–70% of PE cases. PE may cause 10% of inpatient deaths[3)]. The increasing westernization of the lifestyle, the aging population, and a greater rate of diagnosis by the recent imaging techniques have resulted in a larger number of patients with DVT in Japan. The early diagnosis and treatment of PE are mandatory for the good outcome. PE is a fatal disease characterized by a high rate of mortality, therefore early diagnosis and early treatment, including inhibition of DVT progression and prevention of PE recurrence are therefore very important[3)]. The vena cava filter, which presumably prevent the life-threatening PE, will be presented in detail in another section.

Treatment of DVT

The treatment of DVT has advanced significantly in recent years. Standard treatment of DVT involves anticoagulation with low molecular weight heparin or unfractionated heparin, followed by long term therapy with warfarin. This has been shown to effectively reduce the risk of thrombus propagation or recurrence, pulmonary embolism and death[4)]. Furthermore, to overcome the limitation of warfarin (e.g. request of frequent monitoring), new oral anticoagulant agents (NOACs) has been recently applied for the treatment of VTE. It can be given in fixed doses and produce such a predictable anticoagulant response that routine monitoring is unnecessary. Because of their rapid onset of action, the NOACs have the potential to enable all-oral regimens, which can replace parenteral anticoagulants and warfarin for initial, long-term, and extended VTE treatment[5)].

Despite the use of standard and modern anticoagulant therapy, DVT recurs frequently and often leads to the development of permanent sequelae from PTS[6)]. PTS develops in 25–50% of patients with a first episode of proximal lower extremity DVT[7)]. PTS typically causes chronic, lifestyle-limiting symptoms such as swelling, pain, heaviness, and fatigue of the affected limb. Patients with severe PTS may experience short-distance venous claudication that precludes significant physical activity, stasis dermatitis, skin changes such as hyperpigmentation and subcutaneous fibrosis, and skin ulceration. The occurrence of recurrent ipsilateral DVT is associated with a 2 to 6-fold increased risk of PTS[6,7], therefore, adequate anticoagulation should be attempted for DVT patients.

Catheter-based techniques have been used in the management of DVT for many years, but a rigorous evaluation in multicenter randomized controlled trials (RCTs) to determine whether they improve patient outcomes are just undergoing. The feasibility of more invasive techniques aimed at reducing thrombus burden has gained increasing interest in recent years. Initially, systemic thrombolysis (with urokinase or tissue plasminogen activator) demonstrated adequate thrombolysis, but exposed patients to unacceptable side-effects, including intracranial hemorrhage and/or symptomatic retroperitoneal hematomas.

Catheter-directed treatment for DVT

The recent catheter-directed treatment techniques have been widely accepted in large number of fields because of its less invasiveness and higher treatment effects compared with conventional surgical or conservative treatments.

Catheter-directed thrombolysis

The great advantages of image-guided, catheter-directed, intrathrombus drug infusion has been recognized as one potential avenue by which the safety and efficacy of thrombolytic therapy might be enhanced. In DVT patients, the theoretical advantages of catheter placement to infuse pharmacologic thrombolytic agents directly into the thrombosed vein are considered as follows: the ability to achieve a high intra-thrombus drug concentration and to avoid bypass of the drug around the occluded venous segments via collaterals[7]; the ability to reduce thrombolytic agent dose, treatment time, hospital resource utilization, and bleeding complications; and the ability to prevent recurrent DVT episodes by concomitantly using adjunctive catheter-based techniques to treat anatomic venous abnormalities.

<u>Treatment techniques and devices</u>

The careful pre-treatment assessment of the post-contrast CT with several reconstruction techniques may help us to understand the distribution of DVT. For the treatment of ileofemoral DVT, femoral vein can be selected as access route. When the DVT extends to distal common femoral DVT, contralateral femoral venous access may be useful. For the superficial femoral DVT, the patient is placed into the prone position to puncture the popliteal vein under US guidance. After the venous access via each appropriate accessible vein using 5 or 6 French-sized sheath introducers, venogram is subsequently performed to know the extent of DVT. A straight catheter with multiple side holes is advanced to the distal side of the thrombus and connected to the optimal infusion pump to initiate the continuous injection of the thrombolytic agent. For safe and effective infusion, ones should pay attention to fix the sheath and catheter not to slip out and/or kink during the continuous infusion.

