

# Research Progress on Risk Factors for Central Venous Catheter-Related Thrombosis

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## Abstract

Central venous catheterization is widely used in clinical practice. Catheter-related thrombosis (CRT) is one of the most common complications following catheter insertion, significantly impacting patients' quality of life and potentially threatening their lives. This article reviews risk factors from patient-related factors, underlying diseases, puncture-related factors, catheter-related factors, and infection. The aim is to provide a reference for clinical nursing practice to reduce the risk of thrombosis and enhance catheterization safety.

## Keywords

Central Venous Catheterization, Thrombosis, Risk Factors

## 1. Introduction

Central venous catheters (CVC) are inserted via central veins in the neck, chest, or groin, with the tip positioned in the superior vena cava, inferior vena cava, or right atrium. They provide venous access for rapid fluid resuscitation, central venous pressure monitoring, long-term parenteral nutrition support, and other indications [1]. In recent years, CVC have been extensively used clinically for intravenous chemotherapy, blood transfusion, parenteral nutrition, long-term infusion, and administration of irritant medications [2]. With their widespread use, related complications have become increasingly apparent, including catheter-related infections, thrombosis, phlebitis, and catheter occlusion [3]. However, the incidence of catheter-related thrombosis (CRT) post-insertion remains a significant concern and is the most common reason for unplanned catheter removal. Catheter-related thrombosis (CRT) refers to the process in which, after a catheter

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is inserted into the human body, thrombus clots form on the wall of the blood vessel where the catheter is placed and/or on the catheter wall itself due to factors such as damage to the integrity of vascular endothelium caused by puncture and mechanical irritation from the catheter, or the patient's own factors, thereby leading to catheter obstruction or even blockage. B-ultrasound is typically used for the screening and monitoring of CRT. CRT formation leads to discomfort such as limb swelling, pain, and dysfunction, and can even cause pulmonary embolism, endangering the patient's life while increasing treatment burden and suffering [4]. Therefore, early prevention, identification, and timely treatment of CRT are crucial. This article reviews the risk factors for CRT to provide a reference for clinical nursing practice.

The three primary factors for thrombus formation are: blood stasis, vascular endothelial injury, and patient hypercoagulability [5]. Clinical studies report wide variations in the incidence of CRT, ranging from 2% to 67% [6], differing across age groups and health statuses. Although the overall CRT incidence has decreased in recent years, it remains high in patients with specific disease states. In 2025, Liu [7] retrospectively analyzed 161 patients with acute poisoning and found a CRT incidence rate as high as 75%, exceeding the previously reported maximum of 67%. Consequently, implementing appropriate nursing measures for high-risk populations is essential to reduce CRT incidence.

## 2. Patient-Related Factors

### 2.1. Age

Age is a recognized risk factor for thrombosis. Studies indicate that age > 60 years is a significant factor for CRT, and its incidence rate is 2.5 times that of patients under 60 years old [8]. In a large-sample study, Yang analyzed hospitalized patients aged 65 to 104 years and found those over 65 had a higher risk of venous thrombosis, potentially related to declining immune function and reduced resistance [9]. With aging, blood circulation slows, blood viscosity increases, predisposing to thrombosis. Additionally, degeneration of elastic and collagen fibers in blood vessels increases fragility, making the endothelium more susceptible to injury during CVC insertion, leading to fibrin sheath formation and promoting thrombosis [10]. Therefore, healthcare providers should improve puncture techniques to minimize endothelial damage and encourage older patients to increase physical activity to enhance blood flow and reduce thrombosis risk.

### 2.2. Body Mass Index (BMI)

Research by Yuan [11] demonstrated a significant positive correlation between BMI and per catheter thrombosis formation. Studies show that a BMI > 25 kg/m<sup>2</sup> is an independent risk factor for CRT [12] [13]. Reasons include: 1) Higher blood viscosity in obese individuals; obesity also increases the difficulty of catheter insertion, potentially leading to repeated punctures that damage the venous wall, thereby increasing CRT incidence; 2) Obesity increases cardiac load and decreases

