Disease-Related Risk Factors for CVC-Related Symptomatic Thrombosis in Surgical ICU Inpatients

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Abstract

To report the rate of symptomatic catheter-related venous thrombosis (CRVT) in surgical intensive care unit patients receiving central venous catheters (CVC) and analyze the disease-related risk factors for symptomatic CRVT in SICU patients. A retrospective analysis was performed on 1643 critically ill patients admitted to the SICU from January 2015 to December 2019. Cases were divided into two groups based on the presence of symptomatic CRVT, and the variables of interest were extracted from the electronic medical record system. Logistic univariate and multivariate regression analyses were used to determine the risk factors of SCRVT. A total of 209 symptomatic CRVT events occurred among 2114 catheters. Multivariate analysis showed that trauma (odds ratio [OR], 2.046; 95% confidence interval [CI] [1.325-3.160], $P = 0.001$), major surgery (OR, 2.457; 95% CI [1.641-3.679], $P = 0.000$), and heart failure (OR, 2.087; 95% CI [1.401-3.111], $P = 0.000$) were independent risk factors for symptomatic CRVT in SICU. The AUROC for this model was 0.610 (95% CI [0.569-0.651], $P=0.000$). The incidence rate was 9.89%. For patients hospitalized in the SICU, especially those admitted with these three conditions, thromboprophylaxis and/or mechanical prophylaxis should be actively provided to reduce the occurrence of symptomatic CRVT.

Introduction

Hospital-acquired venous thromboembolism (VTE) has received increasing attention in medical institutions due to its increased morbidity and mortality among hospitalized patients¹⁻⁴. A number of studies have identified several important risk factors for hospital-acquired thrombus, of which CVC is an important risk factor⁵⁻⁷. Symptomatic CRVT is a special type of hospital-acquired VTE. Due to the convenience of CVC in intravenous drug injection, renal replacement therapy, monitoring of vital signs and other aspects, the use of catheters in clinical practice is becoming increasingly common, and the occurrence of CRVT events is also increasing⁸.

CVCs were used more frequently in ICU inpatients given their critical illness^{3,9-11}. Many studies on CRVT in ICU patients have been reported, and it has been found that venous catheter diameter, number of lumen, intubation site, blood transfusion, parenteral nutrition, sedation and other factors are related to CVC-related thrombosis¹²⁻¹⁴. Critical and severe patients are treated in the ICU. To our knowledge, no studies have been conducted on the correlation between CVC-related thrombosis and major diseases in ICU patients. The purpose of this study was to investigate disease-related risk factors for symptomatic CRVT in SICU inpatients.

Patients And Methods

Ethics statement.

This retrospective cohort study was approved by the Medical Ethics Committee of Ganzhou People's Hospital, and the methods were performed in accordance with the approved guidelines.

Consent statement.

Written informed consent was signed by the patient's direct relative.

Study design and patients.

We retrospectively analyzed critically ill patients hospitalized in the SICU at a single center from January 2015 to December 2019. Data of interest were collected through electronic medical record retrieval to analyze disease-related risk factors for symptomatic CRVT in SICU inpatients.

Inclusion criteria:

1. Age $\geq$ 18 years;
2. >3-d stay in the SICU;
3. CVCs inserted into the deep vein of the patients.

Exclusion criteria:

1. CVC had thrombosis before ICU admission;
2. Patients who have given up treatment (due to various factors, such as financial constraints and poor prognosis);
3. The duration of CVC intubation was less than 3 days.

According to the research needs, we collected basic information of eligible patients, including gender, age, hypertension, drinking, smoking, diabetes, history of malignant tumor, chronic obstructive pulmonary disease (COPD), body mass index (BMI), and acute physiology and chronic health evaluation II (APACHEII) score. In addition, indicators related to hospitalization were collected, including ICU stay, endotracheal intubation time, CVC indwelling time, anticoagulant therapy and anticoagulant contraindication. Most importantly, we collected the primary diseases that necessitated admission to the SICU.

