CENTRAL VENOUS CATHETER-RELATED DEEP VEIN THROMBOSIS

Thrombosis Canada
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OBJECTIVE:

To provide guidance on the diagnosis, treatment and prevention of central venous catheter-related deep vein thrombosis (DVT).

BACKGROUND:

Central venous catheters are widely used for resuscitation; administration of chemotherapy, antibiotics and other medications; transfusion therapy; apheresis procedures; parenteral nutrition; blood sample acquisition; and supportive care, especially in patients with malignancy. The incidence rates for central venous catheter-related DVT vary widely among studies (ranging from approximately 2 to 70%), due in part to variable criteria for investigation (e.g. symptomatic patients versus routine screening of all patients with central venous catheters), as well as differences in patient populations (e.g. cancer, surgical, pediatrics) and duration of follow-up. Risk factors for catheter-related DVT include use of larger diameter catheters with multiple lumens, catheter tip malposition, left-sided placement, concomitant infection, history of DVT, and, in cancer patients, the type and stage of cancer, and administration of chemotherapy. Peripherally inserted central catheters (PICCs) are associated with a higher risk of DVT than other centrally inserted catheters, including implanted ports. Heritable thrombophilias likely increase the risk, however the magnitude of risk increase is unclear and screening for them is not currently indicated.

DIAGNOSIS OF CATHETER-RELATED DVT:

Patients with central venous catheter-related DVT may develop unilateral hand or arm swelling, pain or swelling in the neck or shoulder, visible collateral veins on the chest, or symptoms of superior vena cava obstruction, such as facial swelling, dyspnea, and headache. Patients with central venous catheter-related DVT may also be asymptomatic. Symptoms of embolization (e.g. pulmonary embolism, paradoxical stroke) should also prompt an evaluation for DVT in patients with central venous catheters. While a combination of clinical decision rules with D-dimer can be effective ruling out DVT in certain populations, its efficiency is limited in those with central venous catheters and is not recommended. The best initial test for diagnosing catheter-related DVT is duplex ultrasonography. Isolated subclavian vein or more central venous thrombosis may not be well seen with ultrasonography due to anatomical hindrance by the clavicle and chest wall. In difficult cases, magnetic resonance imaging (MRI) or computed tomography (CT) may be required. Direct contrast venography is an invasive procedure and may be difficult to obtain.

TREATMENT OF CATHETER-RELATED DVT:

The goals of treatment for catheter-associated DVT are to improve acute symptoms, decrease long-term morbidity, prolong patency and survival of the catheter, and prevent embolization and recurrent

thrombosis. Acute treatment recommendations are based primarily on trials in patients with lower extremity DVT. Removal of the central venous catheter is not required if it is still needed, functioning properly, and not associated with infection; however, if symptoms persist or worsen despite anticoagulation, the central venous catheter may need to be removed.

Use of low molecular weight heparin (LMWH) has been shown to be effective and safe in upper extremity DVT. Longer-term anticoagulation may involve continuation of LMWH alone, or conversion to warfarin. If LMWH is transitioned to warfarin, there should be an overlap for a minimum of 5 days and until the international normalized ratio (INR) is therapeutic. Direct oral anticoagulants (DOACs) have limited data to support use in catheter-related DVT, but they are known to be equivalent to warfarin in non-cancer patients, and LMWH in cancer patients for treatment of lower extremity DVT and pulmonary embolism. In a recent single arm study of rivaroxaban 15 mg orally twice daily for 21 days followed by 20 mg once daily in 70 cancer patients with central venous catheter-related upper extremity DVT, preservation of line function at 12 weeks was 100% and the risk of recurrent venous thromboembolism was 1.43% during the same period. There was, however, one episode of fatal pulmonary embolism, and the risk of clinically relevant bleeding (12.9%) was higher than anticipated. However, the findings from this study are limited by its small size and the lack of a control arm. The use of DOACs in this demographic continue to be studied. Given the limited data, Canadian expert consensus currently favours LMWH over DOACs or warfarin in the treatment of catheter-related DVT.

