CONSENSUS

Consensus among Chinese experts on standard interventional therapy for deep venous thrombosis of lower extremity (second edition)

Chinese College of Interventionalist

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Chinese Venous Interventional Therapy Ally

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ABSTRACT

This is an update on the first edition of the expert consensus. This document discusses the indications and contraindications of interventional treatment methods for deep venous thrombosis such as anticoagulation, catheter-directed thrombolysis, percutaneous mechanical thrombectomy, percutaneous transluminal angioplasty and stent implantation. The operational procedures, considerations, preoperative management, and prevention of complications were also updated, supplemented, and revised. Emphasis is placed on the interventional treatment of acute and subacute deep venous thrombosis to effectively reduce the incidence of post-thrombosis syndrome.

Keywords: deep venous thrombosis; interventional therapy; consensus.

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Conflict of interest: The authors declare that they have no conflict of interest.

Funding: This work was supported by the National Natural Science Foundation of China (81541061), the Special Fund of Jiangsu Province Condition Construction and People's Livelihood Science and Technology (BL2014013), Nanjing Key Projects for the Development of Medical Science and Technology (ZKX15030), 2015 Nanjing Science and Technology Development Plan (201507028).

Ethical approval: Not applicable.

Informed consent: Not applicable.

Journal of Interventional Medicine **2018**, Vol. 1, No. 3, pp. 125–136

INTRODUCTION

Deep venous thrombosis (DVT) is a disease caused by abnormal blood coagulation in the deep veins of the lower extremities. Owing to the obstruction of blood flow, patients may develop lower limb swelling, pain, and dysfunction. Migration of the thrombus may cause pulmonary embolism (PE), resulting in gas exchange disorders, pulmonary hypertension, and right heart failure. More severe cases may also involve dyspnea, shock, and even death. DVT and PE are referred to as venous thromboembolism (VTE) (1,2). DVT leads to the high incidence of PE, and the thrombus of PE mostly comes from DVT. Therefore, DVT and PE can be thought of as different stages of VTE. If effective treatment cannot be administered for acute DVT, the thrombus would become organization, leading to venous insufficiency, which is termed postthrombosis syndrome (PTS) (3,4). Similarly, if PE is not resolved

by thrombolysis on time, pulmonary artery blood flow would be reduced and eventually lead to chronic thromboembolic pulmonary hypertension (CTEPH).

Clinical classification and staging of DVT

1. Clinical classification

1.1 According to the location (5): 1) Peripheral type refers to distal (or calf) DVT in the legs when it is found below the knee. 2) Central type means a proximal (or iliofemoral) DVT in the legs above the knee. 3) Mixed type means both distal and proximal DVT.

1.2 According to the severity (6): 1) the common type of DVT. 2) Severe DVT, including phlegmasia cerulea dolens (severe deep venous congestion) and thrombotic phlegmasia (with persistent arterial spasm of the lower extremity).

2. Clinical staging

According to the onset of the disease: 1) Acute DVT: the thrombus has been present for less than 14 days. 2) Subacute DVT: refers to venous thrombosis in which symptoms have been present for 15–30 days. 3) Chronic DVT refers to venous thrombosis which has been present for more than 30 days. 4) Sequela period means PTS symptom appeared. 5) Acute-on-chronic DVT refers to a venous thrombosis that has both acute (<14 d) and nonacute components.

In 1960, Greenfield tried to aspirate thrombus through the catheter after venotomy under X-ray fluoroscopy In 1984, Sniderman et al. reported for the first time that percutaneous catheter aspiration was used to treat intravascular thrombosis (7). Presently, based on anticoagulant therapy, the main methods of interventional therapy for DVT are as follows: catheter-directed thrombolysis (CDT), percutaneous mechanical thrombectomy (PMT), percutaneous intraluminal angioplasty (PTA), and stent implantation.

Interventional treatment of DVT should consider these four aspects: safety, chronergy, comprehensiveness, and chronicity (8,9).

1) Safety: Placing the vena cava filter prior to interventional treatment could effectively prevent PE in long-segment DVT. Using PMT and/or CDT could significantly reduce the dosage of thrombolytic agents, the occurrence of intracranial, visceral hemorrhage, and other complications (10-14).

