

Thrombosis associated with right internal jugular central venous catheters: A prospective observational study

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Abstract

Background and Aims: Central venous catheters (CVC) are essential in a critical care setting. Thrombosis is one of the very important associated complications that can lead to increased morbidity and mortality. The aim of this study was to find out the incidence of thrombosis in right-sided internal jugular vein (IJV) CVC with the help of color Doppler duplex sonography, its extent, risk factors and clinical impact. **Materials and Methods:** One hundred consecutive patients having right-sided IJV CVC were included in the study. Color Doppler sonography was performed on the 3rd and 6th days after CVC insertion. The size of the thrombus was noted. Presence of diabetes mellitus, hypertension or smoking was noted. Presence of any hypertonic solution and thromboprophylaxis for Deep vein thrombosis (DVT) were also noted. **Results:** Thrombus was detected in 33 of 100 (33.0%) patients. The incidence in males was 32.86% and in females was 33.33%. Males had a significantly higher incidence of small thrombus ($P = 0.05$), whereas females had a significantly higher incidence of large thrombus ($P = 0.05$). DVT thromboprophylaxis was not effective for CVC-related thrombosis. Hypertonic solution, presence of diabetes, hypertension or history of smoking did not increase the risk of thrombosis. **Conclusion:** CVC-related thrombosis is common and has the potential for serious complications. Females appear to be at a higher risk for larger thrombus formation. DVT thromboprophylaxis does not confer protection for CVC-related thrombosis. Color Doppler duplex sonography provides with an easily available, noninvasive means of detecting a thrombus. More studies are needed to establish a consensus for prophylaxis and treatment of asymptomatic CVC-related thrombosis.

Keywords: Central venous catheter, internal jugular vein, thrombosis

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Introduction

Central venous catheters (CVCs) have an essential part to play in the management of a critically ill patient. They are useful for hemodynamic monitoring, for administration of specific medications like vasoactive drugs, parenteral nutrition and for hemodialysis. These are associated with substantial risks of complications, which can be mechanical, septic and thrombotic.^[1]

Upper limb DVT is a well known complication of thrombosis associated with CVCs, which, in its fatal form, can sometimes lead to life-threatening pulmonary embolism.^[2] The incidence of thrombosis varies from 1.9% in subclavian CVCs to 21.5% in femoral catheters.^[3] The incidence is higher in patients with malignancy and in those with hemodialysis catheters. The risk of thrombosis associated with IJV catheters is estimated to be four-times higher than that with subclavian catheters.^[4] Sixty-six percent of the patients with internal jugular vein (IJV) catheters have evidence of thrombus formation either on ultrasound or on autopsy.^[5]

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This was a prospective observational study. The aim of this study was to determine the incidence of thrombosis

associated with right-sided IJV catheters, the extent of thrombosis, its clinical implications and to relate it with the pharmacological prophylaxis for DVT.

Materials and Methods

One hundred consecutive adult patients admitted to our Critical Care Unit, who had right-sided IJV catheters placed for various indications, were included in the study. Informed consent and institutional review board approval was taken. Certofix B Braun CVCs were used every time. CVCs placed with a maximum of two attempts with ease were only included. CVCs were flushed every 2 h with heparinized saline.

CVC insertion was performed by intensivists or doctors having at least 5 years of experience in CVC insertion. Color Doppler sonography was performed by a consultant radiologist.

Color Doppler sonography was done on the 3rd and 6th days of catheter placement. Presence and size of the thrombus was noted. Local signs of inflammation and any clinical signs of upper limb DVT or pulmonary embolism, if any, were noted.

Patient's previous comorbidities were noted. Among the medications, presence of pharmacological prophylaxis for DVT, presence of parenteral nutrition and other medications like mannitol and hypertonic saline were noted.

Patients with diagnosed or suspected malignancy, those with diagnosed prothrombotic states and those having hemodialysis catheters in IJV were excluded from the study.

Results

Among the patients enrolled in our study, there were 70 males and 30 females. There was evidence of thrombus in 33 patients in color Doppler duplex sonography (33.0%). In males, thrombus was found in 23 of 70 patients (32.86%) and in females thrombus was present in 10 of 30 patients (33.33%). There was no difference in the incidence of thrombosis among males and females. The overall incidence was 165.83 per 1000 catheter-days. The

incidence in males was 158.62 per 1000 catheter-days and in females 185.18 per 1000 catheter-days.

