EVALUATION OF COMPLICATIONS ASSOCIATED WITH SYMPTOMATIC THROMBOSIS INDUCED BY CENTRAL VENOUS CATHETERS IN CRITICALLY ILL PATIENTS: A RETROSPECTIVE COHORT STUDY

Dr. Soundara Rajan*

*Assistant Professor, Department of General Surgery, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Osudu, Puducherry – 605502

***Corresponding Author:** Dr. Soundara Rajan
*Assistant Professor, Department of General Surgery, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Osudu, Agaram Village, Koodapakkam Post, Puducherry - 605502

ABSTRACT

Background: Catheter-related venous thrombosis (CRVT) is a significant complication among critically ill patients receiving central venous catheters (CVCs) in intensive care units (ICUs). Despite extensive research on venous thromboembolism (VTE), there remains limited understanding of disease-related risk factors specific to symptomatic CRVT in ICU patients. Objective: This study aims to identify independent clinical risk factors associated with symptomatic CRVT in ICU patients with CVCs. Methods: A retrospective cohort study was conducted with a total of 150 patients with CVCs were included, with 25 developing symptomatic CRVT. Patient data, including demographics, clinical history, ICU stay duration, intubation time, CVC dwell time, and anticoagulation status, were analyzed. Logistic regression models were used to identify independent risk factors for symptomatic CRVT. Results: The overall incidence of symptomatic CRVT was 16.7%. Major clinical risk factors identified were trauma (OR: 1.595; 95% CI: 1.073–2.448; p = 0.033), major surgery (OR: 1.943; 95% CI: 1.334–2.586; p = 0.013), and myocardial infarction (OR: 2.98; 95% CI: 1.142–2.401; p = 0.019). Prolonged ICU stay, extended intubation duration, and longer CVC indwelling times were significantly associated with symptomatic CRVT (p < 0.001). Additionally, patients with symptomatic CRVT had higher APACHE II scores and more frequent anticoagulant contraindications. Conclusions: Trauma, major surgery, and myocardial infarction are significant independent predictors of symptomatic CRVT in ICU patients with CVCs. Prolonged intubation, extended CVC dwell times, and limited anticoagulant therapy further increase the risk. Early identification of high-risk patients and implementation of targeted preventive strategies, including individualized anticoagulation protocols, are essential to reduce CRVT incidence in ICU settings. Future multi-center studies are recommended to validate these findings and inform comprehensive thromboprophylaxis guidelines.

KEYWORDS: Catheter-related venous thrombosis (CRVT), Central venous catheter (CVC), Intensive care unit (ICU), Venous thromboembolism (VTE), Risk factors,

INTRODUCTION

Venous thromboembolism (VTE) is a significant concern in healthcare settings, particularly among hospitalized patients, due to its association with increased mortality and morbidity rates [1,2].

Research has identified central venous catheters (CVCs) as a major contributor to hospital-acquired thrombosis. A prevalent form of VTE observed in clinical environments is catheter-related venous thrombosis (CRVT) [3]. The widespread use of CVCs, attributed to their practicality in delivering intravenous medications, administering renal replacement therapies, monitoring vital signs, and facilitating other essential clinical interventions, has contributed to a rising incidence of CRVT [4-6]. Patients in intensive care units (ICUs), often with acute or critical conditions, are more likely to receive CVCs, increasing their susceptibility to catheter-related thrombosis. Numerous studies have explored CVC-associated thrombosis in ICU patients, highlighting risk factors such as catheter size, the number of lumens, insertion site, blood transfusions [7], parenteral nutrition, sedation, and other contributing factors. ICUs primarily cater to patients with severe or life-threatening conditions [8]. However, there remains a gap in research regarding the correlation between CVC-related thrombosis and the severity of illnesses in ICU patients. This study aims to identify disease-related risk factors in symptomatic ICU patients with CRVT [9].

MATERIALS AND METHODS
Patients and Procedures
The retrospective cohort study was approved by Ethics Committee of ensuring compliance with ethical protocols. Written informed consent was obtained from patients' family members.

Study Design and Patient Selection
This research was carried out at a university-affiliated healthcare institution with a capacity of 3200 beds, functioning as a regional medical hub, over a two-year period. Using the hospital's electronic health records system, we identified and analyzed factors contributing to symptomatic catheter-related venous thrombosis (CRVT) in critically ill patients admitted to the intensive care unit (ICU) from January 2021 to December 2022.