2) Chronergy: Once acute DVT is diagnosed, interventional treatment should be performed as soon as possible. This will shorten the course of disease, increase the complete recanalization rate, reduce or avoid the venous valve adhesion, and reduce the incidence of valvular insufficiency and thrombosis recurrence. It can also prevent the course of disease into the chronic and sequelae phase (15,16).

3) Comprehensiveness: Several methods are often combined to comprehensively treat DVT, for examples, acute DVT could be treated by using CDT, with PMT in combination. For DVT with iliac vein occlusion, PTA and stent implantation can be combined to quickly recover the blood flow, shorten the course of treatment, and improve the curative effect (9,17-19).

4) Chronicity: After comprehensive interventional therapy, long-term anticoagulation (3 months) or prolonged anticoagulation (>3 months) is recommended, and regular follow-up and reexamination could reduce the recurrence of DVT (20).

This expert consensus (Second Edition) is based on the paper "The consensus among Chinese interventional experts on the standard of interventional therapy for deep venous thrombosis of lower extremity" (21,22), published in the *Chinese Journal of Radiology* and the *Journal of Interventional Radiology* in 2011. The second edition has been comprehensively revised based on the national conditions and advances in clinical practice in recent years, and the final version was completed with the assistance of experts in this field.

INDICATIONS AND CONTRAINDICATIONS

1. CDT (10,12,16,23)

1.1 Indications: 1) Central or mixed-type acute DVT. 2) Central or mixed-type subacute DVT. 3) Acute-on-chronic iliofemoral DVT.

1.2 Contraindications: 1) Cerebral hemorrhage and/or major surgery within 3 months, gastrointestinal and other visceral bleeding, and/or organ surgery within 1 month. 2) Serious infection. 3) Many free thrombus in acute iliofemoral or total DVT without inferior vena cava filter placement. 4) Uncontrollable hypertension, i.e. blood pressure>180/100 mmHg, (1 mmHg=0.133 kPa). 5) CDT should be used cautiously

for the patients over 75 years of age and pregnant women.

2. PMT (7,15,24-27)

Percutaneous mechanical thrombectomy (PMT) includes large lumen catheter aspiration and thrombus clearance by thrombectomy device.

2.1 Indications: 1) Acute DVT. 2) Subacute iliofemoral DVT. 3) Acute DVT with contraindications to thrombolysis such as surgery, postpartum ≤ 1 month, and agedness. 4) Severe DVT.

2.2 Contraindications: 1) Chronic DVT. 2) Sequela DVT. 3) DVT below the knee.

3. PTA and stent implantation (28-32)

3.1 Indications: 1) Severe stenosis or occlusion of the iliofemoral vein (Cockett syndrome or May-Thurner syndrome) without acute thrombosis. 2) Iliac vein remains severely stenosed and occluded even after CDT and PMT. 3) Large amount of thrombus in acute iliofemoral DVT with severe obstruction of iliac vein outlet. 4) Iliac vein PTS. 5) Femoral vein PTS (simple PTA is recommended).

3.2 Contraindications: 1) Mild compression of iliac vein. 2) Patients with contraindication of anticoagulant and antiplatelet drugs. 3) Acute iliofemoral DVT with long-segment thrombus without inferior vena cava filter placement.

PREOPERATIVE PREPARATION

1. Physical examination

The following information should be recorded: skin color, superficial vein exposure, blood flow direction in lower extremities, perineum, groin and lower abdomen, skin temperature, lower limb circumference, Homans and Neuhof signs, soft tissue tension of lower extremity, and range of active and passive motion of hip and knee joints.

2. Laboratory examination (33,34)

For blood routine examination, special attention should be paid to platelet count. It is of great significance for the proper diagnosis of acute DVT when plasma D-dimer >500 μg/L (plasma D-dimer detected by enzyme-linked immunosorbent assay-ELISA); prothrombin time (PT), international standard ratio (INR), fibrinogen (FIB), both activated partial thromboplastin time (APTT) and thrombin time (TT); protein C, protein S, and antithrombin III (AT-III) may also be assessed if available.