We categorized the thrombus arbitrarily into three groups: small, medium and large, depending on the size of the thrombus. Small thrombus was just around the catheter, medium-sized thrombus was up to 4 mm in diameter and the large-sized thrombus was more than 4 mm in diameter. In 15 patients the thrombus was small, in nine it was medium sized and in nine it was large. Figures 1a, b and c show the different sized thrombi on vascular doppler studies. The incidence of different sizes of thrombus in males and females has been shown below [Table 1]. The incidence of small-sized



Figure 1a: Small thrombus in the right internal jugular vein



Figure 1b: Medium-sized thrombus in the right internal jugular vein

Table 1: Incidence of CVC-related thrombus in males and females

Size of the thrombus	Males		Females		P-value
	Incidence	% age	Incidence	% age	
Small	13	56.52	2	20.0	0.05
Medium	6	26.09	3	30.0	0.81
Large	4	17.39	5	50.0	0.05

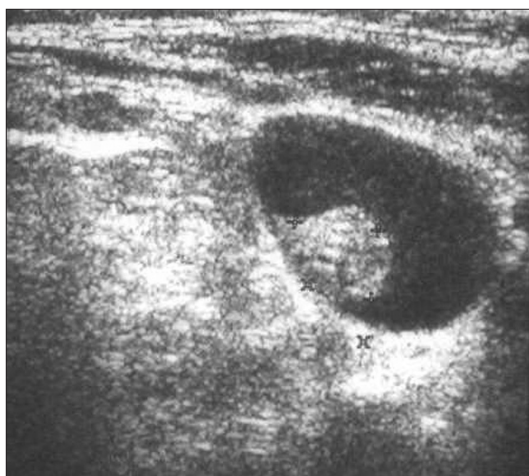


Figure 1c: Large-sized thrombus in the right internal jugular vein

thrombus was significantly higher in males ($P = 0.05$) and the incidence of large-sized thrombus was significantly higher in females ($P = 0.05$).

Of 33 patients found to be having thrombus, in 21 (63.64%) it was detected on the third day after CVC insertion, whereas in 12 patients (36.36%) it was detected on the sixth day. The catheter was removed if the thrombus was large. The patients having large thrombus were followed-up. If the thrombus was small or medium sized, then it was observed and followed-up with a color Doppler sonography after 3 days.

Of 33 patients, 24 had low molecular weight heparin as part of the DVT prophylaxis and nine did not have the same due to some medical contraindications.

None of the patient had total vessel occlusion or pulmonary embolism.

We did not find any significant effect of hypertonic solutions including mannitol and 3% saline as a risk factor for thrombus formation. We did not find diabetes mellitus, hypertension or smoking as increasing the risk of thrombus formation.

Discussion

CVCs are crucial in the management of most of the critically ill patients. They provide an important invasive tool for hemodynamic monitoring. They also allow delivery of certain medications and nutrition to the patient safely. As a result, CVC insertion is one of the most frequently performed invasive procedures in the intensive care unit. Unfortunately, their use is associated with many untoward complications, which increases the morbidity of the patient and can be life threatening.

More than 15% of the patients receiving CVCs have complications.^[3,6] Hirsch and coworkers detected the prevalence of DVT in critically ill patients to be 33% with the help of ultrasonography and color Doppler imaging.^[7] They also noted that among these, 15% were related to CVCs. Merrer and colleagues found the incidence of CVC-associated thrombosis to be 1.9% in the subclavian route and 21.5% in the femoral route.

The incidence of thrombosis is studied extensively in patients with hematological and other malignancies. A review showed that in such patients, the incidence of asymptomatic CVC-related thrombosis varied from 1.5 to 34.1% and that of symptomatic thrombosis from 1.2 to 13%.^[8] Another review found that the prevalence of CVC-related upper torso deep venous thrombosis in asymptomatic cancer patients varies from 11.7 to 44%, whereas in symptomatic patients it varies from 6.7 to 48%.^[9] There have been some studies on catheter-related thrombosis in patients having hemodialysis catheter *in situ*. Terrence and colleagues found the evidence of right IJV thrombus in 25.9% of the patients.^[10] Apart from patients with hematological and other malignancies as well as those having hemodialysis cannula, the incidence of CVC-related thrombosis and its clinical impact have not been studied well. In this study, we found the incidence of catheter-related thrombosis in right-sided IJV catheter to be 33.0%.

The etiology of thrombosis associated with CVCs can be explained on the basis of Virchow's triad of endothelial damage, altered blood flow and hypercoagulability. Vessel endothelium damage can be due to various factors including mechanical injury during the process of CVC insertion, number of vein punctures as well as irritation of endothelium by hypertonic solutions and drugs.^[11,12]

Within hours after insertion of the catheter there is deposition of platelets around the CVCs, reaching its peak in 3–4 h.^[13] This is followed by formation of a sleeve around the CVC, which is an adherent coating of fibrin and collagen. The formation of sleeve is reported to occur in up to 47% of the catheters.^[14,15] The fibrin sleeve in itself is benign, but promotes infection and may lead to thrombus formation.

Mural thrombosis can lead to subtotal stenosis or occlusion of vessel lumen leading to clinical manifestation of thrombosis and its complication. Manifestations also depend on whether thrombus is infected or not. Pulmonary embolism occurred in approximately 12% in most series.^[2] Uncomplicated or noninfected cases present with pain and swelling in the neck and a cord can be palpated beneath the sternocleidomastoid muscle.