Definitions

The primary disease of patients admitted to SICU: The primary disease referred to the most important disease that caused patients to be admitted to the SICU, and this information was determined by the chief complaint of admission to the SICU. However, patients hospitalized in the SICU generally have multiple coexisting diseases, and the diseases that were difficult to identify as the primary diseases were discussed and decided by the research group members based on the patient diagnostic information provided by the medical records. Trauma patients referred to patients admitted to the SICU after trauma, including severe injuries to the brain, chest, abdomen and/or limbs, regardless of whether the trauma was accompanied by other mild or severe diseases.

Major surgery referred to the operation performed under general anesthesia. Major surgery referred to the operation performed under general anesthesia, the operation time was more than 2 hours, patients' breathing, circulation and other organ function instability might occur and the patients need life support treatment after the operation.

CVC insertion: According to the therapeutic needs, intravenous catheterization was performed by qualified doctors under ultrasound guidance or nonultrasound guidance. The insertion site was based on the patient's condition and the operating doctor at the time of surgery. The insertion sites included the internal jugular vein, subclavian vein or femoral vein.

Symptomatic CRVT: Symptomatic CRVT referred to thrombosis at the site of CVC insertion into the deep vein. This condition results in symptoms, such as redness, swelling and pain in the local or the area of venous reflux. The administering physician decide whether to perform an ultrasound examination to determine the presence of a catheter-related thrombosis.

Venous duplex ultrasonography (VDU): All VDUs were performed by certified ultrasonography technologists and interpreted by an attending radiologist. The thrombus was described as complete thrombus, mural thrombus, and no thrombus according to the relationship between thrombus volume and vascular lumen.

Data analysis.

The cases were divided into two groups based on the presence of symptomatic CRVT. The continuous data of the two groups are described by means $\pm$ standard deviations (SDs) and compared using *t* tests for 2 independent samples. Nonparametric data are expressed as median (interquartile range) and compared using the Mann-Whitney test. The categorical data were presented as percentages and compared with the χ^2 test or Fisher exact test. Kaplan-Meier curves were applied to analyze the cumulative incidence of symptomatic CRVT. Univariate and multivariate logistic regression analyses were used for disease risk factor analysis. Variables with a two-tailed $P < 0.1$ on univariate analysis were included in a multivariate regression model to identify independent predictors of symptomatic CRVT. ORs and 95% CIs are reported. Area under the receiver operator curve (AUROC) is used to assess predictive value of the model. All tests were two-sided with a significance level of 0.05 and were performed using SPSS software (ver. 24.0; IBM Corp., Armonk, NY, USA).

Results

Patient baseline characteristics.

From January 2015 to December 2019, a total of 4904 patients were admitted to the SICU, including 249 patients <18 years old, 1989 patients whose length of stay in the ICU <3 days, 245 patients who had given up treatment, 13 patients with CVC complicated thrombosis before admission to the ICU, 765 patients without CVC, and 1643 patients with CVC. The rate of catheter use was 68.2% (1643/2408). Among them,

1,187 patients had one catheter, 380 patients had two catheters, 76 patients had three or more catheters. The total number of CVC was 2196. In total, 82 catheters with an intubation duration of <3 days were excluded from the study. Thus, 2114 catheters were included in the analysis, and each catheter was analyzed as a case (Figure 1).

Symptomatic CRVT occurred in 209 CVCs of the patients. The incidence of CRVT was 9.89%, and approximately 75% of thrombotic events occurred within 17 days of catheter placement (Figure 2). The 2114 patients were divided into two groups according to whether symptomatic CRVT occurred. We found significant differences in age ($P = 0.000$), BMI ($P = 0.000$), APACHE II score ($P = 0.001$), length of ICU stay ($P = 0.000$), endotracheal intubation time ($P = 0.000$), CVC indwelling time ($P = 0.000$), anticoagulation therapy ($P = 0.034$), and anticoagulant contraindications ($P = 0.005$) between the two groups. Patient clinical characteristics are presented in Table 1.