3. Imaging examination

3.1 Venous ultrasound: Color Doppler ultrasound (CDFI) has high sensitivity and specificity in the diagnosis of lower extremity DVT, and can be used for screening and dynamic monitoring of DVT. In the early stage of acute thrombosis, CDFI can detect the change in blood flow as a "Snowstorm". The lumen in normal veins would disappear when compressed by the probe, while the lumen in veins with a thrombus would not disappear and the echoes would appear enhanced. The detection rate of femoral and popliteal vein thrombosis by color Doppler ultrasound is higher than that of lower leg deep vein thrombosis. The detection of iliac vein thrombosis is difficult with the interference of intestinal gas and other cavity organs.

3.2 Anterograde venous DSA: At present, it is still the "gold standard" for the diagnosis of lower extremity DVT. By lifting the affected limb and using indwelling needle instead of a scalp needle through the dorsalis pedis vein or great saphenous vein, the detection rate of iliac vein thrombosis can be improved by increasing the injection rate of contrast agents. Also, consider using a modified tabular sphygmomanometer cuff instead of a tourniquet to block the superficial vein (35,36), which has been shown to increase the detection rate of thrombosis in the femoral popliteal vein and inferior genu vein. What's more, the pressure value can be recorded providing an additional metric for follow-up treatment.

3.3 Computerized tomography venography (CTV) (37-45): According to the different routes of injection contrast agents, lower limb CTV can be divided into indirect, direct, and bidirectional methods. CTV could accurately evaluate the compression of the iliac vein and visualize the relationship between the iliac vein and the surrounding tissue structure. For the patients with iliofemoral vein occlusion detected by anterograde DSA, CTV can also provide intraluminal information of iliofemoral vein, which may be helpful in making treatment plans.

3.4 Magnetic resonance venography (MRV) (46,47): High-field MR can be used as non-enhanced MRV to show thrombosis in the iliofemoral vein and compression of the iliac vein. It can also be used to

screen and diagnose proximal DVT and iliac vein compression. Therefore, MRV has great potential for clinical application. A combination of enhanced MR and non-enhanced MR can evaluate the freshness of thrombus.

Any of the items listed above can be used individually or in conjunction with the remaining three according to the specific clinical case.

4. Intravascular ultrasound (IVUS) (48)

IVUS has a greater advantage over color Doppler ultrasound in the display of iliac vein endovascular lesions, observation of vascular intima, measurement of vascular wall thickness, and external pressure. However, it has only been equipped in a few medical institutions, at great cost. Thus, it is not widely used presently.

5. Anticoagulant therapy

This therapy should start immediately once acute DVT is diagnosed. This is the international consensus among relevant professional physicians (49). Anticoagulant therapy is the basis of interventional therapy for lower extremity DVT. Low molecular weight heparin (LMWH) and some new oral anticoagulants are recommended (50-52). In the case of heparin-induced thrombocytopenia (HIT) (53-55), the anticoagulants can be replaced by agatroban. Heparin and the vitamin K antagonist warfarin are still widely used in the clinic. Pregnancy is a contraindication to warfarin treatment as it is harmful to the fetus. Therefore, LMWH is instead indicated in pregnant women (56). LMWH is also recommended for cancer patients with a hypercoagulable status (57,58).

For inferior vena cava filter placement, details are available in "Expert consensus on the specification of inferior vena cava filter placement and removal."(59)

OPERATIONS

1. CDT (60,61)

Urokinase is a conventionally used thrombolytic agent. However, the individual dose varies depending on the patient's general condition, age, thrombus load, and coagulation function. The usual dose is 200,000–1,000,000 U/d. A lower dose of 500,000 U/d is recommended for long-term CDT. The catheter is usually retained for no more than 7 days (62,63). Commonly used thrombolytic catheters in China are multi-hole thrombolysis catheter, Unifuse thrombolysis catheter and Fountain thrombolysis catheter. According to the different intubation approach (64), CDT can be divided into three categories:

1.1 Antegrade thrombolysis (65-68): Access through 1) the deep vein of the affected leg (posterior tibial vein, anterior tibial vein, and peroneal vein) to the popliteal vein; 2) the popliteal vein, in supine or prone position, to the iliofemoral vein; 3) the affected great saphenous vein to the common femoral vein and iliac vein.