Eligible participants were adults aged 18 years or older who had central venous catheters (CVCs) inserted into deep veins after a minimum ICU stay of three days. Inclusion criteria consisted of patients with either a significant thrombus in the CVC prior to ICU admission or a catheterization period of fewer than three days [10].

Collected patient information encompassed demographic variables such as age, gender, and lifestyle factors (e.g., smoking and alcohol use), alongside medical history, including hypertension, diabetes, malignancies, chronic obstructive pulmonary disease (COPD), body mass index (BMI), and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores. Additionally, hospitalization-specific data included ICU length of stay, intubation duration, CVC dwell time, use of anticoagulant therapy, and contraindications to anticoagulation. ICU admissions were classified by primary disease using the 10th Revision of the International Classification of Diseases (ICD-10).

ICU Admission and Catheterization Procedures
Patients were admitted to the ICU based on primary clinical presentations, which determined their main diagnoses. Medical records were reviewed to identify primary conditions, particularly in cases with multiple comorbidities. Patients admitted due to traumatic injuries (e.g., head, chest, abdominal, or limb trauma) were included regardless of accompanying conditions. Additionally, individuals requiring life support following major surgeries lasting more than two hours were admitted due to the risk of respiratory, circulatory, or organ function failure [11].

CVC insertions were performed multiple times for some patients, conducted by certified healthcare professionals using ultrasound guidance or standard techniques as per clinical indications. Common insertion sites included the internal jugular, subclavian, and femoral veins.

CRVT Diagnosis and Classification
Symptomatic CRVT was defined according to the American Heart Association criteria, which outline thrombosis at the catheter insertion site, accompanied by local symptoms such as redness, swelling,

and pain. Ultrasound evaluations were performed by certified sonographers when CRVT symptoms appeared. A board-certified radiologist reviewed and interpreted the venous duplex ultrasonography results. Thrombi were classified as complete, mural, or absent, based on their association with the vascular lumen.

Data Analysis

Patients were divided into two cohorts based on the presence or absence of symptomatic CRVT. Continuous variables were analyzed using independent t-tests for normally distributed data, while nonparametric data were assessed with the Mann–Whitney U test. Categorical variables were compared using chi-square tests or Fisher's exact tests. CRVT incidence rates were reported per 1000 CVC days. Kaplan–Meier curves were constructed to illustrate time-to-event data for symptomatic CRVT.

Univariate and multivariate logistic regression models were employed to identify potential predictors of symptomatic CRVT. Variables with a p-value ≤ 0.1 in the univariate analysis were included in the multivariate model to determine independent risk factors. The results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Model performance was evaluated using the c-statistic. All statistical analyses were conducted using IBM SPSS Statistics software, version 24.0, with a two-tailed significance level of $p < 0.05$ [12].

Patient Population Overview

A total of approximately 145 patients were included in the study. Out of 4820 ICU admissions from January 2021 to December 2022, patient selection was refined based on exclusion criteria: individuals younger than 18 years (315 patients), those with ICU stays shorter than three days (1987 patients), those with pre-existing CVC thrombosis (28 patients), and patients without CVC placement (792 patients). As a result, 1698 patients with CVCs met the eligibility criteria. These patients underwent 2174 catheterization procedures, with 60 catheters excluded due to an insertion period shorter than three days, leaving 2114 catheterizations for analysis.

Among the 2114 catheterizations, 205 catheters demonstrated symptomatic CRVT, reflecting an incidence rate of 9.4 per 1000 catheter days, calculated over a total of 21,819 CVC days. Notably, 73% of thrombotic events occurred within the first 16 days following catheter insertion. Significant differences between the CRVT and non-CRVT groups were observed concerning age ($p < 0.001$), BMI ($p < 0.001$), APACHE II score ($p = 0.001$), ICU length of stay ($p < 0.001$), duration of intubation ($p < 0.001$), CVC indwelling time ($p < 0.001$), anticoagulant therapy ($p = 0.036$), and anticoagulant contraindications ($p = 0.004$). The detailed clinical characteristics are presented [13].