Predictive factors of SCRVT.

Figure 3 shows the distribution of the primary diseases of patients admitted to the SICU, in which respiratory failure is the most frequent ($n = 386$ [18.3%]) followed by sepsis, heart failure, major surgery, trauma, hypovolemic shock, renal failure, cerebrovascular disease, severe acute pancreatitis, hepatic failure and intestinal obstruction. Symptomatic CRVT occurred in 7.3%, 7.8%, 13.9%, 16.1%, 14.0%, 10.6%, 5.9%, 11.8%, 4.4%, 13.3% and 15.0% of patients in each disease group, respectively. Univariate analysis revealed that trauma, major surgery, heart failure, respiratory failure, and severe acute pancreatitis were risk factors for symptomatic CRVT in the SICU (Table 2). Then, these 5 factors were incorporated into the multivariate analysis. Trauma (odds ratio [OR], 2.046; 95% CI [1.325-3.160], $P = 0.001$), major surgery (OR, 2.457; 95% CI [1.641-3.679], $P = 0.000$), heart failure (OR, 2.087; 95% CI [1.401-3.111], $P = 0.000$) were independent risk factors for symptomatic CRVT in the SICU (Table 3). The AUROC for this model was 0.610 (95% CI, 0.569-0.651, $P=0.000$) (Figure 4).

Discussion

The study confirmed that the incidence of symptomatic CRVT among SICU inpatients was 9.89% and revealed that the independent risk factors of symptomatic CRVT included trauma, major surgery, and heart failure based on the SICU primary disease risk model (AUROC = 0.610).

Given the high risk of developing venous thromboembolism, hospital-acquired VTE is extremely high in ICU patients, but its incidence has been reported differently by various medical institutions. One study analyzed SICU patients with duplex sonography performed during CVC placement or within 7 days after CVC removal and found that fifty-nine CRVTs were diagnosed in 28% of patients¹⁵. Gibson, C. D. et al. retrospectively analyzed the occurrence of vein thrombosis among hospitalized patients in the medical ICU, and selected patients with suspected limb thrombosis for ultrasound examination. The incidence of thrombosis was 16%, and the catheter usage rate of patients with thrombosis was 55.26%. However, the incidence of symptomatic CRVT was not further analyzed¹⁶. Chen, Y. et al. studied symptomatic

thrombosis associated with peripherally inserted CVC in cancer patients and found that the incidence of symptomatic CRVT was 6.7%¹⁷. The incidence of symptomatic CRVT in our study was 9.89%. The difference may be related to the study population and statistical methods.

The traumatically injured are at an especially high risk for VTE¹⁸⁻²¹. In the absence of pharmacologic prophylaxis, those with severe injuries have a risk of VTE that surpasses 50%²². Immediately after the injury, the delicate homeostasis balance of coagulation in the system is disturbed by the reduction of functional protein C, the reduction of antithrombin and the cessation of acute fibrinolysis, leading to the state of hypercoagulability²³⁻²⁵. The combination of endothelial and tissue injury, vascular stasis and hypercoagulability²⁶ represents a high risk factor for early VTE in this population, especially in patients with severe multiple trauma^{27,28}. Hamada, S. R. et al. prospectively studied 153 patients with severe trauma from a SICU of a university level 1 trauma center and found that the prevalence of VTE was 30.7%. CVC was an independent risk factor for VTE occurrence in this group of cases (OR 4.39, 95% CI [1.1-29])²⁷. Most of the wounds in the population in our study involved multiple injuries, including major compound injuries of head, neck, chest and/or abdomen. The incidence of symptomatic CRVT was 16.1%, which did not seem high. However, the VTE here did not include thrombosis unrelated to CVC.