1.2 Retrograde thrombolysis (69,70): Access through 1) the healthy femoral vein to the affected iliofemoral vein; 2) the internal jugular vein to the affected iliofemoral vein.

1.3 Antegrade thrombolysis via artery (71): Access through the femoral artery to the iliofemoral artery of the affected side.

For an iliofemoral DVT, it is recommended to use ipsilateral popliteal vein puncture for anterograde thrombolysis or retrograde thrombolysis via internal jugular vein and healthy femoral vein. For femoral and popliteal vein thrombosis, it is recommended to perform anterograde thrombolysis through deep vein puncture of the affected leg or catheterization through the healthy femoral artery to the affected femoral artery.

2. PMT (7,13,26,27,72-74)

2.1 Large lumen catheter aspiration: an 8-10F catheter sheath and guiding catheter can be used (elbow guiding catheter is recommended). Insert the guiding catheter along the guide wire to thrombus, and aspirate repeatedly with a 30 mL or 50 mL syringe.

2.2 Thrombus clearance by thrombectomy device: The available thrombectomy devices in China are: 1) AngioJet thrombectomy system: Under high pressure, a prescribed amount of thrombolytic agent (200,000–250,000 U urokinase dissolved in 500 mL saline) can be sprayed into the thrombus, crushing the thrombus and increasing the contact area with the thrombus. Then, thrombus aspiration is performed, which can be called chemical-physical coupled thrombus reduction. This is suitable for acute thrombosis of iliac, femoral, and popliteal veins. 2) Straub Aspirex thrombectomy system: The thrombus

was cut using high-speed rotary blade and subsequently aspirated. It is suitable for both acute and subacute thrombosis of iliofemoral vein. Both AngioJet and Straub Aspirex thrombectomy system can be inserted along the guide wire and be propelled to the thrombus site under fluoroscopic surveillance to activate the thrombus defibrillator for clearance.

3. PTA and stent implantation (75-79)

3.1 PTA: 1) For obstructions in the common iliac vein and the superior part of the external iliac vein, puncture through the ipsilateral femoral vein is recommended. 2) For obstruction involving the inferior segment of the external iliac vein, the common femoral vein, and the femoral vein, an ipsilateral popliteal vein approach is recommended. 3) For PTS involving bilateral iliac veins, PTA should be performed simultaneously in bilateral iliac veins. 4) PTA for iliac vein should use a balloon catheter with 10–12 mm diameter, and PTA for common femoral vein and femoral vein is recommended to use balloon catheter of 8–10 mm. 5) It is recommended to use a pressure pump to fill the balloon and maintain pressure for 1–3 min.

3.2 Stent implantation: 1) Iliofemoral vein stenting must be performed after sufficient PTA. 2) Select self-expanding stents with a larger internal diameter, stronger radial supporting force and smaller shortening rate for the iliac vein. Special venous stents are recommended. 3) Self-expandable stents with a diameter of 12–14 mm are recommended for the common iliac vein and the upper part of the external iliac vein. 4) Self-expandable stents with a diameter of 10–12 mm are recommended for the inferior segment of the external iliac vein and the common femoral vein.

CONSIDERATIONS

1. Considerations for CDT

1.1 For a peripheral DVT, anterograde thrombolysis could be performed through the superficial vein of dorsum pedis or ankle based on adequate anticoagulation.

1.2 If there is a thrombus in the lower part of femoral vein or popliteal vein, popliteal vein puncture for CDT is not suitable, as it would injure the femoral and popliteal vein which leads to thrombosis aggravation. At this point, it is advisable to choose the following route to puncture: 1) Through the ipsilateral anterior tibial, posterior tibial or peroneal veins. 2) Through the contralateral femoral vein to the affected side. 3) Retrograde catheterization of internal jugular vein to femoral and popliteal vein of the affected limb.