Tovi *et al.* described the following clinical manifestation in a large series of patients with septic IJV thrombosis: fever (83%), leucocytosis (78%), cervical pain (66%), neck swelling (72%), cord sign (39%), sepsis syndrome (39%), pleuropulmonary complications (28%), superior vena cava syndrome (11%), chylothorax (5%) and jugular foramen syndrome (6%).^[16]

There are several risk factors identified that can potentiate thrombus formation. They are thrombogenicity of the catheter material, circumferential size of the catheter, catheter tip position, side of insertion, puncture site of insertion, multiple venipuncture attempts, composition of infusate, thrombophilic abnormalities, CVC-related infection and duration of catheter placement.^[8,13]

Borow and Crowley studied the adhesion of Chromium-51-labeled platelets to the different CVC materials and found that the least thrombogenic catheters were hydromer-coated polyurethane catheters.

The position of the catheter tip is an important risk factor for thrombosis. The incidence of CVC-related thrombosis is found to be higher in patients in whom the catheter tip is placed in the innominate vein or proximal superior vena cava as compared with the distal superior vena cava/right atrial junction.^[17,18] Tesselaar *et al.* showed a 2.6-fold higher risk when the catheter was located in the superior vena cava compared with the right atrium.^[19]

Other important risk factors are side of insertion of the catheter and puncture site of CVC. Tesselaar *et al.* also showed that the placement of CVC on the left side was associated with a 3.5-times higher risk of thrombosis as compared with the right side. In children, the incidence of catheter-related thrombosis was 44% in subclavian vein CVCs compared with 20% in jugular vein CVCs.^[20] This difference in the relative risk can be possibly explained by the anatomy of the venous system in the upper torso. As compared with the right side, the left brachiocephalic vein is longer and has a more horizontal course, leading to a sharper angle to the superior vena cava. Further, compared with the jugular CVCs, the subclavian CVCs follow a sharper curve into the superior vena cava, facilitating wall adherence. The subclavian CVCs enter where the vein passes between the clavicle and the first rib, which may cause vein compression and kinking of the CVC.

CVC-related infection is also an important risk factor that can lead to increased propensity for thrombus formation. Van Rooden *et al.* showed an increased incidence of CVC-associated thrombosis in patients

with CVC-related infection as compared with those without infection in a population of patients with hematological malignancy.^[21] There seems to be a bidirectional relationship between CVC-related infection and thrombosis.^[8] The major contributing factor for both of them is the formation of a fibrin sheath around the catheter. Microorganisms like *Staphylococcus aureus* and *Staph. epidermidis* easily adhere to the fibrin sheath. They also produce a coagulase enzyme that enhances the thrombogenic process.^[22] On the other hand, thrombin has been shown to upregulate many proinflammatory mediators *in vitro*.^[23]

Contrast venography is the gold standard for the diagnosis of upper limb DVT. But, it can dislodge the thrombus and cause embolism. Other modalities used to diagnose upper limb DVT are computed tomography scan with contrast, magnetic resonance imaging and nuclear medicine scan.^[24] Color Doppler duplex sonography is a noninvasive, safe and convenient means of diagnosing upper limb DVT and CVC-related thrombus. A systematic review of studies reported a sensitivity of compression ultrasound ranging from 56 to 100% and a specificity of 94–100% for the diagnosis of upper limb DVT.^[25]

It still remains a matter of debate whether antithrombotic prophylaxis is effective in preventing CVC-related thrombosis. There have been studies using unfractionated heparin, minidose warfarin and low molecular weight heparin for antithrombotic prophylaxis but, due to lack of well-designed prospective studies, it still remains a matter of debate.^[8]

The management of patients who develop a CVC-related thrombosis is not standardized. Treatment strategies consist of thrombolytic therapy, initiation of systemic anticoagulation, removal of the catheter or both. For CVC-related thrombosis, the preferred treatment is a combination of low molecular weight heparin followed by oral anticoagulant for 3–6 months, but no prospective randomized studies have been published on this subject.^[26,27]

Conclusions

CVC-related thrombosis is common. It appears to be more common in patients with hematological and other malignancies and in patients having hemodialysis cannula *in situ*. Many risk factors have been identified in different studies that have a strong association with thrombus formation. In this study, those patients who had CVC in the right IJV were only included. Females had significantly higher risk of developing larger

thrombus than males. Males had a significantly higher incidence of small-sized thrombus. In 63.64% patients, the thrombus could be detected on the 3rd day after CVC placement. The low molecular weight heparin used for DVT prophylaxis was not effective in preventing the CVC-related thrombus. The risk of thrombosis was not increased with the use of hypertonic solutions or with the presence of factors like diabetes mellitus, hypertension and history of smoking. There is no consensus regarding management of asymptomatic CVC-related thrombus, and more prospective randomized studies are required. Till then, knowledge of the different risk factors for the thrombus, its prevention and effective treatment of CVC-related infection remains the mainstay to avoid CVC-related thrombosis and its dreaded complications.

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