cardiac function, weakening the heart's pumping capacity and slowing circulation, creating favorable conditions for thrombosis. Adipocytokines affect fat and carbohydrate metabolism, increasing coagulant activity and decreasing fibrinolytic activity. The resulting accumulation of fibrin promotes platelet aggregation, increases blood viscosity, and enhances erythrocyte adhesion, all favoring thrombosis. Furthermore, elevated triglyceride levels in obese patients lead to deposits on venous walls, forming plaques that reduce vascular lumen diameter and slow blood flow, further promoting thrombosis [14]. Thus, for obese patients, education on dietary adjustments (increasing intake of low-calorie, high-fiber foods like vegetables and fruits), adequate hydration to reduce blood viscosity, weight control, and proactive preventive measures are crucial. Guide patients and set weight management goals, with a monthly weight loss of 0.5 - 1 kg being appropriate to avoid metabolic disorders caused by rapid weight loss. Monitor body weight and BMI every 2 weeks, and dynamically adjust the plan.

### **2.3. Smoking**

Smoking has been confirmed as a risk factor for CRT in multiple studies [15]. Delgado [16] found that fibrin formation is significantly enhanced in smokers, promoting coagulation. Nicotine, tar, and carbon monoxide in cigarettes induce vascular endothelial cells to release inflammatory factors, accelerate activation of the inflammatory response system, exacerbate endothelial injury, and activate platelets, accelerating the coagulation cascade and leading to thrombosis [17]. Research by Wei [18] indicated a correlation between CRT and smoking history, although the small sample size and older study population necessitate further validation. Nevertheless, the harmful effects of smoking on health are well-established, and smoking cessation prior to surgery is necessary [19], as smoking increases perioperative and postoperative complication rates. Therefore, for patients who smoke, vigorous encouragement and support for scientific smoking cessation are essential to improve overall health and reduce treatment-related risks. Working with the patient to develop a "smoking cessation plan", clarify the quit date (it is recommended to start within 1 - 2 weeks), inform the family members to supervise, and remove triggers such as cigarettes and lighters from the environment.

## **3. Underlying Patient Diseases**

### **3.1. Hypertension**

Hypertension, characterized by elevated blood pressure, often reflects aggravated vascular endothelial dysfunction. This leads to increased release of vasoconstrictors and decreased release of vasodilators, promoting vascular smooth muscle hyperplasia, lumen narrowing, and increased vascular resistance. Under these conditions, blood is more likely to reflux into the catheter and accumulate, accelerating thrombus formation [20] [21]. Niu [22] found that among hypertensive patients, elevated diastolic pressure had a greater impact on thrombosis risk than

elevated systolic pressure, and the combined incidence of thrombosis caused by both reaches as high as 27.89%. Chen [23] noted that patients receiving antihypertensive medication had a lower CRT incidence. Antihypertensive drugs (ACEIs, ARBs, CCBs,  $\beta$ -blockers) may improve endothelial function by modulating nitric oxide bioavailability or oxidative stress, thereby preventing thrombotic events. Thus, hypertension is a CRT risk factor, and antihypertensive medication can mitigate this risk. Hypertensive patients requiring CVC should strictly adhere to prescribed medications and blood pressure monitoring. Further clinical research exploring combinations of different antihypertensive drugs on endothelial function and CRT prevention is needed to identify optimal regimens for both blood pressure control and thrombosis risk reduction.

### 3.2. Cancer

Malignant tumor cells can directly activate the coagulation system. Interaction between monocytes/macrophages and tumor cells can cause vascular endothelial injury, inducing a hypercoagulable state. Tumor cells can also directly invade endothelial cells, releasing vascular permeability factors that disrupt endothelial integrity [24]. Tao [25] confirmed that cancer patients have a 7-fold higher risk of CVC-related thromboembolism than the general population. The incidence of CRT in cancer patients across different series ranges from 2.4% to 61.5%, and the incidence of symptomatic thrombosis also varies significantly, ranging from 0.3% to 28% [26] [27]. Prolonged disease duration in advanced stages (especially stage IV), long-term chemotherapy (particularly vascular-damaging agents like etoposide) [28] [29], and reduced activity due to extreme weakness during chemotherapy slow blood flow, predisposing to thrombosis [30]. A valuable prospective cohort study by Yu [31] involving 255 hospitalized cancer patients with catheters monitored by regular vascular ultrasound for 3 months found that patients with metastatic disease had a significantly higher thrombosis risk than those without metastasis (OR = 2.358). However, current research primarily focuses on cancer stage and metastasis; differences related to specific tumor types or locations remain unclear. Moreover, a recent meta-analysis shows that articles in this regard are generally of low quality, which calls for further research in the future.