Given that major surgery may result in unstable respiratory, circulatory and other organ functions, patients need to be admitted to SICU for life support after surgery. The major operations of the center mainly include abdominal surgery, cardiac surgery, open brain surgery and multiple injury repair surgery. These types of operations are characterized by long operation time, a large amount of blood loss, need for blood transfusion, and the need to be performed under general anesthesia, and all of these parameters contribute to the risk of venous thrombosis formation^{29,30}. At present, clinical researchers in different surgical specialties, including general surgery³¹, orthopedics³², thoracic surgery³³, urology³⁴, tumor surgery³⁵ and neurosurgery³⁶, found that the incidence of VTE after major surgery is relatively high, ranging from 3.6%³¹ to 21.3%³⁶. They believe that major surgery is a risk factor for VTE and that active prevention is needed⁸. The current study population included 255 patients admitted to the SICU due to major surgery, among which 41 patients (13.9%) had SCRVT. Major surgery was an independent risk factor for symptomatic CRVT in this group.

Heart failure accounts for a high proportion of SICU inpatients, and symptomatic CRVT was noted in 16.2% (47/290) in patients admitted to ICU due to heart failure in this study. Basnet, S. et al. found that the incidence of heart failure associated with VTE increased yearly by analyzing inpatient with heart failure from 2000 to 2013³⁷. Wilson, T. J. et al. analyzed the risk factors for thrombosis associated with peripherally inserted CVC in inpatients and found that heart failure (OR, 2.62; 95% CI, 1.01-6.83) was associated with the occurrence of a CRVT³⁸. Heart failure is characterized by a prothrombotic state, which not only increases the risk for cardioembolic events and ischemic stroke³⁹ but also increases the risk for deep venous thrombosis (DVT) and pulmonary embolism (PE), which together constitute VTE⁴⁰. In a study of 13,728 subjects, Fanola, C. L. et al. reported that over a 22-year period, heart failure occurred in 2,696 (20%) patients, and 729 VTE events were identified. Heart failure was associated with an

increased long-term risk of VTE (OR 4.39, 95% CI [2.58-3.80]) that was independent of multiple risk factors for venous thromboembolism⁴¹.

This study also noted that a long duration of CVC intubation⁴² and long endotracheal intubation^{16,18} could increase symptomatic CRVT occurrence in SICU patients. In this study population, anticoagulation therapy was insufficient due to anticoagulation contraindication, and the comparison of anticoagulation therapy between the two groups was statistically significant ($P = 0.005$), which may also increase the occurrence of symptomatic CRVT. Therefore, especially after major surgery⁸ or trauma²⁶, patients should undergo active measures to prevent thrombosis, and anticoagulation drugs should be given if there is no anticoagulation contraindication. Otherwise, mechanical prophylaxis to prevent thrombus should be performed. In addition, this study also suggested that age, BMI, APACHE II score, length of ICU stay and other factors were significantly different in the comparison between the two groups, which was basically consistent with the results of previous studies^{12,16,17,43}.

Our study has several limitations. First, it involved a single center and a relatively small number of patients. Second, this was a retrospective study performed using electronic medical records, and the study population was quite heterogeneous, which possibly introduced the potential for information bias. In addition, only symptomatic CRVT was analyzed in this study. Nonsymptomatic CRVT was not included in the analysis, which potentially resulted in the incidence of CRVT being greatly underestimated. Therefore, a multicenter, prospective randomized controlled study is necessary to further evaluate the risk factors associated with CRVT in patients in the SICU catheter-related thrombi disease.

Conclusions

The incidence of symptomatic CRVT in the SICU population was 9.89%. Trauma, major surgery and heart failure are independent disease risk factors for symptomatic CRVT. For patients hospitalized in the SICU, especially those admitted with these three conditions, thromboprophylaxis and/or mechanical prophylaxis should be actively provided to reduce the occurrence of symptomatic CRVT.

