# A retrospective analysis of risk factors associated with catheter-related thrombosis: a single-center study

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# Abstract

Background: Catheter-related thrombosis (CRT) may lead to catheter infections and failure, further deep venous thrombosis (DVT), and pulmonary embolism (PE). Recognizing the risk factors for CRT is extremely important to inform the development of catheter-nursing guidelines.

Methods: Data were collected from a total of 1532 patients who had undergone venous catheterization, including indwelling catheterization from March 19 to March 30, 2019 in Sun Yat-sen Memorial Hospital. The factors for which data were to be collected included the patients' physical characteristics, catheter-associated factors, and factors associated with catheter nursing. Logistic regression analysis, the chi-square test, Fisher's exact test, and the t-test were used to analyze the data.

Results: Of the 1532 patients studied, 28 developed intraductal thrombi, and of the factors analyzed, tumor, a catheterization history, a history of thrombophilia, surgery during the week before catheterization, the catheterization duration were significant risk factors associated with CRT (all $P < 0.05$). There were no significant associations between the catheter brand, the number of lumens, the insertion direction, or the factors associated with catheter nursing and CRT (all $P > 0.05$). Anticoagulation therapy significantly decreases the risk of CRT ( $P < 0.05$ ). Conclusion: Tumor, a history of thrombophilia, a history of catheterization, surgery during the week before catheterization, and catheterization duration were associated with increased risks of CRT. Prophylactic anticoagulation is effective for preventing and treating CRT. Our study incorporates clear and systematic risk factors associated with CRT. The results are different from those of previous studies.


# Background

Implanting central venous catheters (CVCs) into patients can lead to catheter-related thrombosis (CRT). However, implanting CVCs into patients with tumors and those who need long-term parenteral nutrition infusion is useful to establish good infusion channels, avoid the pain of repeated punctures, and to accelerate the critical transport of chemicals, blood, antibiotics, and parenteral nutrition [1]. In the United States of America, over five million CVCs are implanted into patients' blood vessels each year, and this number is increasing [2]. Thus, the causes of and the risk factors for CRT are the foci of current research. The pathophysiological mechanism underlying CRT suggests that catheter insertion causes mechanical damage to the vein, fibrin is deposited onto the surface of the catheter, and a large number of smooth muscle and endothelial cells quickly become embedded within the fibrin. The continuous movement of the catheter in the vein erodes the endothelial cells, which enter the catheter cavity, and this may trigger mural thrombus formation, catheter infections, DVT, and persistent vascular damage if they are not detected and treated promptly [3]. Patients with CRT may develop persistent vascular occlusion many years after catheter removal, thereby increasing their risk of post-thrombotic syndrome and recurrent thrombosis [4]. Furthermore, CRT may lead to PE, which may cause death [5]. Therefore, the presence of and possible harm caused by CRT should be considered, and the risk factors associated with CRT should be determined and mitigated.

While studies' findings indicate that many risk factors may be associated with CRT, they are yet to be clearly defined [1]. The risk factors associated with CRT can be categorized into three groups, namely, patients' physical characteristics, catheter-associated factors, and factors associated with catheter nursing [1,3]. Patients' physical factors include the presence of a tumor, their embolism history, and their infectious disease history [6–10]. Catheter-associated factors include the type of catheter implanted, catheter placement location, catheter insertion location, and the catheterization duration [11–14]. Catheter-nursing-associated factors include the infusion order and the composition of the liquid because intraductal thrombosis may be caused by drug and parenteral nutrition preparations [15,16]. However, clear and systematic descriptions of the risk factors that may be associated with CRT and its prevention do not exist. Therefore, we collected data describing the baseline characteristics of patients who had CVCs inserted, catheter-associated factors, and catheter-nursing-associated factors to analyze a variety of potential risk factors that may contribute to CRT. This study aimed to identify the main hospital-based risk factors for CRT and to provide benchmarks for the clinical prevention and treatment of adverse events, including infections, catheter failure, catheter-related DVT and its sequelae, and PE, which are caused by CRT.