### 3.3. Diabetes Mellitus

Hypercoagulability in diabetic patients involves multiple mechanisms, including endothelial damage, altered platelet structure and function, and disordered coagulation factor activity, increasing thrombotic risk [32]. Hyperglycemia also enhances erythrocyte aggregation and impairs flow [33]. Concurrent microangiopathy in some diabetic patients further increases thrombosis risk. Most epidemiological studies suggest diabetes promotes CRT and is an independent risk factor [34]-[36]. Diabetes patients often have multiple chronic diseases, and the incidence of CRT varies significantly depending on the different comorbid chronic conditions, ranging from 33% to 72% [18] [37].

However, these studies are retrospective analyses of specific disease groups; research in the general population is lacking. Gao [38] in a multifactorial linear regression analysis of patients over 18 requiring subclavian vein puncture, did not identify diabetes as a CRT risk factor, possibly due to good glycemic control or mild disease without severe complications in the study population. Furthermore, this study focuses on the specific scenario of subclavian vein catheterization, and the mechanism of catheter-related thrombosis formation may differ from that of catheterization in other sites (such as internal jugular vein and femoral vein). However, other studies may not have restricted the catheterization site, leading to inconsistent results. Despite conflicting evidence, considering the underlying pathological basis in diabetics (hypercoagulability, erythrocyte dysfunction, microangiopathy), a potentially hidden increased risk of thrombosis post-CVC insertion may exist. Therefore, for diabetic patients receiving CVC, healthcare providers should emphasize health education, strengthen blood glucose monitoring, maintain normal glycemic levels, and reduce the likelihood of CRT.

### 3.4. Elevated D-Dimer

Analysis of 647 cancer patients with CVC by Liu [39] showed that D-dimer level is an independent risk factor for CRT. Serum D-dimer is a key indicator of coagulation function and a specific marker of hyperfibrinolysis. Elevated D-dimer levels indicate increased fibrinolytic activity and are associated with a 4.094-fold higher risk of CRT [40] [41]. Guidelines report D-dimer sensitivity ranging from 75% to 100% and specificity from 26% to 83% [42]. However, many studies [43] [44] report sensitivity above 90%, and D-dimer often has the highest predictive importance in models. Notably, D-dimer levels peak post-thrombosis and then decline over time [45]. Therefore, the timing of D-dimer testing relative to symptom onset influences its diagnostic value for thrombotic disease. Patients should undergo coagulation testing before catheterization; those with elevated D-dimer may require anticoagulation therapy or avoidance of catheterization.

### 3.5. History of Thrombosis

Patients with a history of thrombosis often have hereditary or acquired coagulation disorders (e.g., antithrombin III deficiency, protein C/S deficiency, factor V Leiden mutation) or underlying conditions (e.g., cancer, autoimmune disease, nephrotic syndrome) causing chronic hypercoagulability. This state may persist after catheterization, making blood more prone to clotting on the catheter surface or vessel wall. Gao [38] found that a history of thrombosis increased the risk of CRT in critically ill patients, and the recurrence rate of thrombosis within 10 years in patients with a history of venous thrombosis can be as high as 30% - 50% [46]. A meta-analysis showed a significant odds ratio for CRT in patients with a thrombotic history undergoing CVC insertion (OR = 3.75, 95% CI: 1.02 - 13.85) [47]. However, a study on subclavian catheters did not find vascular disease history to be a CRT risk factor [38], possibly because patients with prior thrombosis received

anticoagulants, which may have mitigated the risk associated with their history.