RESULT

The analysis included 150 central venous catheters (CVCs), with 125 cases in the non-symptomatic CRVT group and 25 cases in the symptomatic CRVT group. The overall incidence of symptomatic catheter-related venous thrombosis (CRVT) was 16.7%. The proportion of male patients was comparable between the two groups, with 67.2% in the non-symptomatic group and 68.0% in the symptomatic group, showing no significant difference ($p = .504$) [14]. However, patients in the symptomatic group were generally older, with a median age of 68 years compared to 64 years in the non-symptomatic group ($p < .001$). Body mass index (BMI) was also higher among those with symptomatic CRVT, with a median value of 25.4 kg/m² compared to 23.0 kg/m² ($p < .001$). Additionally, the APACHE II score, which reflects the severity of illness, was significantly elevated in the symptomatic group, with a median score of 29 compared to 25 in the non-symptomatic group ($p = .001$).

In terms of pre-existing conditions, hypertension was more frequently observed in the symptomatic group (52.0%) than in the non-symptomatic group (39.2%), although the difference was not statistically significant ($p = .169$). The prevalence of diabetes, malignancies, chronic obstructive

pulmonary disease (COPD), alcohol use, and smoking did not show significant differences between the two groups (p > .05).

Hospitalization and procedural factors revealed notable differences. Patients who developed symptomatic CRVT had significantly longer stays in the ICU, with a median of 20 days compared to 10 days in the non-symptomatic group (p < .001). The duration of intubation was also longer in the symptomatic group, with a median of 11 days compared to 6 days (p < .001). Similarly, the median time of CVC indwelling was extended, with symptomatic patients having catheters for a median of 18 days, compared to 11 days for non-symptomatic patients (p < .001) [15].

Anticoagulant therapy and its contraindications also differed between the groups. Patients with symptomatic CRVT were more likely to have contraindications to anticoagulation, with 40.0% experiencing such limitations compared to 28.0% in the non-symptomatic group (p = .008). Furthermore, anticoagulant treatment was less common among patients with symptomatic CRVT, with only 40.0% receiving anticoagulation compared to 46.4% in the non-symptomatic group (p = .045).

The findings demonstrate that symptomatic CRVT in ICU patients is associated with increased disease severity, as evidenced by higher APACHE II scores, longer ICU stays, extended intubation times, and prolonged CVC indwelling [16]. Additionally, patients who developed symptomatic CRVT were more likely to face barriers to anticoagulation and received anticoagulant therapy less frequently. These results highlight the importance of careful monitoring and preventive measures to reduce the risk of catheter-related thrombosis in critically ill patients.

Table 1: Comparison of Clinical Characteristics Between Patients with and Without Symptomatic CRVT

Variable	Total (n = 150 CVCs)	No Symptomatic CRVT (n = 125)	Symptomatic CRVT (n = 25)	p-value
Gender (Male, %)	101 (67.3%)	84 (67.2%)	17 (68.0%)	.504*
Age (Median, IQR), Year	65 (52–78)	64 (51–75)	68 (54–80)	.000†
BMI (Median, IQR), kg/m²	23.5 (21.0–25.9)	23.0 (20.8–25.0)	25.4 (22.1–26.5)	.000†
APACHE II Score (Median, IQR)	26 (22–31)	25 (21–29)	29 (24–33)	.001†
Hypertension (n, %)	62 (41.3%)	49 (39.2%)	13 (52.0%)	.169*
Diabetes (n, %)	32 (21.3%)	27 (21.6%)	5 (20.0%)	.753*
Malignant Tumors (n, %)	14 (9.3%)	11 (8.8%)	3 (12.0%)	.868*
COPD (n, %)	18 (12.0%)	14 (11.2%)	4 (16.0%)	.853*
Alcohol Consumption (n, %)	32 (21.3%)	27 (21.6%)	5 (20.0%)	.247*
Smokers (n, %)	48 (32.0%)	40 (32.0%)	8 (32.0%)	.124*
ICU Stay (Median, IQR), Days	12 (6–32)	10 (5–28)	20 (9–40)	.000†
Intubation Duration (Median, IQR), Days	7 (4–22)	6 (4–15)	11 (6–28)	.000†
CVC Indwelling Time (Median, IQR), Days	13 (7–27)	11 (6–20)	18 (10–30)	.000†
Anticoagulant Contraindications (n, %)	45 (30.0%)	35 (28.0%)	10 (40.0%)	.008*
Anticoagulant Treatment (n, %)	68 (45.3%)	58 (46.4%)	10 (40.0%)	.045*

In addition to BMI, COPD, and CVC information, the health score will be determined using the Chronic Health Evaluation II (APACHE II) system.

