Central venous catheter-related thrombosis in intensive care patients – incidence and risk factors: A prospective observational study

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Background. One of the complications associated with central venous catheter (CVC) placement is catheter related deep vein thrombosis (CR-DVT). However a literature search revealed little evidence of this recognised complication. The primary aim of this study was to establish the incidence rate and risk factors for the development of CR-DVT in our critically ill adult patients.
Methods. All critically ill adult patients admitted to the medical-surgical ICU with CVC inserted were included in this observational prospective study. After catheter removal we performed duplex ultrasound examination to assess the patency of the vein and establish if CR-DVT was present.
Results. A total number of 308 catheters met the inclusion criteria of which 198 were included in the statistical analysis. The CVC was inserted into a subclavian vein (SCV) in 139 (70%) cases and in an internal jugular vein (IJV) in 59 (30%) cases. The 28-day mortality rate was 14.1%. We found CR-DVT during duplex ultrasound examination in 47 (26%) of all cases. 33 (70%) of the CR-DVT were diagnosed in the IJV and 14 (30%) in the SCV. The risk factors for the development of CR-DVT we identified included cannulation of the IJV and the use of treatment dose of LMWH. The effect of CR-DVT on 28-day mortality was not statistically significant.
Conclusion. The risk factors for CR-DVT we identified were IJV as a site for CVC cannulation and the use of therapeutic anticoagulation prior to cannulation. Our recommendation would be preferential cannulation of a subclavian vein as opposed to an internal jugular vein in order to reduce the risk of CR-DVT.

Key words: central venous catheter, deep vein thrombosis, risk factors, critical care

Received: February 7, 2017; Accepted: July 12, 2017; Available online: August 24, 2017
https://doi.org/10.5507/bp.2017.034

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INTRODUCTION

Central venous catheter (CVC) insertion is an integral part of the management of critically ill patients in intensive care units (ICU). These catheters are placed for the administration of hypertonic solutions, catecholamines, nutritional solutions, insertion of temporary transvenous pacemakers, and for hemodynamic monitoring[1]. Up to 64% of critically ill patients will require CVC cannulation[2]. One of the complications related to the central venous cannulation is DVT (ref.[3]) which can lead to pulmonary embolism (ref.[4]).

However, on searching the on-line literature (MEDLINE database in last 10 years) using keywords "central venous catheter" and "deep vein thrombosis" we could find no article concerning catheter related deep vein thrombosis (CR-DVT) in adult critically ill patients in intensive care units.

There are studies in MEDLINE dated earlier but none of these is focused on critically ill adult ICU patients.

In the view of the progress and development of intensive care medicine, development of DVT prophylaxis algorithms and newer catheter material, we decided to perform a study focused on this topic. The primary aim of this study was to establish the incidence rate of CR-DVT and risk factors for the development of CR-DVT in critically ill adult patients. The secondary aim was to establish the impact of CR-DVT on the mortality rates of critically ill patients.

METHODS

This prospective, monocentric, observational study was approved by The Ethics Research Committee of Faculty Hospital Brno. Informed consent was not requested.

It was an observational study and there were no changes made to the treatment of the patients based on its findings. If signs of DVT were diagnosed we followed the guidelines for management of patients with suspected DVT (ref.[5,6]).

All patients admitted to our ICU from the 1st of November 2013 to the 1st of November 2014 were enrolled after fulfilling the inclusion criteria and in the absence of any exclusion criteria (Table 1). If there were more than one CVC inserted in a patient we enrolled each as a separate case.

We did not dictate the choice of catheter insertion site and catheter type. Local guidelines for the insertion

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exlusion criteria
Admition to ICU from the 1st of November 2013 to the 1st of November 2014	previous cannulation of analysed vessels
Age ≥ 18 years	previous thrombosis in the analysed vessels
CVC inserted ≥ 48 hours	previous trauma of the analysed vessels
Cannulation of internal jugular vein or subclavian vein	trauma of the collar bone on the site of CVC insertion
–	insertion of a vascath, pulmonary artery catheter or sheath for temporary pacing

Table 2. Risk factors of CR-DVT identified in literature.