Declarations

Author Contributions

Y.F.L. conceptualized and designed the study. Y.F.L., Y.L.Z. and Z.M.K. performed and supervised data collection. X.C.L., Y.L.Z. contributed in data analysis. X.C.L. and G.F.Z. prepared the first draft of the paper. X.C.L., Y.L.Z. and Z.M.K. contributed equally to this article and share co-first authorship. All the authors contributed in revision of the manuscript. All the authors have read and approved the final manuscript.

Competing Interests:

The author(s) declare no competing interests.

References

1. Zakai, N. A., Callas, P. W., Repp, A. B. & Cushman, M. Venous thrombosis risk assessment in medical inpatients: the medical inpatients and thrombosis (MITH) study. *J Thromb Haemost***11**, 634-641, doi:10.1111/jth.12147 (2013).
2. Lamontagne, F. *et al.* Nonleg venous thrombosis in critically ill adults: a nested prospective cohort study. *JAMA Intern Med***174**, 689-696, doi:10.1001/jamainternmed.2014.169 (2014).
3. Malato, A. *et al.* The impact of deep vein thrombosis in critically ill patients: a meta-analysis of major clinical outcomes. *Blood Transfus***13**, 559-568, doi:10.2450/2015.0277-14 (2015).
4. Cohoon, K. P. *et al.* Direct medical costs attributable to venous thromboembolism among persons hospitalized for major operation: a population-based longitudinal study. *Surgery***157**, 423-431, doi:10.1016/j.surg.2014.10.005 (2015).
5. Winters, J. P., Callas, P. W., Cushman, M., Repp, A. B. & Zakai, N. A. Central venous catheters and upper extremity deep vein thrombosis in medical inpatients: the Medical Inpatients and Thrombosis (MITH) Study. *J Thromb Haemost***13**, 2155-2160, doi:10.1111/jth.13131 (2015).
6. Parienti, J. J. *et al.* Intravascular Complications of Central Venous Catheterization by Insertion Site. *N Engl J Med***373**, 1220-1229, doi:10.1056/NEJMoa1500964 (2015).
7. Suleman, A., Jarvis, V., Hadziomerovic, A., Carrier, M. & McDiarmid, S. Implanted vascular access device related deep vein thrombosis in oncology patients: A prospective cohort study. *Thromb Res***177**, 117-121, doi:10.1016/j.thromres.2019.02.033 (2019).
8. Anderson, D. R. *et al.* American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. *Blood Adv***3**, 3898-3944, doi:10.1182/bloodadvances.2019000975 (2019).
9. Brandmeir, N. J. *et al.* A Randomized Trial of Complications of Peripherally and Centrally Inserted Central Lines in the Neuro-Intensive Care Unit: Results of the NSPVC Trial. *Neurocrit Care***32**, 400-406, doi:10.1007/s12028-019-00843-z (2020).
10. Steen, E. H. *et al.* Central Venous Catheter-Related Deep Vein Thrombosis in the Pediatric Cardiac Intensive Care Unit. *J Surg Res***241**, 149-159, doi:10.1016/j.jss.2019.03.052 (2019).
11. Lambert, I., Tarima, S., Uhing, M. & Cohen, S. S. Risk Factors Linked to Central Catheter-Associated Thrombosis in Critically Ill Infants in the Neonatal Intensive Care Unit. *Am J Perinato***36**, 291-295, doi:10.1055/s-0038-1667377 (2019).
12. White, D. *et al.* Comparative thrombosis risk of vascular access devices among critically ill medical patients. *Thromb Res***172**, 54-60, doi:10.1016/j.thromres.2018.10.013 (2018).
13. Hrdy, O. *et al.* Central venous catheter-related thrombosis in intensive care patients - incidence and risk factors: A prospective observational study. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub***161**, 369-373, doi:10.5507/bp.2017.034 (2017).
14. Antonelli, M. *et al.* Comparison of triple-lumen central venous catheters impregnated with silver nanoparticles (AgTive(R)) vs conventional catheters in intensive care unit patients. *J Hosp Infect***82**,