## 4. Puncture-Related Factors

### 4.1. Puncture Vein

Common CVC insertion sites include the subclavian, internal jugular, and femoral veins. The 2020 American Society of Anesthesiologists “Practice Guidelines for Central Venous Access” did not provide a definitive preference between jugular and subclavian sites. A meta-analysis by Liu [1] indicated a higher risk of deep vein thrombosis with internal jugular vein catheterization. The subclavian vein has relatively constant anatomy, a larger diameter less affected by blood pressure changes, facilitates puncture in various positions, allows secure catheter fixation, and offers higher patient comfort, making it an ideal choice for CVC insertion [48] [49]. Subclavian vein puncture typically has two approaches: infraclavicular and supraclavicular. The choice of approach significantly impacts outcomes [50]. Studies suggest the supraclavicular approach offers higher safety and accuracy and may prolong catheter dwell time. By avoiding the lung apex and staying distant from the pleura and subclavian artery, the supraclavicular route significantly reduces complication risk. Left and right subclavian insertions differ: the optimal catheter length is 14 - 16 cm for the right side and 16 - 18 cm for the left [51]. Catheters inserted via the left subclavian vein make two bends before reaching the superior vena cava (SVC), and research indicates the left side carries a 3.5-fold higher thrombosis risk than the right [52], likely because left-sided CVC are more prone to abut the right wall of the SVC, causing greater endothelial damage. Given the high quality of these studies, prioritizing the right supraclavicular approach is recommended to reduce thrombosis risk and insertion difficulty.

### 4.2. Catheter Tip Position

Catheter tip position is a major determinant of CRT. The tip should ideally reside in the lower third of the SVC or the upper third of the right atrium [53]. This location has high blood flow (2 - 2.5 L/min), which rapidly dilutes concentrated infusates (e.g., chemotherapy), minimizing endothelial damage [54]. If the tip is malpositioned outside the SVC, slower surrounding blood flow allows the tip to move with cardiac or respiratory cycles, causing continuous mechanical irritation to the endothelium. This facilitates the aggregation of clotting factors and thrombus formation [55]. Therefore, post-insertion confirmation of tip position is mandatory. Expert consensus recommends post-procedural chest X-ray for verification [56]; infusion therapy should only commence after confirming correct placement. Liu [57] found that patient movement, positional changes, and respiration can cause tip migration, necessitating ongoing clinical vigilance. Principles of tip movement can also be utilized for repositioning malpositioned catheters.

### 4.3. Puncture Success Rate

Failed puncture attempts cause vascular trauma and local tissue damage, increas-

ing infection risk. Studies show that multiple unsuccessful attempts significantly increase infection risk compared to successful insertion on the first attempt; infection risk was 7.04 times higher when two or more insertion attempts were needed [58]. Repeated punctures easily damage skin and vessels, compromising natural defense barriers. Pathogen invasion under these conditions readily leads to catheter-related infection, subsequently promoting thrombosis [59]. Therefore, nurses must enhance catheterization skills, mastering knowledge of vascular anatomy, puncture angles, and depth. For obese patients with obscured landmarks and thick subcutaneous fat, ultrasound guidance can significantly improve success rates. Similarly, while improving the success rate of puncture, ultrasound also reduces the three most common complications of CVC insertion (such as arterial puncture, catheter kinking, and catheter malposition), thereby enhancing its safety [60].

## 5. Catheter-Related Factors

### 5.1. Catheter Material

Catheter material is a significant risk factor for deep vein thrombosis. As a foreign body, the catheter can provoke reactive inflammation of the vascular intima. Materials with better biocompatibility should be prioritized. The chemical composition of CVC affects microbial adhesion and thrombogenesis [61]. The thrombosis risk associated with different materials generally decreases in the order: polyvinyl chloride (PVC) > polyethylene > polyurethane > silicone [62]. However, some studies suggest silicone is too soft, increasing insertion difficulty, and recommend polyethylene for CVC [63]. The relative superiority of silicone versus polyurethane remains inconclusive, and no relevant systematic reviews or meta-analyses were retrieved. Large-scale RCT comparing the biocompatibility of these materials are needed to provide evidence-based selection guidance. Nevertheless, modern materials (polyurethane, silicone) offer advantages in softness, surface smoothness, and reduced endothelial damage, helping lower thrombosis risk.

### 5.2. Dwell Time

Catheter dwell time is a risk factor for CRT [64]. Misirlioglu [65] reported that prolonged dwell time increases thrombosis risk. Catheter-related bloodstream infection (CRBSI) was also associated with longer catheter duration; the inflammatory response from infection activates coagulation and suppresses fibrinolysis, directly or indirectly contributing to CRT. The Asia Pacific Society of Infection Control (APSIC) recommends CVC dwell time should not exceed 15 days [66]. However, a large retrospective analysis by Wang [41] found that CRT in cancer patients predominantly occurred within the first week post-insertion, with fluctuating rates thereafter, highlighting the critical importance of intensive CRT prevention within the first 2 weeks for this population. Qiao [67] found that each additional day of dwell time significantly increased CRT risk. Therefore, dwell time is a CRT risk factor, but optimal durations likely vary significantly across different patient

populations and diseases, necessitating evidence-based summaries for specific groups.