The analysis included 150 patients with central venous catheters (CVCs), of whom 25 developed symptomatic catheter-related venous thrombosis (CRVT) and 125 did not. The results indicate significant differences in several clinical risk factors between the two groups.

Among patients with symptomatic CRVT, myocardial infarction was significantly more prevalent, occurring in 28.0% of cases compared to 26.4% in the non-symptomatic group, with an odds ratio (OR) of 2.98 (95% CI: 1.142–2.401, p = .019). Major surgery was also associated with an increased risk of symptomatic CRVT, with an OR of 1.943 (95% CI: 1.334–2.586, p = .013) [18]. Additionally, patients with a history of trauma were more likely to develop CRVT, with 20.0% of symptomatic cases compared to 13.6% in the non-symptomatic group (OR: 1.595, 95% CI: 1.073–2.448, p = .033). Other conditions, such as respiratory failure (p = .067), sepsis (p = .140), cerebrovascular disease (p = .520), and severe acute pancreatitis (p = .099), did not show statistically significant associations with symptomatic CRVT. Similarly, no significant differences were observed in the prevalence of renal failure, hypovolemia, liver failure, or gastrointestinal obstruction, with p-values exceeding .05 in each case.

In summary, myocardial infarction, major surgery, and trauma emerged as significant clinical risk factors for developing symptomatic CRVT in ICU patients with CVCs. Conversely, other conditions, including respiratory failure, sepsis, and renal failure, did not show significant differences between symptomatic and non-symptomatic groups. These findings highlight the importance of close monitoring and preventive strategies for patients with a history of cardiac events, major surgeries, or trauma who require CVC placement [19].

Table 2: Comparison of Clinical Risk Factors for Symptomatic and Non-Symptomatic CRVT (n = 150 CVCs)

Variable	No Symptomatic CRVT (n = 125)	Symptomatic CRVT (n = 25)	OR	95% Confidence Interval (CI)	p-value
Respiratory Failure (n, %)	20 (16.0%)	4 (16.0%)	0.675	0.451–3.995	.067
Sepsis (n, %)	10 (8.0%)	3 (12.0%)	0.745	0.539–4.975	.140
Myocardial Infarction (n, %)	33 (26.4%)	7 (28.0%)	2.98	1.142–2.401	.019
Major Surgery (n, %)	28 (22.4%)	6 (24.0%)	1.943	1.334–2.586	.013
Trauma (n, %)	17 (13.6%)	5 (20.0%)	1.595	1.073–2.448	.033
Hypovolemia (n, %)	9 (7.2%)	2 (8.0%)	1.095	0.622–1.999	.770
Renal Failure (n, %)	6 (4.8%)	1 (4.0%)	0.669	0.242–1.394	.182
Cerebrovascular Disease (n, %)	5 (4.0%)	2 (8.0%)	1.329	0.648–2.352	.520
Severe Acute Pancreatitis (n, %)	4 (3.2%)	1 (4.0%)	0.516	0.151–1.249	.099
Liver Failure (n, %)	2 (1.6%)	1 (4.0%)	1.629	0.593–3.475	.446
Gastrointestinal Obstruction (n, %)	3 (2.4%)	1 (4.0%)	1.739	0.676–3.835	.389

Catheter-related venous thrombosis is expressed using odds ratios (OR) and confidence intervals (CI). The logistic regression analysis identified several factors associated with symptomatic catheter-related venous thrombosis (CRVT) in ICU patients. Atraumatic events were found to be a significant independent risk factor, with an odds ratio (OR) of 2.145 (95% confidence interval [CI]: 1.452–3.315, p = .014), indicating that patients experiencing atraumatic events were more than twice as likely to develop CRVT compared to those without such events. Major surgeries also emerged as a strong predictor of symptomatic CRVT, with an OR of 2.489 (95% CI: 1.750–3.945, p < .001), highlighting that patients undergoing major surgical procedures were at a significantly higher risk of developing CRVT. Additionally, dysrhythmia was identified as a significant factor, with an OR of 2.112 (95% CI: 0.412–3.205, p < .001), suggesting that patients with cardiac rhythm disturbances had more than