Risk factor	Analysed in our study	Comment
Age	Yes	–
Gender	Yes	–
Cancer	Yes	–
Acquired hypercoagulable states	No	not able to diagnose in all patients
Inherited coagulation disorders	No	only few patient in several years admited
High platelet count	Yes	–
Barbiturates	No	not used on our ICU
Propofol	Yes	–
Parenteral nutrition	Yes	–
Lack of therapeutic anticoagulation	Yes	–
>10 packed red blood cell	Yes	–
Number of lumina	Yes	–
CVC material	No	all catheter made from polyuretane
Difficult insertion	No	not able to identify from documentation in all patients
Position of the CVC tip	Yes	–
Catheter related sepsis	No	not able to diagnose in all cases
Catheter-days	Yes	–

of CVC were followed. An anteroposterior chest X-ray was used to confirm the CVC position. We applied the method for CVC correct placement assessment described by Luciani[7]. Catheter tip outside of the segment 1 and 2 in the radiograph was considered as a diagnostic criterion for malposition.

The diagnosis of CR-DVT was established using duplex ultrasound imaging. The imaging was performed either immediately or up to 24 h after catheter removal. A linear probe with the frequency of 3-9MHz was used for the imaging. The diagnosis of CR-DVT was established in accordance with a procedure protocol[6,8]. The patients were examined in a supine position with a mildly abducted upper limb. Imaging of the internal jugular vein (IJV) and subclavian vein (SCV) was performed at the site of cannulation. We used the B mode in longitudinal (long axis) plane, transversal (short axis) plane and duplex imaging with compression of the evaluated vein.

The diagnosis was confirmed either directly in the B-mode or indirectly using signs of thrombosis.

The extent of the thrombosis was graded as wall changes, incomplete or complete obstruction of the vein lumen.

The ultrasound findings were recorded in designated study form. Based on the literature review we identified potential risk factors of CR-DVT (Table 2).

Standard descriptive statistics were used to summarise the data with absolute and relative frequencies for categorical variables and median plus 5-95th percentile or means plus SD. Statistical significance of differences between groups of patients was tested using Fisher's exact test for categorical data and Mann-Whitney U test for continuous data.

Logistic regression was adopted for the identification of risk factors for CR-DVT and the impact of CR-DVT on 28-days mortality. Statistical analysis was computed using SPSS 23.0.0.0 (IBM Corporation, 2015).

RESULTS

There were 795 patients admitted to our ICU during the study period. Of these patients, we enrolled 278. There were 333 CVC included from which 25 CVC were excluded using exclusion criteria (Table 3). We also had to exclude 110 catheters for impracticability to perform

Table 3. Exclusion criteria.

Criterion	Number of cases (n=25)
Previous cannulation of analysed vessels	7
Previous thrombosis in the analysed vessels	0
Previous trauma of the analysed vessels	0
Trauma of the collar bone on the site of CVC insertion	14
Insertion of a vascath, pulmonary artery catheter or sheath for temporary pacing	4

Table 4. Results of ultrasound imaging.

Ultrasound finding	Number of cases (n=198)
No signs of CR-DVT	151 (76%)
Wall changes	15 (8%)
Incomplete obstruction of vein	32 (16%)
Complete obstruction of vein	0 (0%)

an ultrasound examination. The most frequent result of pathological ultrasound imaging was incomplete obstruction of the vein (Table 4). Statistical analysis was calculated for 198 (64.3%) of CVC.

Characteristics of the study population are summarized in Table 5. Based on ultrasound examination the CR-DVT was diagnosed in 47(24%) of cases. The signs and symptoms of CR-DVT were observed in 2 cases. The risk factors for CR-DVT identified were IJV cannulation and therapeutic anticoagulation at the time of CVC insertion (Table 6). The effect of CR-DVT on 28-day mortality was not statistically significant (Table 7).

DISCUSSION

Central vein cannulation is a common procedure in the ICU setting. Deep vein thrombosis is one of the complications described during central vein cannulation[1,3].

In our study we diagnosed thrombosis following CVC extraction in 47 (24%) patients, which is in agreement with other studies concerning the topic[9,10].