1.3 When antegrade thrombolysis is performed via artery for total DVT, the location of the catheter head depends on the level and degree of involvement of the thrombus. If the thrombus is in the iliofemoral vein, popliteal vein, and the deep genu vein, the catheter head could be placed in the affected common iliac artery. The anticoagulants would pass through the internal iliac artery and the deep femoral artery, and act on the thrombus in the internal iliac vein, the deep femoral vein, and their branches, with better therapeutic effect.

1.4 Monitoring clotting function is essential in the use of the anticoagulants. The dosage of heparin anticoagulant should consider body weight. APTT must be monitored when heparin is used. If APTT is prolonged to 1.5–2.5 times the normal value, the anticoagulant effect is strong, and the risk of bleeding is relatively small. PT and INR values should be regularly monitored during warfarin use. The dose must be adjusted to maintain an INR value between 1.8 and 2.5.

1.5 The dosage of thrombolytic agent should not be too high, and the dosage of urokinase should not be > 1.2 million U/d (20,62,63,80). During the use of thrombolytic agents, it is advisable to monitor routine blood tests daily. Once the FIB < 1.5 g/L, the dosage of thrombolytic agents should be reduced. However, if the thrombus is still much, we can use PMT in combination or alternately infuse the cryoprecipitation containing FIB. Once the peripheral blood FIB is above 1.5 g/L, CDT treatment can be continued.

1.6 However, if the thrombolytic efficiency of urokinase is dissatisfactory, and anticoagulant deficiency and HIT are excluded, the recombinant tissue-type plasminogen activator (rt-PA) should be used instead. The recommended dose is 20 mg every 24–36 h by transcatheter administration for 2–3 days (63,80-82). The level of plasma FIB should be closely monitored during the use of rt-PA.

1.7 CDT is just one comprehensive interventional therapy method for DVT (24,83). For patients with much thrombus in the iliofemoral vein, combining CDT with PMT can improve treatment and shorten the course of the disease. PTA and stenting are recommended as early as possible in patients with

severe obstruction of reflux and DVT caused by severe stenosis and occlusion of common iliac vein (Cockett syndrome or May-Thurner syndrome) (31,32).

2. Consideration for PMT

2.1 Thrombus aspiration (7,74): 1) When thrombus aspiration is to be performed for lower limb DVT with much thrombus, it is recommended that an IVC filter be inserted in advance to prevent PE caused by thrombus exfoliation. 2) A constant negative pressure should be maintained during aspiration to minimize the probability of dislodging a secondary thrombus 3) Thrombus aspiration often results in blood loss. The amount of total blood loss should be strictly controlled and should not exceed 200 mL. 4) Thrombectomy should be combined with anticoagulation therapy and CDT to improve treatment and reduce the recurrence of thrombosis.

2.2 Thrombus clearance by thrombectomy device (13,72,73): 1) Choose an anterograde puncture site as close to the popliteal vein as possible to avoid the injury of a deep vein valve. 2) In the process of using a thrombectomy device, close attention should be paid to prevent the device from overheating and potential breakage caused by the following rotation of the guide wire. 3) The operation of thrombus clearance in each segment should not exceed 3 times, and total operation time should not be too long to reduce the influence of the instrument on vascular intima and normal blood components. 4) Vital signs must be closely monitored during operation.

3. Consideration for PTA and stent implantation (19,29-32,84)

3.1 After iliofemoral DVT underwent CDT and PMT, venography showed that the targeted stenosis was less than 30%. PTA and stent implantation would not be suitable. After treatment with PTA, moderate to severe short segment stenosis (<2 cm) shows patency, smooth walls, no obvious residual stenosis, and no obvious retention of contrast medium; thus stent implantation could proceed without consideration. Stent implantation is necessary after PTA for long-segment severe stenosis and occlusion of the iliac vein.

3.2 For PTS patients with obvious symptoms, especially those with ulceration, PTA can be performed selectively in superficial femoral, femoral total, external iliac, and common iliac veins. It is recommended to use a small diameter (4–5 mm) long balloon for predilatation. Then, employ a large diameter long balloon to further dilate the femoral vein (6–8 mm) and the iliac vein (10–12 mm).

3.3 Stents are usually placed in the common iliac vein and the external iliac vein. There are many venous valves in the superficial femoral vein, and thus stent implanting would lead to venous insufficiency. Therefore, the cross-joint stenting should be cautious.