# Methods

## Data sources

The data were collected from departments that used CVCs from March 19, 2019 until March 30, 2019 at the Sun Yat-Sen Memorial Hospital of Sun Yat-Sen University for this retrospective analysis. The study was approved by the hospital ethics committee. We distributed questionnaires to the critical care and pediatric intensive care units, and the biliary and pancreatic surgery, pediatric, otorhinolaryngology, gynecological oncology, hepatobiliary surgery, orthopedic, respiratory, emergency, rehabilitation, stomatology, urology, thoracic surgery, general medicine, cardiovascular surgery, cardiothoracic surgery, cardiothoracic surgery, neurorheumatology, neurosurgery, nephrology, gastrointestinal surgery, gastroenterology, hematology, ophthalmology, plastic surgery, oncology, and intensive care departments, and we collected data describing pertinent factors to analyse their association with CRT.

## Patient inclusion and exclusion criteria

The inclusion criteria were patients aged <75 years who had received CVC implantations in the aforementioned departments, including patients who received systemic tumor treatment. The exclusion criteria were patients with CRT, DVT, and PE that were detected two weeks before their inclusion in the study, and patients with brain tumors. *Table 1* presents the patients' baseline data.

## Catheter-related thrombosis risk factors

*Table 1* presents the patients' baseline data which included the physical characteristics factors that are associated with CRT. The catheter-related risk factors for CRT included the catheter brand, number of catheter lumens, catheter placement position, and the catheterization duration. The catheter-nursing-related risk factors for CRT included a comparison of prefilled saline delivery devices with syringes used to draw saline.

## Study endpoints

The study's clinical endpoints were the presence of intraductal thrombosis during the observation period, CRT detected using Doppler ultrasound, computed tomography, or venography, infections caused by CRT, further DVT, and PE. *Figure 1* illustrates the clinical pathway for CRT detection.

## Data analysis

The data were analyzed using IBM®SPSS® software, version 20.0 (IBM Corporation, Armonk, NY, USA). The risk factors associated with CRT were determined using univariate and logistic regression analyses, and the odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from the data describing the patients' baseline characteristics, and catheter- and catheter-nursing-related factors. The group of patients that did not have CRT represented the reference group. Chi-square and Fisher's exact tests were used to calculate the P values for the aforementioned factors. The t-test was used to determine the significance of the catheterization duration. The associations between CRT and the presence of tumors, a history of thrombophilia, and the use of anticoagulants were analyzed using univariate analysis only, because the data that all departments submitted was the sum.

## Results

From 19 March until 30 March 2019, a total of 1532 patients who underwent catheterization were included in the survey. Of the patients, 51.1% were male, 48.9% were female, 13.3% were aged 5–15 years, 58.3% were aged 15–60 years, and 28.4% were aged 60–75 years. CRT occurred in 28 patients (1.83%) (*Table 1).* Further DVT, PE, post-thrombotic syndrome, and catheter infections and failure did not occur during the observation period. No bleeding events were reported in association with the use of prophylactic anticoagulants. *Tables 1* and *2* present comparisons of the patients' baseline data and the catheter- and catheter-nursing-related factors, respectively.

There were no significant differences between the groups in relation to sex (P = 0.31) or age (P = 0.63). The univariate analysis of the patients' physical factors showed that the risk of CRT was lower in the patients without tumors than that in the patients with tumors (OR = 0.39 [95% CI = 0.18–0.82]), and the chi-square test showed that the presence of a tumor was significantly associated with CRT (P = 0.01). The patients without a catheterization history had a lower risk of CRT compared with that in the patients with a catheterization history (OR = 0.42 [95% CI = 0.18–0.95]), and the chi-square test showed that the

result was statistically significant (P = 0.04). The risk of CRT was lower among the patients who did not have a history of thrombophilia (OR = 0.41 [95% CI = 0.17–0.98]). Compared with the patients who had undergone surgery during the week before catheterization, those who had not undergone surgery had a significantly reduced risk of CRT (P < 0.01) (OR = 0.15 [95% CI = 0.06–0.37]). The patients who did not use anticoagulant therapy had a significantly increased risk of CRT (OR = 6.34 [95% CI = 0.86–46.81]) (P = 0.04).

Among the catheter- and catheter-nursing-associated factors, the risk of CRT did not differ in relation to the catheter brand (P = 0.17), catheter lumen number (P = 0.50), or the catheter insertion direction (P = 0.63). A longer catheterization duration significantly increased the risk of CRT (P = 0.036), and although prefilled saline delivery devices seemed to reduce the risk of CRT compared with the use of syringes (OR = 0.51 [95% CI = 0.22–1.21]), the difference was not significant based on the chi-square test ( P = 0.12). *Table 3* presents data describing the types of and numbers of patients with tumors within the study population, and the patients' histories of thrombophilia and their use of anticoagulants.