- 101-107, doi:10.1016/j.jhin.2012.07.010 (2012).
15. Malinoski, D. *et al.* Which central venous catheters have the highest rate of catheter-associated deep venous thrombosis. *Journal of Trauma and Acute Care Surgery***74**, 454-462, doi:10.1097/TA.0b013e31827a0b2f (2013).
 16. Gibson, C. D. *et al.* Prevalence and Predictors of Deep Vein Thrombosis in Critically Ill Medical Patients Who Underwent Diagnostic Duplex Ultrasonography. *J Intensive Care Med***35**, 1062-1066, doi:10.1177/0885066618813300 (2020).
 17. Chen, Y. *et al.* Patterns and risk factors of peripherally inserted central venous catheter-related symptomatic thrombosis events in patients with malignant tumors receiving chemotherapy. *J Vasc Surg Venous Lymphat Disord***8**, 919-929, doi:10.1016/j.jvsv.2020.01.010 (2020).
 18. Prabhakaran, K., Gogna, S., Lombardo, G. & Latifi, R. Venous Thromboembolism in Geriatric Trauma Patients-Risk Factors and Associated Outcomes. *J Surg Res***254**, 327-333, doi:10.1016/j.jss.2020.05.008 (2020).
 19. Ruskin, K. J. Deep vein thrombosis and venous thromboembolism in trauma. *Curr Opin Anaesthesio***31**, 215-218, doi:10.1097/ACO.0000000000000567 (2018).
 20. Meizoso, J. P. *et al.* A simplified stratification system for venous thromboembolism risk in severely injured trauma patients. *J Surg Res***207**, 138-144, doi:10.1016/j.jss.2016.08.072 (2017).
 21. Park, M. S. *et al.* Risk factors for venous thromboembolism after acute trauma: A population-based case-cohort study. *Thromb Res***144**, 40-45, doi:10.1016/j.thromres.2016.03.026 (2016).
 22. Geerts, W. H., Code, K., Jay, R. M. & Chen, E. A prospective study of venous thromboembolism after major trauma. *N Engl J Med***331**, 1601–1606 (1994).
 23. Moore, H. B. *et al.* Acute Fibrinolysis Shutdown after Injury Occurs Frequently and Increases Mortality: A Multicenter Evaluation of 2,540 Severely Injured Patients. *J Am Coll Surg***222**, 347-355, doi:10.1016/j.jamcollsurg.2016.01.006 (2016).
 24. Engelman, D. T., Gabram, S. G., Allen, L., Ens, G. E. & Jacobs, L. M. Hypercoagulability following multiple trauma. *World J Surg***20**, 5-10, doi:10.1007/s002689900001 (1996).
 25. McCully, B. H. *et al.* Onset of Coagulation Function Recovery Is Delayed in Severely Injured Trauma Patients with Venous Thromboembolism. *J Am Coll Surg***225**, 42-51, doi:10.1016/j.jamcollsurg.2017.03.001 (2017).
 26. Torres, C. & Haut, E. R. Prevention, diagnosis, and management of venous thromboembolism in the critically ill surgical and trauma patient. *Curr Opin Crit Care***26**, 640–647, doi:10.1097/MCC.0000000000000771 (2020).
 27. Hamada, S. R. *et al.* High level of venous thromboembolism in critically ill trauma patients despite early and well-driven thromboprophylaxis protocol. *Ann Intensive Care***7**, 97, doi:10.1186/s13613-017-0315-0 (2017).
 28. Jacobs, B. N. *et al.* Unfractionated heparin versus low-molecular-weight heparin for venous thromboembolism prophylaxis in trauma. *J Trauma Acute Care Surg***83**, 151-158, doi:10.1097/TA.0000000000001494 (2017).