3.4 Special venous stents are recommended. In addition, a laser engraving stent with accurate positioning and preferable perspective visibility is a viable alternative. Closed loop stents can be used in the cross-joint segment from the external iliac vein to the common femoral vein. The shortening rate should be considered when the braided stent is used in the common iliac vein. The head of the braided stent should enter into the inferior vena cava approximately 10 mm when releasing the stent. The head of the laser engraving stent should enter into the inferior vena cava 3–4 mm.

3.5 The diameter of the stent should be equal to or slightly larger than that of the adjacent normal vessel. The stent should be long enough to cover the narrow segment. In long-segment lesions, a single long stent should be used if possible and overlapping implantation of multiple stents is avoided.

3.6 Adequate predilatation ensures sufficient blood flow at the stent's inlet (femoral vein side) and outlet (inferior vena cava side), with no retained contrast media. If there is not enough blood flow after stent implantation (e.g., such as femoral vein diameter <8 mm), or the stent is insufficient to cover the entire narrowed/occlusive segment, it is not appropriate to choose stent implantation.

POSTOPERATIVE TREATMENT

During CDT and after PMT, PTA and stent implantation, the appropriate height of the affected limb should be 15 cm from horizontal to facilitate the blood reflux and swelling subsidence of the affected limb.

Mild fever occurs 2–3 days after CDT. Body temperature is generally between 37.5 and 38.5 ℃. The cause of fever may be thrombolysis, retention of the catheter itself with a heat source, or both. This situation does not often require special treatment. If

necessary, replace the catheter or extubate after strict disinfection.

During anterograde thrombolysis through the dorsum pedis or great saphenous vein, the modified sphygmomanometer cuff can be used instead of the tourniquet to intermittently block the superficial veins, to improve patient tolerance and comfort. Furthermore, the pressure is readable and controllable, which may assist in thrombolytic effect and facilitate ward management (35,36).

For CDT, the administration of thrombolytic agents included intermittent pulse injection and continuous uniform injection.

Postoperatively, detect and treat other underlying diseases that may cause hypercoagulability. For young patients, attention should be paid to primary risk factors such as connective tissue disease, antiphospholipid thrombosis syndrome, AT-III deficiency, protein C, and protein S deficiency. For elderly patients, special attention should be paid to secondary risk factors such as a malignant tumor, long-term drug use, or cardiopulmonary dysfunction.

New oral anticoagulants are recommended after interventional treatment. As for rivaroxaban, 15 mg twice a day for three weeks, and then 20 mg once a day for up to 3 months, followed by oral aspirin 100 mg bridged, once a day until 6 months (49). LMWH may also be administered subcutaneously once every 12 hours for 5–7 days, followed by oral warfarin bridged from day 4 to 6 months.

For patients with venous insufficiency and diagnosed as PTS by the Villata score, symptoms can be ameliorated by long-term treatment of interspace pneumatic compression and/or wearing medical elastic stockings on the affected limb (4,85-88).

Follow-up is required at 1, 3, 6 and 12 months after the operation, and reexamination with venography or color Doppler ultrasound is required at 6 and 12 months. Follow-up visits are then conducted once a year. If recurrence of DVT is found, it should be dealt with in time. If DVT recrudesces, it should be treated in time.

COMPLICATIONS PREVENTION AND TREATMENT

1. Hemorrhage and hemolysis

During anticoagulant and thrombolytic therapy, subcutaneous, mucosal, and visceral bleeding signs should be closely noticed. Subcutaneous ecchymosis and gingival bleeding are common, and hemoptysis and hematemesis occur occasionally. When patients have nervous system symptoms such as headache and vomiting, the possibility of cerebral hemorrhage should be considered first. In this case, anticoagulant and thrombolytic drugs must be stopped immediately, and the patient should undergo emergency cranial CT examination definite diagnosis. If there is a hemorrhage, relevant specialized referral should consult as soon as possible, and the patient should be transferred to cerebral surgery if necessary. The traumatic hemolysis caused by PMT is usually transient, and manifests as red urine, which indicates hemoglobin in the urine and not true hematuria. It needs no special treatment and will resolve after 2 days.