Although treatment duration for catheter-related DVT is controversial, it is reasonable to treat patients with a DVT in the axillary or a more proximal upper extremity deep vein for a minimum of 3 months or longer if the catheter remains in place. In those with a DVT involving only the brachial vein or thrombosis confined to the superficial veins, such as the cephalic or basilic vein, treatment with anticoagulation has not been studied. In this situation, anticoagulation with either full dose anticoagulation or less than therapeutic doses of LMWH (e.g. approximately 50% of a treatment dose) to prevent progression of the thrombus while the catheter remains in place is reasonable. There are few data to guide the use of catheter-directed thrombolysis in patients with extensive central catheter-related DVT and so the use of this intervention remains a case-by-case decision, best guided by consultation with a thrombosis expert and/or interventional radiologist.

PREVENTION OF CATHETER-RELATED DVT:

The most important aspects of prevention of catheter-related DVT include use of central venous catheters only when necessary, insertion of the smallest catheters that satisfy their purpose and prompt removal when no longer needed. The process of PICC exchange has recently been identified as a risk factor for developing DVT, so should be done only when absolutely necessary.

Routine use of thromboprophylaxis in patients with central venous catheters with anticoagulation is not recommended by most guidelines. A systematic review and meta-analysis evaluating anticoagulation thromboprophylaxis (LMWH, warfarin) in cancer patients with central venous catheters, found that LMWH compared to no prophylaxis probably decreases the risk of symptomatic catheter-related VTE by approximately 50%, with no difference in major bleeding or mortality. Low dose warfarin compared to no warfarin did not decrease the incidence of symptomatic catheter-related VTE and had no beneficial effect on mortality. Low dose apixaban and rivaroxaban have been

shown to be effective as thromboprophylaxis in ambulatory cancer patients at high risk for VTE (Khorana score >=2), but these studies did not specifically assess those with central venous catheters. A study is currently underway to compare low dose rivaroxaban to placebo as thromboprophylaxis in cancer patients with central venous catheters. Thromboprophylaxis may be considered in higher-risk cancer patients when the perceived risk of thrombosis outweighs the risk of bleeding and the burden of anticoagulation (e.g. in those with prior venous thrombosis).

PEDIATRICS:

Central venous catheters are a frequent necessity in children who require supportive care to manage their illness (e.g. chemotherapy, parenteral nutrition, antibiotics, transfusions). The incidence of thrombosis related to catheter use in children is estimated at 3% to 34% of children with central venous catheters, varying between patient populations and with different diagnostic modalities. Without a previous history of thrombosis, thromboprophylaxis in children with central venous catheters is not routinely recommended, but could be considered in children with long-term VTE risk including those on home total parenteral nutrition, or undergoing hemodialysis. In children with cancer without previous VTE, central venous catheters alone are not an indication for thromboprophylaxis, but if other VTE risk factors are present (including asparaginase chemotherapy, obesity, hormonal contraceptives, adolescence, or hospitalization for surgery), thromboprophylaxis with LMWH could be considered.

LMWH and VKA remain the mainstay of the treatment for catheter-related DVT in pediatrics. Both dabigatran and rivaroxaban have been compared to standard of care as treatment of VTE in randomized controlled trials in the pediatric population, which included catheter-related DVT, demonstrating similar efficacy and bleeding risk. Widespread adoption of rivaroxaban and dabigatran is expected once pediatric oral formulations are available. Studies assessing apixaban and edoxaban in the pediatric population are still ongoing.

Pediatricians with expertise in thromboembolism should be involved in decisions about thrombosis prophylaxis and management of thromboembolism in pediatric patients where possible. When this is not possible, a combination of a neonatologist/pediatrician and an adult hematologist, supported by consultation with an experienced pediatric hematologist, is recommended.

OTHER RELEVANT THROMBOSIS CANADA CLINICAL GUIDES:

- Cancer and Thrombosis
- Deep Vein Thrombosis: Treatment

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