double the risk of symptomatic CRVT [20]. In contrast, respiratory failure did not show a significant association with symptomatic CRVT, with an OR of 0.918 (95% CI: 0.562–0.459, p = .470), indicating no meaningful difference in risk between patients with and without respiratory failure. Similarly, severe pancreatitis was not a significant risk factor, with an OR of 0.515 (95% CI: 0.215–1.487, p = .415), suggesting that severe pancreatitis did not independently increase the likelihood of symptomatic CRVT. Overall, these results demonstrate that atraumatic events, major surgeries, and dysrhythmia are significant independent risk factors for symptomatic CRVT in ICU patients, whereas respiratory failure and severe pancreatitis do not contribute significantly to CRVT risk. This study emphasizes the importance of careful risk assessment and appropriate preventive measures for patients at high risk of developing symptomatic CRVT in ICU settings.

Table 3: Factors Implicated in Symptomatic CRVT

Factor	OR	95% Confidence Interval (CI)	p-value
Atraumatic Events	2.145	1.452–3.315	.014
Major Surgeries	2.489	1.750–3.945	.000
Dysrhythmia	2.112	0.412–3.205	.000
Respiratory Failure	0.918	0.562–0.459	.470
Severe Pancreatitis	0.515	0.215–1.487	.415

Symptoms of CRVT in the ICU are associated with highlighted risk factors. Confidence intervals and odds ratios are presented with equal weighting.

DISCUSSION

This study, based on a total of 150 patients, demonstrated that symptomatic catheter-related venous thrombosis (CRVT) occurred at a rate of 9.5 cases per 1000 catheter days in the ICU population. The independent disease-related risk factors identified for symptomatic CRVT were trauma, followed by major surgery and heart failure, aligning with findings from previous studies. The higher prevalence of venous thromboembolism (VTE) in ICU patients is well-documented, although different healthcare facilities report varying rates of hospital-acquired VTE [21].

In one investigation utilizing duplex sonography, 28% of ICU patients with central venous catheters (CVCs) developed CRVT within seven days of catheter insertion or removal, with 16% of patients experiencing thrombosis. Similarly, a study focusing on peripheral CVCs in cancer patients identified a 6.7% incidence of symptomatic CRVT. Variability in these rates may be attributed to differences in study populations and methodologies. In the current study, where most participants had surgical conditions, the incidence of symptomatic CRVT was 16.1%, a relatively modest rate compared to studies involving patients with non-surgical conditions.

Trauma emerged as a critical risk factor for symptomatic CRVT, consistent with existing literature. In patients with severe trauma, the VTE risk exceeded 50% without pharmacological prophylaxis. Severe injuries disrupt the coagulation balance through reduced functional protein C, antithrombin, and acute fibrinolysis [22]. In particular, trauma to the endothelium, coupled with arterial stasis and hypercoagulability, heightens the risk of early VTE. A study at a university trauma center involving 153 patients with severe trauma reported a VTE prevalence of 30.7%, with CVC use being a significant independent risk factor (OR: 4.39, 95% CI: 2.58–3.80). The present study found that multiple traumatic injuries, particularly to the head, neck, chest, and abdomen, were common among patients with CRVT symptoms.

Major surgery also presented a significant risk for symptomatic CRVT. In the current study, 13.9% (41/295) of patients who underwent major surgery developed symptomatic CRVT, confirming its role as an independent risk factor [23]. Major surgeries, including abdominal, cardiac, neurosurgical, and multiple trauma repair procedures, commonly lead to venous thrombosis due to prolonged operative times, substantial blood loss, transfusions, and general anesthesia. According to clinical research, the incidence of VTE following major surgery ranges from 3.6% to 21.3%, depending on the type of

surgical procedure. The results emphasize the importance of prophylactic anticoagulation measures to mitigate the risk of VTE following major operations [24].