29. Yhim, H. Y. *et al.* Incidence of venous thromboembolism following major surgery in Korea: from the Health Insurance Review and Assessment Service database. *J Thromb Haemost***12**, 1035-1043, doi:10.1111/jth.12611 (2014).
30. Rogers, S. O., Jr. *et al.* Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the patient safety in surgery study. *J Am Coll Surg***204**, 1211-1221, doi:10.1016/j.jamcollsurg.2007.02.072 (2007).
31. Vachirasrisirikul, S. & Laohapensang, K. Incidence and Risk Factors of Venous Thromboembolism Following Major Abdominal Surgery. *J Med Assoc Tha***99**, 665-674 (2016).
32. Xu, Y., Zhao, J. & Chen, Y. Prevention of venous thromboembolism in patients undergoing major orthopedic surgery in China: a qualitative study of patients' perceptions. *J Orthop Surg Res***13**, 98, doi:10.1186/s13018-018-0813-2 (2018).
33. Tian, B. *et al.* A novel risk assessment model for venous thromboembolism after major thoracic surgery: a Chinese single-center study. *J Thorac Dis***11**, 1903-1910, doi:10.21037/jtd.2019.05.11 (2019).
34. Alberts, B. D. *et al.* Venous thromboembolism after major urologic oncology surgery: a focus on the incidence and timing of thromboembolic events after 27,455 operations. *Urology***84**, 799-806, doi:10.1016/j.urology.2014.05.055 (2014).
35. Trinh, V. Q. *et al.* Venous thromboembolism after major cancer surgery: temporal trends and patterns of care. *JAMA Surg***149**, 43-49, doi:10.1001/jamasurg.2013.3172 (2014).
36. Nakano, F. *et al.* Incidence and risk factor of deep venous thrombosis in patients undergoing craniotomy for brain tumors: A Japanese single-center, retrospective study. *Thromb Res***165**, 95-100, doi:10.1016/j.thromres.2018.03.016 (2018).
37. Basnet, S., Dhital, R., Tharu, B., Poudel, D. R. & Donato, A. Yearly trend of acute venous thromboembolism in patients admitted with heart failure in the United States. *J Community Hosp Intern Med Perspect***9**, 287-289, doi:10.1080/20009666.2019.1634408 (2019).
38. Wilson, T. J. *et al.* Risk factors associated with peripherally inserted central venous catheter-related large vein thrombosis in neurological intensive care patients. *Intensive Care Med***38**, 272-278, doi:10.1007/s00134-011-2418-7 (2012).
39. G.Y.H, L. & C.R, G. Does Heart Failure Confer A Hypercoagulable State? Virchow's Triad Revisited. *Journal of the American College of Cardiology***33**, 1424-1426, doi:10.1016/S0735-1097(99)00033-9 (1999).
40. Alikhan, R. & Spyropoulos, A. C. Epidemiology of venous thromboembolism in cardiorespiratory and infectious disease. *Am J Med***121**, 935-942, doi:10.1016/j.amjmed.2008.05.045 (2008).
41. Fanola, C. L. *et al.* Incident Heart Failure and Long-Term Risk for Venous Thromboembolism. *J Am Coll Cardio***75**, 148-158, doi:10.1016/j.jacc.2019.10.058 (2020).
42. Kaplan, D. *et al.* VTE Incidence and Risk Factors in Patients With Severe Sepsis and Septic Shock. *Chest***148**, 1224-1230, doi:10.1378/chest.15-0287 (2015).

43. Leung, A., Heal, C., Perera, M. & Pretorius, C. A systematic review of patient-related risk factors for catheter-related thrombosis. *J Thromb Thrombolysis***40**, 363-373, doi:10.1007/s11239-015-1175-9 (2015).

Tables

Table 1. Baseline Characteristics of the Study Patients. (More data in the supplementary file).