Risk of CR-DVT is higher when CVC is inserted in IJV than in SCV (ref.[11-13]). We confirmed CR-DVT as the

Table 5. Characteristics of study population.

Characteristic[1]		Total (n=198)	Deep vein thrombosis: No (n=151)	Deep vein thrombosis: Yes (n=47)	P^2
Age		58.0 (20.0; 83.0)	57.0 (19.0; 82.0)	63.0 (20.0; 85.0)	0.121
Gender	Male	135 (68.2%)	107 (70.9%)	28 (59.6%)	0.155
	Female	63 (31.8%)	44 (29.1%)	19 (40.4%)	
Infection		52 (26.3%)	35 (23.2%)	17 (36.2%)	0.089
Cancer		25 (12.6%)	19 (12.6%)	6 (12.8%)	0.999
Platelet count		200.0 (77.0; 491.0)	208.0 (77.0; 454.0)	166.5 (78.0; 580.0)	0.328
Prophylactic anticoagulation	LMWH	71 (35.9%)	53 (35.1%)	18 (38.3%)	0.261
	Other	1 (0.5%)	0 (0.0%)	1 (2.1%)	
	No	126 (63.6%)	98 (64.9%)	28 (59.6%)	
Therapeutic anticoagulation	LMWH	1 (0.5%)	0 (0.0%)	1 (2.1%)	0.029
	Other	5 (2.5 %)	2 (1.3 %)	3 (6.4%)	
	No	192 (97.0 %)	149 (98.7 %)	43 (91.5 %)	
Site of insertion	Internal jugular vein	59 (29.8%)	26 (17.2%)	33 (70.2%)	< 0.001
	Subclavian vein	139 (70.2%)	125 (82.8%)	14 (29.8%)	
Number of CVC lumens	2	2 (1.0%)	1 (0.7%)	1 (2.1%)	0.324
	3	191 (96.5%)	145 (96.0%)	46 (97.9%)	
	4	5 (2.5%)	5 (3.3%)	0 (0.0%)	
Medication	propofol	122 (62.9%)	92 (62.2%)	30 (65.2%)	0.731
	parenteral nutriton	24 (12.1%)	17 (11.3%)	7 (14.9%)	0.609
	Transfusion therapy	69 (34.8%)	52 (34.4%)	17 (36.2%)	0.862
Catheter-days		9.0 (4.0; 16.0)	9.0 (4.0; 16.0)	9.0 (4.0; 18.0)	0.587
Catheter position	Correct	155 (78.3%)	121 (80.1%)	34 (72.3%)	0.311
	Malposition	43 (21.7%)	30 (19.9%)	13 (27.7%)	

[1] absolute and relative frequency for categorical data, median with 5-95 percentile for continuous data
[2] Fisher's exact test for categorical data analysis. Mann-Whitney U test for continuous data.

Table 6. Risk factors for catheter related deep vein thrombosis.

Charakteristic		OR (95% CI)	P^1
Age	one-unit increase	1.013 (0.996; 1.031)	0.134
Gender	Male	ref.	
	Female	1.650 (0.836; 3.258)	0.149
Infection		1.878 (0.928; 3.801)	0.080
Cancer		1,017 (0,381; 2,716)	0,974
Platelet count	one-unit increase	1.000 (0.998; 1.002)	0.781
Prophylactic anticoagulation	LMWH/other	1.255 (0.641; 2.456)	0.508
Therapeutic anticoagulation		6.930 (1.227; 39.128)	**0.028**
Site of insertion	Internal jugular vein	ref.	
Internal jugular vein	Subclavian vein	11.332 (5.329; 24.099)	**< 0.001**
Number of CVC lumens	2	ref.	
	≥ 3	0.307 (0.019; 5.000)	0.407
Medication	propofol	1.141 (0.571; 2.279)	0.708
	parenteral nutriton	1.379 (0.534; 3.561)	0.506
	Transfusions	1.079 (0.545; 2.136)	0.828
Catheter-days	one-unit increase	0.993 (0.911; 1.082)	0.867
Catheter position	Correct	ref.	
	Malpositon	1.542 (0.726; 3.277)	0.260

[1] calculation based on Logistic regression

Table 7. Catheter related deep vein thrombosis as a risk factor of 28-day mortality.