# Discussion

Our result had shown that the presence of a tumor, a catheterization history, a history of thrombophilia, surgery during the week before catheterization, the catheterization duration were significant risk factors associated with CRT (all P < 0.05). Anticoagulation therapy significantly decreases the risk of CRT ( P < 0.05). There were no significant associations between the catheter brand, the number of lumens, the insertion direction, or the factors associated with catheter nursing and CRT (all P > 0.05). Our result may be different with previous studies.

A previous study's findings showed that among catheterized patients, the CRT rate can be as high as 66% [17]. CRT can cause post-thrombotic syndrome, further DVT, PE, catheter occlusion, and catheter infections [18–20]. Up to 10% of patients with symptomatic CRT may have a PE [21]. Another study's findings from 112 patients with CRT showed that post-thrombotic syndrome was difficult to relieve without removal of the CVC and anticoagulation [22]. Although this study's findings did not indicate the presence of further venous thromboembolism, events associated with post-thrombotic syndrome were detected, and we must consider the factors that may trigger CRT to prevent more dangerous complications caused by CRT.

Thrombosis occurs more frequently in patients with tumors [23]. In this analysis, the presence of a tumor increased the risk of CRT. A review of the relationship between tumors and thrombosis at the molecular level suggested that tumor cells can show the abnormal expression of tissue factor (TF), release tumor cell-derived TF particles, and express cancer coagulation factors and cell surface proteases that directly promote coagulation. In addition, cancer cells can release cytokines, factor X-activating cysteine protease, mucinous glycoproteins, or circulating TF-bearing microparticles that affect platelets, white blood cells, and endothelial cells, thereby promoting thrombosis indirectly [24]. Meanwhile, tumors may differentially express the *RAS, PTEN,* and *P53* genes that influence the genesis of thrombosis [25,26]. Tumors are

associated with a high risk of CRT, especially among patients with advanced or active tumors[23], and this demands clinical attention. The 2019 version of the National Comprehensive Cancer Network (NCCN) guidelines on cancer-associated venous thromboembolic diseases recommends that prophylactic anticoagulation therapy should administered to patients who have been diagnosed with cancer or are clinically suspected of having cancer [27]. Many studies' findings have demonstrated the efficacy and safety of rivaroxaban administered to cancer patients to prevent thrombosis [28–32]. Our clinical practice indicated that rivaroxaban may be the first choice for anticoagulation in cancer patients with CVC; these findings will be verified in future trials.

This study's data demonstrated that a history of thrombophilia was associated with a greater risk of CRT. Previous study's findings have shown that a history of venous thromboembolism was the most important external risk factor for predicting CRT (OR = 2.0 [95% CI = 1.1–3.9]) [33]. Virchow's triad describes changes in the flow and composition of blood, endothelial damage, and inflammation as components that may cause thrombosis [34–36]; this may help to explain why a history of catheterization and surgery during the week preceding catheterization increased the risk of CRT. Surgery during the week before catheterization may be associated with a high risk of thrombosis [37]; hence, reasonable catheter maintenance should be achieved during the perioperative period. The 2019 version of the NCCN guidelines also recommends that prophylactic anticoagulation therapy should be administered to hospitalized and surgical patients [27]; this is a recommendation that we follow in our hospital to prevent CRT. However, a fixed-dose schedule for the anticoagulation of CRT in surgical patients with CVC is yet to be agreed, and the anticoagulation of CRT requires further investigation.