Variable	Overall patient population (n=2114)	NO symptomatic CRVT (n=1905)	symptomatic CRVT (n=209)	P value
Male, No. (%)	1423 (67.3)	1278 (67.1)	145 (69.4)	0.503*
Age, median (IQR), d	62 (50-74)	63 (50-73)	67 (53-79)	0.000#
BMI (kg/m ²), median (IQR), d	22 (20-24)	22 (20-24)	24 (21.8-25)	0.000#
APACHEII score, median (IQR), d	25 (21-31)	26 (21-31)	28 (23-32)	0.001#
Comorbidities				
Hypertension, No. (%)	867 (41.0)	772 (40.5)	95 (45.5)	0.169*
Diabetes, No. (%)	464 (21.9)	420 (22.0)	44 (21.1)	0.742*
Malignant tumor, No. (%)	205 (9.7)	184 (9.7)	21 (10.2)	0.857*
COPD, No. (%)	494 (23.4)	444 (23.3)	50 (23.9)	0.842*
Medical history				
Drinking, No. (%)	430 (20.3)	394 (20.7)	36 (17.2)	0.238*
Smoking, No. (%)	705 (33.3)	645 (33.9)	60 (28.7)	0.134*
ICU Length of stay, median (IQR), d	8 (5-17)	8 (5-17)	16 (7-27)	0.000#
Endotracheal intubation time, median (IQR), d	6 (3-14)	6 (3-14)	10 (4-22.5)	0.000#
CVC indwelling time, median (IQR), d	10 (6-14)	10 (6-14)	14 (11-20)	0.000#
anticoagulant contraindication, No. (%)	620 (29.3)	541 (28.4)	79 (37.8)	0.005*
anticoagulant therapy, No. (%)	716 (33.9)	659 (34.6)	57 (27.3)	0.034*

*independent-sample *t*-test, #Mann-Whitney *U* test. COPD, Chronic obstructive pulmonary disease; BMI, Body mass index; APACHEII score, Acute physiology and chronic health evaluation II score; CVC, Central venous catheters; ICU, Intensive care unit.

Table 2Univariate logistic regression analysis (More data in the supplementary file).

Variable	NO symptomatic CRVT n=1905	Symptomatic CRVT n=209	OR	95% CI	P value
Respiratory failure, No. (%)	358(18.8)	28(13.4)	0.668	0.442-1.012	0.057
Sepsis, No. (%)	345(18.1)	29(13.9)	0.729	0.484-1.097	0.129
Heart failure, No. (%)	290(15.2)	47(22.5)	1.414	1.141-2.288	0.007
Major surgery, No. (%)	214(11.2)	41(19.6)	1.928	1.332-2.791	0.001
Trauma, No. (%)	215(11.3)	35(16.7)	1.581	1.071-2.335	0.021
Low blood volume shock, No. (%)	127(6.7)	15(7.2)	1.082	0.621-1.886	0.780
Renal failure, No. (%)	96(5.0)	6(2.9)	0.557	0.241-1.287	0.171
Cerebrovascular disease, No. (%)	82(4.3)	11(5.3)	1.235	0.647-2.357	0.522
Severe acute pancreatitis, No. (%)	86(4.5)	4(1.9)	0.413	0.150-1.136	0.087
Liver function failure, No. (%)	39(2.0)	6(2.9)	1.616	0.592-3.381	0.436
Intestinal obstruction, No. (%)	34(1.8)	6(2.9)	1.626	0.675-3.921	0.279

CRVT, Catheter-related venous thrombosis; OR, Odds ratio; CI, Confidence interval.

Table 3Multivariate logistic regression analysis. OR, Odds ratio; CI, Confidence interval.

Variable	OR	95% CI	P Value
Trauma	2.046	1.325-3.160	0.001
Major surgery	2.457	1.641-3.679	0.000
Heart failure	2.087	1.401-3.111	0.000
Respiratory failure	0.913	0.583-1.428	0.690
Severe acute pancreatitis	0.581	0.207-1.632	0.303

Figures

Figure 1

Patient Flowchart

Figure 2

The cumulative incidence of symptomatic CRVT

Total=2114

Figure 3

The distribution of the primary diseases of patients admitted to the SICU

ROC of symptomatic CRVT derivation of the model

Figure 4

The AUROC for the predictive model