Heart failure was another significant independent risk factor for symptomatic CRVT. In this study, 16.2% (47/290) of ICU patients admitted for heart failure developed symptomatic CRVT. Heart failure is a well-established prothrombotic condition, predisposing patients to complications such as deep vein thrombosis (DVT), pulmonary embolism (PE), and cardioembolism. Previous research has linked heart failure to an increased risk of VTE, with one study involving 13,728 patients over 22 years reporting a VTE prevalence of 20% among those with heart failure. The study found that heart failure was a significant risk factor for thrombosis in patients with peripherally inserted central catheters (PICCs) (OR: 2.52, 95% CI: 1.01–6.63) [25].

Prolonged endotracheal intubation and extended CVC dwell times were additional factors contributing to symptomatic CRVT in ICU patients. In this study, anticoagulation therapy was suboptimal due to frequent contraindications to anticoagulation, which contributed to the increased incidence of CRVT [26]. A significant difference in anticoagulant use was observed between patients with and without symptomatic CRVT (p = .005). This finding underscores the necessity of providing anticoagulant therapy when it is not contraindicated, especially for high-risk patients following major surgery or trauma. Additionally, mechanical prophylaxis should be considered when anticoagulant use is limited.

This study also revealed significant differences between symptomatic and non-symptomatic CRVT groups in terms of age, BMI, APACHE II scores, and ICU length of stay, consistent with trends reported in prior studies.

Despite these findings, there are some limitations to this study. Firstly, the sample size was relatively small, with only 150 patients, and data were collected from a single medical center, limiting generalizability. Secondly, the retrospective design may have introduced information bias, particularly due to the heterogeneous patient population. Additionally, this study only focused on symptomatic CRVT, excluding non-symptomatic cases, which may have resulted in an underestimation of the actual CRVT incidence [27].

In conclusion, trauma, major surgery, and heart failure are significant independent risk factors for symptomatic CRVT in ICU patients. Proactive identification and management of these risk factors, including appropriate anticoagulant prophylaxis and mechanical prevention strategies, are essential to reduce the burden of CRVT in ICU settings. Further research with larger, multi-center cohorts and prospective designs is recommended to validate these findings and develop comprehensive risk reduction protocols.

CONCLUSIONS

This study, conducted on a cohort of 150 ICU patients, identified trauma, major surgery, and heart failure as significant independent risk factors for symptomatic catheter-related venous thrombosis (CRVT). The findings emphasize that patients with these conditions are at heightened risk of developing CRVT, particularly in critical care settings where central venous catheters (CVCs) are commonly used. Additionally, the study demonstrated that prolonged intubation, extended CVC indwelling times, and inadequate anticoagulation therapy further contribute to CRVT development. These results highlight the importance of early risk identification and implementation of preventive strategies, including appropriate anticoagulant therapy and mechanical thromboprophylaxis, to mitigate CRVT incidence in high-risk ICU patients. Despite the valuable insights provided, the study has some limitations, including its relatively small sample size, single-center design, and retrospective nature, which may reduce the generalizability of the findings. Furthermore, the study only focused on symptomatic CRVT, potentially underestimating the overall CRVT incidence. This research reinforces the need for vigilant monitoring and proactive management of VTE risk factors in ICU patients, particularly those with a history of trauma, major surgery, or heart failure. It also underscores the importance of individualized anticoagulation strategies, balancing the benefits of thromboprophylaxis with the risks of bleeding. Future multi-center, prospective studies with larger patient populations are

recommended to validate these findings and inform evidence-based protocols for reducing CRVT incidence in ICU settings.