Urokinase (UK) is a commonly used agent for the thrombolysis. UK is continuously infused at a low dose (typically 10,000 U/hr with total duration of 24 or 48 hrs) with simultaneous systemic anticoagulation. After completing the thrombolysis, physicians should evaluate the therapeutic effect of the thrombolysis by the physiological findings and imaging findings using US or contrast-enhanced CT. When the sufficient thrombolytic effect is not achieved, the treatment is continued.

Catheter-directed thrombectomy

Commercially available mechanical thrombectomy devices are designed to aspirate, fragment, macerate, or disrupt venous thrombus[8)]. This technique is frequently used in combination with catheter-directed thrombolysis to remove fresh thrombus. Moreover, the partial removal of DVT may accelerate the exposure of thrombolytic agent and minimize the dose of agents. Although these 2 techniques are frequently used in combination to treat lower extremity DVT, the AHA guidelines indicate that performing percutaneous mechanical thrombectomy alone is reasonable if the patient has contraindications to thrombolytic agents.

Treatment techniques and devices

The mechanical methods include simple aspiration, rheolytic aspiration, rotational thrombectomy, balloon thrombectomy, pharmacomechanical thrombectomy combined with lytic agents, and ultrasonic fragmentation. Rheolytic devices remove the thrombus based on the Venturi effect[9,10)]. Various types of the devices, which are designed for mechanical thrombectomy, have been launched previously and some of them are not commercially available now. Though the high clearance of DVT has been reported using these devices, they have a risk of procedure-related complications (as described in "complication" paragraph).

Among them, the simple aspiration technique is safe and effective one. The 6F size thrombectomy catheter is usually used for the aspiration thrombectomy. However, the aspiration lumen of these catheters is often insufficient to aspirate the DVT in the large-size vein. The large-size catheter, such as the guiding catheter, delivery catheters for IVC filters, etc, are sometimes useful for the DVT in large veins[11)]. After advancing the aspiration catheter and removal of guidewire, thrombectomy is performed by aspirating through the catheter using a 50-mL syringe or Vaclok syringe while gradually pulling the catheter out **(figure)**.