Regarding our investigation of catheter-related factors, neither the catheter brand nor the number of lumens influenced the risk of CRT. One study's findings showed that a greater number of lumens was associated with an increased risk of CRT [38]. The findings from a large randomized controlled trial have shown that among the three types of CVC implantation, a subclavian vein placement decreased the risk of CRT compared with femoral vein (hazard ratio = 3.4 [95% CI = 1.2–9.3]), jugular, and subclavian vein placements that had similar levels of risk [39]. However, our analysis showed there were no statistical differences among the three different types of catheter implantation in relation to the risk of CRT. Previous studies' findings have also shown that femoral and subclavian vein catheterization did not differ regarding the overall rate of mechanical complications (17.3% vs 18.8%; P = 0.74) [40]. Subclavian vein catheterization can injure patients; consequently, we do not recommend this type of catheterization. Regarding the catheterization duration, we have found that a longer catheter exposure time is associated with an increased risk of CRT, which is a finding that is supported by other studies' data [39,40]. Catheter movement can damage vessels, and as the catheterization duration increases, the greater the possibility that smooth muscle cells and endothelial cells will become embedded in the fibrin on the surface or in the cavity of the catheter, thereby increasing the risks of blood infection and CRT. In terms of the catheter-nursing-related factors, using prefilled saline delivery devices did not differ from syringes regarding the CRT risk. A meta-analysis showed that there was no statistical difference between heparin saline and 0.9% normal saline used for catheter maintenance [41]. However, no studies have explored the differences between prefilled saline delivery devices and syringes in relation to the risk of CRT. Compared with

syringes, prefilled saline delivery devices can reduce the occurrence of infections and accurately control the volume of liquid administered, and they are extremely safe [42]. Prefilled saline delivery devices may reduce the frequency of catheter infections, thereby helping to prevent CRT; however, the data do not support this notion. At present, most hospitals use syringes to draw normal saline and heparin saline to seal the tube. Catheter-nursing-related factors should be explored further.

Our study has limitations. Only single-factor logistic regression and chi-square analyses were conducted, because the data submitted was the sum. In addition, confounding factor analysis was not undertaken. The number of patients who participated in the study may be not be adequate, and further studies involving larger numbers of patients are needed. While adverse events, including catheter failure, catheter infections, catheter-related DVT, and PE, did not occur during this investigation, a longer follow-up duration is needed to determine the evolution of CRT.

## Conclusions

Our findings showed that the presence of a tumor, a history of thrombophilia, a history of catheterization, surgery during the week before catheterization, catheterization duration were associated with increased risks of CRT. Prophylactic anticoagulation, which we highly recommend, is effective and safe for the prevention and treatment of CRT in hospitalized and surgical patients with CVC.

## Abbreviations

## CRT: Catheter-related thrombosis

## DVT: Deep venous thrombosis

## PE: Pulmonary embolism

## OR: odds ratio

## CI: confidence interval

## SD: standard deviation

## CT: computed tomography

## Declarations

## Ethics approval and consent to participate

## The study was approved by the Sun Yat-sen memorial hospital ethics committee.

## Consent for publication

## We had used our agency's consent form.

## Availability of data and materials

## The data is shown in this article.

## Competing interests

## The authors declare that they have no competing interests.


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*Authors's contributions*

Kai huang, Runnan Shen and Xuezhen Zhou are the main authors to design the study and to write the manuscript. Yingying Qu, Chunling Mo, Yan Li contributed in designing questionnaires and collecting data from departments. Xi lin, Qingchang Chen, Guitao wu and Zhenhong chen analyzed the data and helped writing the manuscript. All authors read and approved the final manuscript.


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## Tables

**Table 1** Patients' baseline demographic and clinical data.

| Baseline characteristics | | All (n=1532 100%) | No CRT found  n=1504 98.17%  | CRT (n=28 1.83%) | OR | 95%CI | Chi-square value | P value |
|---|---|---|---|---|---|---|---|---|
| Sex, n (%) | Male | 783 51.1 | 766 50.9 | 17(60.7) | 1.489 | 0.69-3.20 | 1.05 | 0.31 |
| | Female | 749 48.9 | 738 49.1 | 11(39.3) | | | | |
| Age, years, n (%) | 5-15 | 203 13.3 | 200 13.3 | 3(10.7) | - | - | 0.85 | 0.63 |
| | 15-60 | 894 (58.3) | 875 (58.2) | 19(67.9) | | | | |
| | 60-75 | 435(28.4) | 429(28.5) | 6(21.4) | | | | |
| Tumor presence[a], n (%) | Absent | 1148 74.9 | 1128(75.0) | 15(53.6) | 0.39 | 0.18-0.82 | 6.66 | 0.01 |
| | Present | 384 25.1 | 376(25.0) | 13(46.4) | | | | |
| History of catheterization[a], n (%) | No | 1308 85.4 | 1288(85.6) | 20(71.4) | 0.42 | 0.18-0.95 | 3.67[b] | 0.04 |
| | Yes | 224 14.6 | 216(14.4) | 8(28.6) | | | | |
| Sugery in the week before catheterization[a], n (%) | No | 983 64.2 | 977(65.0) | 6(21.4) | 0.15 | 0.06-0.37 | 22.65 | 0.01 |
| | Yes | 549 35.8 | 527(35.0) | 22(78.6) | | | | |
| Anticoagulant drug use[a], n (%) | No | 1246 81.3 | 1219(81.1) | 27(96.4) | 6.34 | 0.86-46.81 | 4.30 | 0.04 |
| | Yes | 286 18.7 | 285(18.9) | 1(3.6) | | | | |
| History of thrombophilia[a], n (%) | No | 1345 87.8 | 1323(88.0) | 21(78.6) | 0.41 | 0.17-0.98 | 4.29 | 0.04 |
| | Yes | 187 12.2 | 181(12.0) | 7(21.4) | | | | |