### 5.3. Catheter Diameter

Research by Jay [68] reported CRT incidence rates of 0%, 1%, 6.6%, and 9.8% for 3Fr, 4Fr, 5Fr, and 6Fr catheters, respectively. Larger catheter diameter correlates with higher thrombosis rates. Maintaining the catheter-to-vein ratio (CVR) below 50% is considered relatively safe [69]. However, exceeding 41% not only increases the risk of failed first-attempt insertion but also significantly raises venous thrombosis incidence [70]. Larger catheters also cause greater endothelial damage, slowing blood flow and promoting hypercoagulability. Other studies recommend keeping the CVR between 33% and 45% to minimize impact on blood flow [71]. Similarly, catheters with more lumens are associated with higher thrombosis rates [72]. Therefore, for patients with smaller or fragile veins (e.g., children, elderly), pre-insertion assessment using visualization tools (ultrasound) to evaluate vein size and select an appropriately sized catheter can proactively prevent CRT.

## 6. Infection

Catheter-related bloodstream infection (CRBSI) triggers local inflammation at the insertion site. If inadequately managed, this can lead to thrombosis [73]. Yu [74] identified infection as a CRT risk factor in hemodialysis patients. Qian [75] demonstrated a positive correlation between CVC related infection and intraluminal thrombosis formation. Baskin [73] noted that risk factors for CRT include previous catheter infection, and conversely, CRT can predispose to catheter infection. Infection activates the coagulation system and impairs fibrinolysis, directly or indirectly contributing to CRT. The precise mechanisms linking infection to thrombosis are still under investigation. A plausible explanation involves a bidirectional relationship: CRT can serve as a nidus for infection, promoting local bacterial colonization, while bacterial infection and inflammation activate platelets, releasing substances like serotonin and clotting factors that accelerate thrombosis. Data on CVC related infection and thrombosis primarily stem from small retrospective studies. Prospective randomized studies on preventive measures for both CVC related thrombosis and infection are needed to develop effective prevention strategies.

In summary, based on the identified risk factors for central venous catheter-related thrombosis (CRT), nurses can implement the following evidence-based preventive measures: During the puncture process, ultrasound-guided technology should be adopted to improve the success rate of one-time puncture and reduce vascular endothelial damage. This is particularly beneficial for obese patients or those with poor vascular conditions, as it can lower the risk of thrombosis caused by repeated punctures. Before catheterization, the ratio of catheter to vein diameter should be evaluated, and catheters with appropriate diameters should be preferred (it is recommended to control the ratio within 33% to 45%) to reduce blood

stasis. For high-risk patients such as the elderly and those with tumors, early mobilization plans should be formulated according to their activity ability, such as assisting in turning over in bed and performing active or passive limb exercises, to improve blood circulation. Meanwhile, post-catheterization maintenance should be strengthened, including standardized flushing and sealing operations, regular monitoring of white blood cell count and D-dimer levels. For patients with indwelling catheters for more than 10 days, the frequency of thrombosis risk assessment should be increased to promptly identify potential risks and intervene, thereby reducing the incidence of CRT.

## 7. Conclusion

The use of CVCs reduces the discomfort of repeated venipuncture, protects peripheral veins, and provides convenience for patients and healthcare providers. However, CRT remains a significant risk post-insertion. Patient-related factors (age, BMI, smoking), underlying diseases (hypertension, cancer, diabetes, elevated D-dimer, history of thrombosis), puncture-related factors (vein choice, tip position, success rate), catheter-related factors (material, dwell time, diameter), and infection contribute to CRT formation. Current research on CRT predominantly consists of retrospective studies; large-scale, multi-center prospective studies incorporating regular ultrasound screening until catheter removal are scarce, and many asymptomatic thrombi are easily overlooked. This underscores the need for nurses to comprehensively assess risk factors throughout the entire CVC management process (pre-insertion, insertion, maintenance) and enhance their technical skills to reduce CRT incidence and alleviate patient suffering.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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