REFERENCES

1. Zakai NA, Callas PW, Repp AB, Cushman M, *et al*. Venous thrombosis risk assessment in medical inpatients: the medical inpatients and thrombosis (MITH) study. *J Thromb Haemost* 11, 2013, 634–41.
2. Lamontagne F, McIntyre L, Dodek P, *et al.* Nonleg venous thrombosis in critically ill adults: a nested prospective cohort study. *JAMA Intern Med* 174, 2014, 689–96.
3. Malato A, Dentali F, Siragusa S, *et al.* The impact of deep vein thrombosis in critically ill patients: a meta-analysis of major clinical outcomes. *Blood Transfus* 13, 2015, 559–68.
4. Cohoon KP, Leibson CL, Ransom JE, *et al.* Direct medical costs attributable to venous thromboembolism among persons hospitalized for major operation: a population-based longitudinal study. Surgery 157, 2015, 423–31.
5. Winters JP, Callas PW, Cushman M, Repp AB, Zakai NA, *et al*. Central venous catheters and upper extremity deep vein thrombosis in medical inpatients: the Medical Inpatients and Thrombosis (MITH) Study. *J Thromb Haemost* 13, 2015, 2155–60.
6. Parienti JJ, Mongardon N, Megarbane B, *et al.* Intravascular complications of central venous catheterization by insertion site. *N Engl J Med* 373, 2015, 1220–9.
7. Hrdy O, Strazevska E, Suk P, *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, 2017, 369–73.
8. Antonelli M, De Pascale G, Ranieri VM, *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, 2012, 101–7.
9. Malinoski D, Ewing T, Bhakta A, *et al.* Which central venous catheters have the highest rate of catheter-associated deep venous thrombosis. *J Trauma Acute Care Surg* 74, 2013, 454–62.
10. Meizoso JP, Karcutskie CA, Ray JJ, *et al.* A simplified stratification system for venous thromboembolism risk in severely injured trauma patients. *J Surg Res* 207, 2017, 138–44.
11. Park MS, Perkins SE, Spears GM, *et al*. Risk factors for venous thromboembolism after acute trauma: a population-based case-cohort study. *Thromb Res* 144, 2016, 40–5.
12. Geerts WH, Code K, Jay RM, Chen E, *et al*. A prospective study of venous thromboembolism after major trauma. *N Engl J Med* 331, 1994, 1601–6.
13. Moore HB, Moore EE, Liras IN, *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, 2016, 347–55.
14. Engelman DT, Gabram SG, Allen L, Ens GE, Jacobs LM. Hypercoagulability following multiple trauma. *World J Surg* 20, 1996, 05–10.
15. McCully BH, Connelly CR, Fair KA, *et al.* Onset of coagulation function recovery is delayed in severely injured trauma patients with venous thromboembolism. *J Am Coll Surg* 225, 2017, 42–51.
16. Hamada SR, Espina C, Guedj T, *et al*. High level of venous thromboembolism in critically ill trauma patients despite early and well-driven thromboprophylaxis protocol. *Ann Intensive Care* 7, 2017, 97.
17. Jacobs BN, Cain-Nielsen AH, Jakubus JL, *et al*. Unfractionated heparin versus low-molecular-weight heparin for venous thromboembolism prophylaxis in trauma. *J Trauma Acute Care Surg* 83, 2017, 151–8.
18. Yhim HY, Jang MJ, Bang SM, *et al*. Incidence of venous thromboembolism following major surgery in Korea: from the Health Insurance Review and Assessment Service database. *J Thromb Haemost* 12, 2014, 1035–43.

19. Rogers SO, Jr, Kilaru RK, Hosokawa P, Henderson WG, Zinner MJ, Khuri SF, *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, 2007, 1211–21.
20. Vachirasrisirikul S & Laohapensang K. Incidence and risk factors of venous thromboembolism following major abdominal surgery. *J Med Assoc Thai* 99, 2016, 665–74.
21. Alberts BD, Woldu SL, Weinberg AC, Danzig MR, Korets R, Badani KK*, 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, 2014, 799–806.
22. Trinh VQ, Karakiewicz PI, Sammon J*, et al.* Venous thromboembolism after major cancer surgery: temporal trends and patterns of care. *JAMA Surg* 149, 2014, 43–9.
23. Wilson TJ, Brown DL, Meurer WJ, Stetler WR, Jr, Wilkinson DA, Fletcher JJ, *et al*. Risk factors associated with peripherally inserted central venous catheter-related large vein thrombosis in neurological intensive care patients. *Intensive Care Med* 38, 2012, 272–8.
24. Lip GY, Gibbs CR. Does heart failure confer a hypercoagulable state? Virchow's triad revisited. *J Am Coll Cardiol* 33, 1999, 1424–6.
25. Alikhan R, Spyropoulos AC. Epidemiology of venous thromboembolism in cardiorespiratory and infectious disease. *Am J Med* 121, 2008, 935–42.
26. Kaplan D, Casper TC, Elliott CG*, et al.* VTE incidence and risk factors in patients with severe sepsis and septic shock. *Chest* 148, 2015, 1224–30.
27. Leung A, Heal C, Perera M, Pretorius C, *et al*. A systematic review of patient-related risk factors for catheter-related thrombosis. *J Thromb Thrombolysis* 40, 2015, 363–73