CRT, catheter-related thrombosis; OR, odds ratio; CI, confidence interval.

a Factors that may induce CRT in patients.

b Fisher exact test

**Table 2** Catheter- and catheter-nursing-related factors among the patients.

| Catheter related factors | | All (n=1532 100%) | No CRT found  n=1504 98.17%) | CRT (n=28 1.83%) | OR | 95%CI | Chi-square value | P value |
|---|---|---|---|---|---|---|---|---|
| Cather brand, n (%) | Braun | 183(11.9) | 179 (11.9) | 4 (14.3) | | | 3.66[a] | 0.17 |
| | Arrow | 756(49.3) | 747 (49.7) | 9 (32.1) | - | - | | |
| | SungWon | 593(38.7) | 578 (38.4) | 15 (53.6) | | | | |
| Number of lumens, n (%) | 1 | 46(3.0) | 45(3.0) | 1(3.6) | | | 0.95[a] | 0.50 |
| | 2 | 1364(89.0) | 1340(89.1) | 24(85.7) | - | - | | |
| | 3 | 122(8.0) | 119(7.9) | 3(10.7) | | | | |
| Catheter insertion direction, n (%) | Femoral vein | 487(31.8) | 476(31.6) | 11(39.3) | | | 0.94 | 0.63 |
| | Subclavian vein | 433(28.3) | 425(28.3) | 8(28.6) | - | - | | |
| | Jugular vein | 612(40.0) | 603(40.1) | 9(32.1) | | | | |
| Catheterization duration, mean±SD | | 12.7±3.2 | 11.2±2.5 | 14.1±3.4 | - | - | - | 0.036[b] |
| Catheter nursing factors | | | | | | | | |
| Flashing catheter, n (%) | Prefilled drug delivery | 602(39.3) | 595(39.6) | 7(25.0) | 0.51 | 0.22-1.21 | 2.4 | 0.12 |
| | device | | | | | | | |
| | delivers | | | | | | | |
| | saline / heparin saline | | | | | | | |
| | Syringe suction of | 930(60.7) | 909(60.4) | 21(75.0) | | | | |

| | | |
|---|---|---|
| | saline / heparin | |
| | saline | |

CRT, catheter-related thrombosis; OR, odds ratio; CI, confidence interval; SD, standard deviation.

a Fisher exact test

b Catheter duration was calculated with t-test.