2. Vascular wall injury

During procedures, vascular wall injury can be caused by a catheter, guide wire, thrombectomy device, or balloon. During the intervention, patient complaints of pain and/or contrast agent retention or diffusion in the tissue space could be identified as a vascular injury or rupture of the vessel wall. When the catheter and guide wire proceeds to explore and pass through a severe stenosis or occlusion, it is advisable to use a guide wire with supple head. After the catheter passes through the long segment occlusion vessel, it is advisable to exchange the thrombolytic catheter for angiography to confirm whether the catheter is in the true cavity. When using large lumen catheter aspiration, such as AngioJet or Straub Aspirex for thrombus clearance, patients should also be monitored for any discomfort at any time. Heart rate and blood pressure should be closely monitored, and symptomatic treatment should be taken at continuously (89-91). For patients with severe venous occlusion, especially the iliofemoral PTS, a small diameter balloon is recommended for pre-dilatation. For vascular wall injury with active bleeding, local pressure on the body surface can be used to stop bleeding in the groin and below. Temporary balloon occlusion may also be used for the iliac vein. Covered stents can be considered if necessary.

3. Residual thrombus and thrombus recurrence

It is sometimes difficult for CDT and PMT to completely clear the thrombus in the vein cavity. Continuing CDT for several days, increasing the dose of urokinase or replacing urokinase with rt-PA can often reduce the residual thrombus. During CDT, if the amount of thrombus increases abnormally, or even increases with thrombolysis, HIT should be considered. Platelets counts should be measured in time and the recent changes in platelets should be analyzed retrospectively. If necessary, platelet function tests and HIT IgG antibody tests should be done. After definite diagnosis, all forms of heparin (including LMWH) should be discontinued, and anticoagulant agents such as agatroban should be used. Satisfactory results can be obtained by CDT for several days. The recurrence of thrombus is related to the blood hypercoagulable state caused by basic pathological changes, nonstandard anticoagulant therapy, and incomplete thrombus treatment. The principles, methods and steps of treatment are similar to those of acute DVT (80,92).

4. PE

During thrombolysis, PMT or PTA, patients can present with symptoms such as dyspnea, chest tightness, cough, hemoptysis, decreased oxygen saturation, and shock. If this happens, PE should be considered. Before interventional therapy, if there is fresh or floating thrombus in the inferior vena cava or iliac vein, the effective method to prevent PE is implantation of an inferior vena cava filter (14,59). For patients with no inferior vena cava filter implantation, only simple anticoagulant therapy can be used. In case of symptomatic PE, comprehensive interventional treatment can be selected according to the specific situation.

5. Vascular occlusion and restenosis after PTA and stent implantation (93,94)

After PTA and stent implantation, if the swelling and pain do not decrease or the symptoms recur or aggravate, and the level of plasma D-dimer increases again, acute thrombosis should be considered. Diagnosis and treatment are similar to acute DVT. Adequate intraoperative and postoperative anticoagulation, thrombolysis for 1–2 days after PTA, and stent implantation could reduce the incidence of acute thrombosis. Long-term anticoagulation or prolonged anticoagulation after PTA and stent implantation as well as bridging antiplatelet therapy are recommended to reduce the incidence and severity of restenosis.