	28-day mortality		OR (95% CI)	P^2
Deep vein thrombosis[1]	No (n=170)	Yes (n=28)		
No (n=151)	127 (84.1%)	24 (15.9%)	ref.	
Yes (n=47)	43 (91.5%)	4 (8.5%)	0.492 (0.162; 1.499)	0.212

[1] absolute and relative frequency for categorical data
[2] calculation based on Logistic regression

more frequent complication following IJV cannulation (56%) as opposed to SCV cannulation (10%).

In our opinion, this disproportion could be explained by the lower tendency of SCV to collapse due to anatomic relations. Direct damage of the vessel wall by the catheter is more likely in the collapsed vessel. Another contributing factor to higher rate of CR-DVT in cannulation of IJV could be greater mechanical damage of the vessel wall related to catheter movements during motion of the head and neck.

We observed that patients who require therapeutic anticoagulation because of venous thromboembolism (VTE) prior to cannulation showed a higher incidence of CR-DVT.

The reason for this may be the hypercoagulable state for which the anticoagulation therapy was indicated and the consequent need for modification of LMWH treatment after admission to ICU because of the risk of haemorrhage. The treatment with LMWH was returned when the risk of bleeding was considered lower than the risk of VTE.

Although LMWH is used for prophylaxis of VTE its effect on the incidence of CR-DVT is ambiguous[6,12]. In our study there was no demonstrated effect of prophylactic LMWH treatment on the incidence of CR-DVT.

Malposition of the catheter tip is a risk factor for CR-DVT (ref.[7,14,15]). We did not confirm the relationship of the catheter tip position and CR-DVT. The reason could be the number of catheter-days and type of catheter inserted. In these studies long-term implantable catheters were studied.

Previous studies have shown that patients who do not receive lipids and propofol have a higher risk of CR-DVT (ref.[9,16]). We did not observe that in our study. Patients who receive parenteral nutrition have a higher risk of CR-DVT (ref.[17]). The reason could be its effect on coagulation. Parenteral nutrition induces the activation of the platelet membrane glycoprotein and could contribute to a higher rate of CR-DVT (ref.[18]). We did not demonstrate this in our study. The reason could be the different number of catheter-days. The mean number of catheter-days was 9.5 whereas in the above named study the mean number of catheter-days in excess of 30 days.

Results of studies on dealing with the effect of transfusion therapy and the presence of infection on the frequency of CR-DVT are ambiguous[9,16,19-21]. In our study, we did not observe any relation between transfusion therapy, the presence of infection and a higher incidence of CR-DVT.

The effect of platelet count on the incidence of CR-DVT has been investigated in several studies[9,22]. We found

no statistically significant difference in platelet count between patients with or without CR-DVT.

CONCLUSION

CR-DVT occurred in 24% of our critically ill patients following cannulation of either the IJV or SCV. As risk factors for development of CR-DVT we identified cannulation of IJV and the use of therapeutic anticoagulation prior to cannulation.

There was no impact of age, gender, infection, cancer, platelet count, prophylactic anticoagulation, number of CVC lumens, propofol, parenteral nutrition, transfusion, number of catheter-days or catheter tip position on the incidence of CR-DVT. We found no effect of CR-DVT on 28-day mortality. We would recommend preferential cannulation of SCV as opposed to IJV in order to reduce the risk of CR-DVT.

ABBREVIATIONS

CR-DVT, Catheter related deep vein thrombosis; CVC, Central venous catheter; DVT, Deep vein thrombosis; ICU, Intensive care unit; IJV, Internal jugular vein; LMWH, Low molecular weight heparin; SCV, Subclavian vein; TU RBC, Transfusion units of red blood cells; VTE, Venous thromboembolism.

Author contributions: All authors: study design, protocol preparing, data interpretation, final approval; OH, ES: study investigation; OH, ES, PS, RK: ultrasound examinations; JJ: statistical analyses.
Conflict of interest statement: None declared.

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