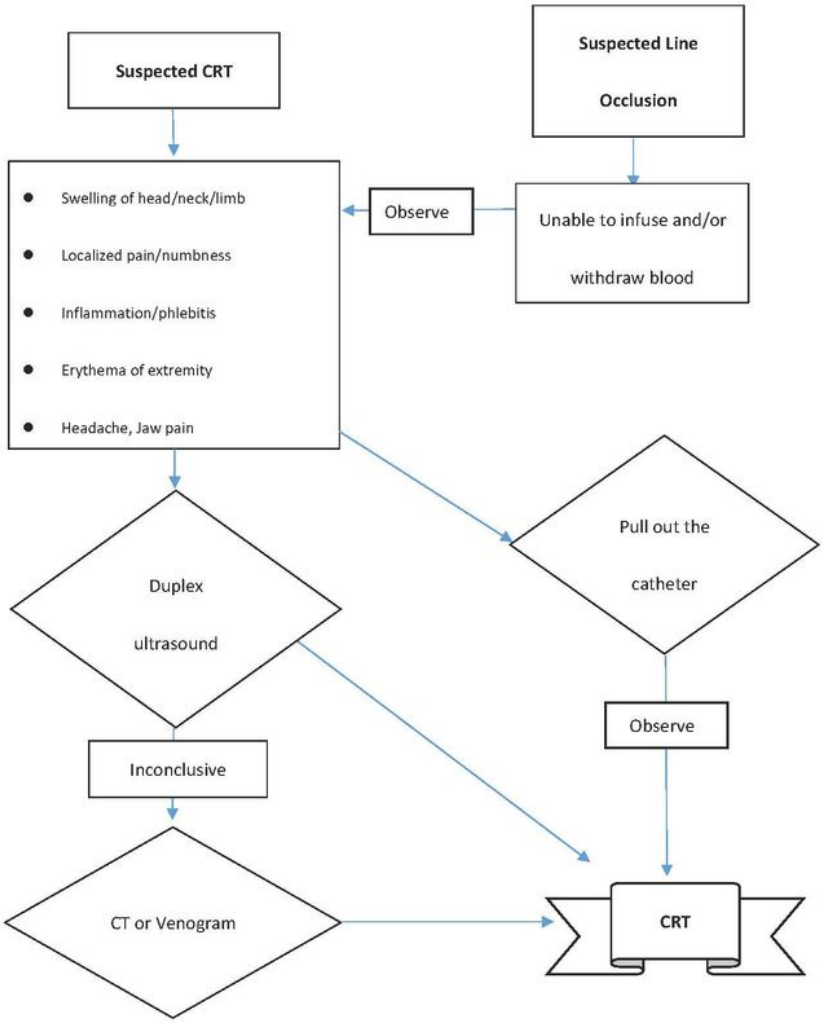
**Table 3** Conditions of tumors, previous thrombophilia diseases history and anticoagulant therapy of patients selected.

| Baseline characteristics | | All (n=1532 100%) | No CRT found (n=1504 98.17%) | CRT (n=28 1.83%) |
|---|---|---|---|---|
| Tumor patients, n (%) | No | 1148(74.9) | 1128(75.0) | 20(71.4) |
| | Yes | 384(25.1) | 376(25.0) | 8(28.6) |
| Type of tumor, n (%) | Breast cancer | 89(5.8) | 86(5.7) | 3(10.7) |
| | colorectal cancer | 32(2.1) | 31(2.1) | 1(3.6) |
| | lung cancer | 54(3.5) | 52(3.5) | 2(7.1) |
| | Gastric cancer | 33(2.2) | 32(2.1) | 1(3.6) |
| | Gynecological tumor | 30(2.0) | 30(2.0) | 0 |
| | Lymphomas | 35(2.3) | 35(2.3) | 0 |
| | Liver tumor | 65(4.2) | 64(4.3) | 1(3.6) |
| | Renal tumor | 46(3.0) | 46(3.1) | 0 |
| History of thrombophilia, n (%) | Deep venous thrombosis | 58(3.8) | 56(3.7) | 2(7.1) |
| | Pulmonary embolism | 13(0.8) | 12(0.8) | 1(3.6) |
| | Septicemia | 5(0.3) | 5(0.3) | 0 |
| | Sickle cell disease | 3(0.2) | 3(0.2) | 0 |
| | inherited thrombophilia | 6(0.4) | 5(0.3) | 1(3.6) |
| | Enteritis | 54(3.5) | 54(3.6) | 0 |
| | Infectious diseases | 48(3.1) | 46(3.1) | 2(7.1) |
| | Others or missed | 1345(87.8) | 1323(88.0) | 22(78.6) |
| Use of anticoagulant, n (%) | No | 1236(80.7) | 1209(80.4) | 27(96.4) |
| | Low molecular weight | 81(5.3) | 81(5.3) | 0 |

| | | | |
|---|---|---|---|
| **heparin** | | | |
| **Warfarin** | 59(3.9) | 59(3.9) | 0 |
| **Rivaroxaban** | 156(10.2) | 155(10.1) | 1(3.6) |

CRT, catheter-related thrombosis.

# Figures




## Figure 1

The catheter-related thrombosis detection pathway.