TREATMENT EFFECT EVALUATION

The curative effect varies greatly with clinical classification, clinical stage, and interventional treatment methods. It is generally considered that CDT is effective in treating acute and subacute DVT (60-71). PMT can rapidly reduce the amount of thrombus, alleviate the symptoms, and shorten the course of disease (24,72-74). PTA and stent implantation have excellent effects on iliac vein obstruction with or without DVT (75-77,83,84,95-98). The efficacy of interventional therapy can be evaluated before discharge and 6 months, 1, 3, 5 years after discharge. There are many methods to evaluate the efficacy of interventional therapy, and they are as follows: 1) Calculate the circumference difference and get the detumescence rate of limbs. 2) Thrombolytic rate and venous patency rate are obtained by comparing venography. 3) PTS is assessed to obtain the incidence of sequelae. According to the results of physical examination and venography, this expert consensus divides the curative effect into 4 grades: Excellent (grade 1): the circumference, tension and range of motion of the affected limb are basically normal, the difference of circumferential diameter between the affected and the healthy side is ≤1.0 cm after treatment, the blood flow is recovered completely or abnormal collateral vessels are not shown, the contrast medium is not retained, and the vessel wall is smooth. Good (grade 2): the circumference, tension, and range of motion of the affected limb are close to normal; the difference of circumferential diameter compared with the healthy side ranges from 1.0 to 1.5 cm; most of the blood flow has recovered; a small number of collateral vessels are found; the contrast medium is not obviously retained; and the vessel wall is relatively smooth. Middle (grade 3): the circumference, tension, and range of motion of the affected limb are obviously improved; the difference of circumferential diameter compared with the healthy side ranges from 1.5 to 2.0 cm; blood flow is partially recovered; there are many collateral vessels; contrast medium is slightly retained; and the vessel wall is not smooth. Poor (grade 4): there is no significant improvement in circumference, tension, or range of motion of the affected limb. After treatment,

the difference of circumference is more than 2.0 cm as compared with that of the healthy side. Venography shows that blood flow has not recovered, there are many collateral vessels, the contrast medium obviously remains, and the vessel wall is not smooth. Gradings of excellent, good, and moderate are regarded as an effective treatment (29,99).

CONCLUSIONS

The methods of interventional therapy for lower extremity DVT are varied, and contemporary research progress is fast. Methods should be selected according to the clinical classification and stage of the patient. Comprehensive interventional therapy can improve the curative effect. Anticoagulant therapy is just the foundation of DVT treatment, and application of new oral anticoagulants will be applied more extensively. LMWH can be used safely to treat DVT in pregnant women. Patients with a malignant tumor often need prolonged anticoagulation treatment. Agatroxobin can be used as an anticoagulant for HIT. In the experience of Chinese experts, CDT can reduce the incidence and degree of PTS, but more medical evidence is needed to confirm. PMT can shorten the course of disease and can be used selectively in patients with severe symptoms and much thrombus. The long-term patency rate of an iliac vein stent is high, and can be considered for patients with venous obstruction and venous hypertension.

ACKNOWLEDGMENTS

Jianping Gu, MD, and Cheng Qian, MD, authored the first draft of this document and subsequent revisions of the draft. The authors would like to thank the following professors for their contributions to this work: Bin Xiong, MD, Caifang Ni, MD, Duanming Du, MD, Feng Wang, MD, Fuxian Zhang, MD, Gang Deng, MD, Gaojun Teng, MD, Guohong Han, MD, Haibin Shi, MD, Haiying Jin, MD, Hao Xu, MD, Haobo Su, MD, Hong Shan, MD, Hong Gao, MD, Hongshan Zhong, MD, Hongyao Hu, MD, Hua Xiang, MD, Jianguo Chu, MD, Jianhua Wang, MD, Jianjun Luo, MD, Jianmin Cao, MD, Jianping Gu, MD, Jianyang Peng, MD, Jing Zhang, MD, Jinguo Cui, MD, Ke Xu, MD, Lei Yu, MD, Liang Xiao, MD, Linan Du, MD, Linsun Li, MD, Maoheng Zu, MD, Min Yang, MD, Ning Yang, MD, Renyou Zhai, MD, Shaoxin Yao, MD, Shixi Chen, MD, Wanyong Zhang, MD, Wei Liang, MD, Weizhu Yang, MD, Wensheng Lou, MD, Xiangsheng Xiao, MD, Xiaobai Wang, MD, Xiaofeng He, MD, Xindong Fan, MD, Xinwu Lu, MD, Xu He, MD, Xuan Li, MD, Xuesong Liu, MD, Yanbo Zheng, MD, Yanhao Li, MD, Yanxian Deng, MD, Yaochang Luo, MD, Yinghua Zou, MD, Yongde Cheng, MD, Yongli Wang, MD, Yubin Zhou, MD, Yu-e Liu, MD, Yuming Gu, MD, Zhaoyu Liu, MD, Zhenhua Zhao, MD, Zhiping Yan, MD.

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