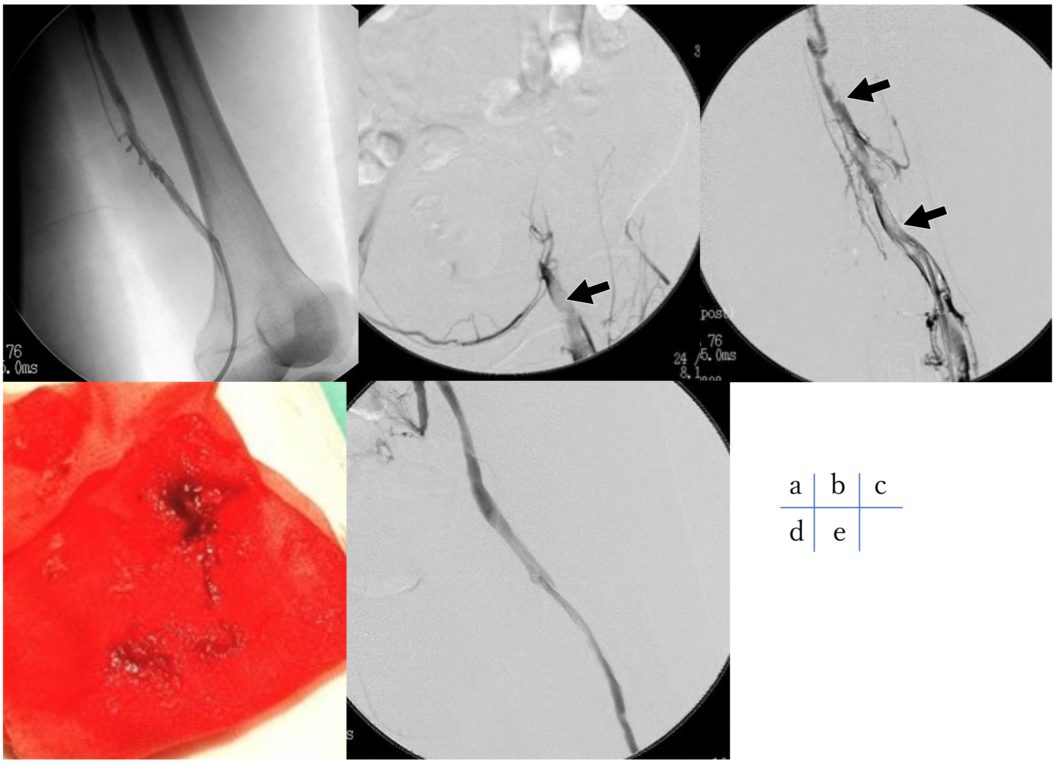

Figure. 30-year-old obese pregnant with DVT diagnosed by US and CT.
After delivery, she underwent catheter-directed thrombectomy and thrombolysis.
a,b. After antegrade puncture of popliteal vein and placement of 5F sheath (a), venography shows filling defect at the level of the left common femoral vein and complete occlusion of the external iliac vein (b, arrow).
c. Catheter-directed aspiration thrombectomy was performed by using thrombectomy catheter. Venography shows partial recanalization of the external iliac vein (arrows).
d. Gross finding of the removed thrombus.
e. After catheter-directed thrombolysis by 2days continuous infusion of urokinase (10,000 U/hr) via the placed infusion catheter, venography shows good clearance of DVT in iliofemoral vein.

Clinical results of catheter-directed treatments

Catheter-directed delivery of thrombolytic agent into the thrombus accelerates thrombolysis, increasing the likelihood of a successful outcome. Accelerated thrombolysis reduces the overall dose and duration of plasminogen activator infusion; therefore, it is reasonable to expect that complications also will be reduced. Acceptable clinical outcomes of catheter-directed thrombolysis for acute DVT have been reported in a number of articles[12-18]. Previous reports have emerged demonstrating acceptable outcomes of catheter-directed thrombolysis for acute DVT. Three large reports documented approximately an 80% success rate[12-14]. According to these reports, when the treatment is aimed at the acute ileofemoral DVT, a high initial success rate can be obtained. In contrast, for the patients having more extensive DVT and/or more chronic DVT, the treatment may result in lower success rates compared with ileofemoral acute DVT.

The ability of catheter-directed thrombolysis to achieve sustainable venous patency is crucial in determining its role in preventing PTS. It has been reported that up to 75% of the catheter-directed thrombolysis-treated limbs demonstrated complete clot lysis at 1 year, and that patency was maintained at 3-years follow-up[19,20]. In addition, catheter-directed thrombolysis has been shown to reduce long term venous reflux compared to anticoagulation alone, reflecting its ability to preserve valve function and protect against the development of PTS[21]. DVT recurrence rates have also been reported to be low at 6 months (thrombolysis and warfarin vs. anticoagulation alone: 72% vs. 12% patency rates) [22] and 3 years (75% of patients free of recurrent DVT) [20].

Complications

Major complications from catheter-directed thrombolysis occur in approximately 9% of cases [23]. The most relevant major complications identified in a pooled analysis of more than 1,000 patients included major hemorrhage (8.3%), symptomatic PE (0.9%), death (0.3%), and intracranial hemorrhage (0.2%) [23].

The mechanical thrombectomy devices have risks of vessel wall and valve damage due to aggressive and prolonged procedures[24], hemolysis which can lead to hemoglobinuria with a damage of renal function[24], anemia due to over-aspiration, and hemorrhagic complication due to the requirement of the large-size access route.

Conclusion

Catheter-directed treatment techniques are available for the treatment of patients with DVT. The procedure and the device used will depend on the clinical nature of the patients with a strong discussion of risks, benefits, and alternatives. It is likely that IR will reinforce its important role in the treatment of patients with DVT.

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