Peripherally Inserted Central Venous Catheter in Upper Extremities Could be a Risk for Deep Vein Thrombosis in Lower Extremities and D-Dimer in Neurology Department

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Research

Keywords: peripherally inserted central venous catheter, lower extremity deep venous thrombosis , D-dimer, Neurology department

Abstract

Background: With the in-depth study of Peripherally Inserted Central venous Catheter (PICC) related venous thrombosis, it is found that the incidence of lower extremity deep venous thrombosis (LEDVT) in patients with PICC in upper extremities is higher than that in patients without PICC . However, there is no explanation for this clinical phenomenon that PICC related venous thrombosis seems to have exceeded the range of PICC travel . The purpose of this study is to elucidate this association between PICC in upper extremities and LEDVT by observing the changes of D-dimer .

Methods: This was a retrospective cohort study of adults in Neurology department who underwent Color Doppler ultrasound and D-dimer test between 1 April 2017 to 1 April 2020. We analyzed the related factors of LEDVT and the change of D-dimer value, compared the changes of D-dimer before and after PICC insertion, and evaluated the predictive value of D-dimer in patients with and without PICC.

Results: ⬚ It was found that the presence of PICC increased the risk of lower extremity venous thrombosis by 7 times (OR = 7.048 [95% CI: 4.486-11.074]; ⬚It was found that the presence of PICC promoted the increase of D-dimer value (OR = 5.133 [95% CI: 3.072-8.575]). ⬚ For patients without LEDVT, the level of D-dimer in patients with PICC was higher than that in patients without PICC (P < 0.05). ⬚ The level of D-dimer after PICC insertion was significantly higher than that before PICC insertion(P < 0.05). ⬚ In patients with PICC, the AUC value of D-dimer in the diagnosis of LEDVT was 0.657 (95% CI: 0.549-0.765), and the negative predictive value was 82.35%.

*Conclusion:*PICC insertion may increase the level of D-dimer and become an important risk factor of LEDVT; For patients with PICC , D-dimer value is not suitable to rule out LEDVT.

Introduction

Peripherally Inserted Central venous Catheter (PICC) is a catheter with tip located in superior vena cava or inferior vena cava through superior limb basilic vein, median cubital vein, cephalic vein, brachial vein, external jugular vein (newborns PICC insertion can also through great saphenous vein of lower limb, temporal vein of head, retroauricular vein, etc.). As a new infusion tool, PICC can reduce the pain of repeated puncture and reduce the incidence of drug extravasation, which is welcomed by clinical medical staff, patients and family members. However, PICC insertion and displacement will damage the vascular intima [2], The presence of PICC occupies part of the inner diameter of the vein [3, 4], coupled with the patients' own diseases and medication induced hypercoagulable state [5], just meet the Virchow's triad [6]. The incidence of PICC related upper extremity deep venous thrombosis(UEDVT) was 51.4% – 71.9% [7–9]. Among them,patients who appear peripheral symptoms like limb swelling, local tenderness, skin temperature rise, skin color cyanosis, limb dysesthesia and dyskinesia or shoulder discomfort were 2.0% – 27.9% [10–12].

Previous studies have suggested that PICC related venous thrombosis is mainly mural thrombus, which is mainly limited to the venous route where the catheter is located [13–15]. With the deepening of the study,

some data show that the incidence of lower extremity deep venous thrombosis (LEDVT) in patients with PICC is higher than that of patients without PICC, and PICC related venous thrombosis seems to have exceeded the range of the venous route where the catheter is located [2] [6, 16–18]. How to explain this clinical phenomenon? The purpose of this study is to elucidate this association by observing the changes of D-dimer. D-dimer is a specific degradation product of cross-linked fibrin. The increase of D-dimer reflects the enhancement of coagulation and fibrinolysis system, and can be used as a sensitive index of hypercoagulability [14, 19] The normal value of D-dimer can be used to assist in the exclusion of venous thrombosis [20] [21] [22] [23] [24]. Previous studies have shown that D-dimer can predict catheter-related venous thrombosis, and when venous thrombosis occurs, the D-dimer value can also increase [19, 25]. It is not clear whether D-dimer is the medium or by-product of catheter-related venous thrombosis events [26]. Based on the above understanding, we conducted a cohort study to to elucidate the association between PICC in upper extremities and LEDVT by observing the changes of D-dimer in neurology department.

Patients And Methods

Patients and study design

The study was approved by the ethics committee of Xiangya Hospital of Central South University(202004327) and was conducted according to the Helsinki Declaration of Ethical Principles for Medical Research involving Human Subjects.

This was a retrospective case cohort study that evaluated patients in neurology department who received Color Doppler ultrasound in Xiangya Hospital of Central South University, Hunan Province, Changsha between April 1, 2017 to April 1, 2020. The exclusion criteria were 1)Under 18 years old;2）Pregnant；3）Patients with PICC in lower extremities；4）Patients with upper extremity venous thrombosis ;5) diagnosed with venous thromboembolism in the 6 months before admission; 6) admitted for presumed venous thromboembolism;7）LEDVT occurred after PICC extubation.

Data, including on basic demographic characteristics, PICC, test results, disease course, and medications, were collected using the standard form in the Reasonable Safety Infusion Monitoring System of Xiangya Hospital of Central South University.Malignant tumor is defined as the malignant tumor patients who are under treatment within 6 months; recent surgery refers to neurosurgical operation that takes more than 2 hours within 6 months; PICC status only includes patients with PICC after insertion and before extubation; diabetes, liver dysfunction and renal dysfunction are defined as the disease status within 6 months after hospitalization.

Statistical analysis

This was a case cohort study, descriptive statistics were reported as means and standard deviations for continuous variables and frequencies for categorical variables. Proportions of events were compared by use of the Pearson χ^2 test. Continuous variables were compared by use of Student's t-test or the Mann–

Whitney rank sum test, according to normality of their distribution. Risk factors for lower extremity deep vein thrombosis(LEDVT) and D-dimer group were studied by performing univariate and multivariate logistic. A Student's t-test for association between D-dimer value in patients with PICC and those without PICC. A Student's t-test for the changes of D-dimer value before and after PICC insertion. Risk assessments are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Receiver operating characteristic (ROC) analysis was used to plot the sensitivity and specificity of the with PICC related / non- PICC related D-dimer level respect to LEDVT. PICC related and non- PICC related D-dimer level as an independent biomarker for LEDVT was evaluated according to its area under the curve (AUC). The Youden's index were determined to identify the optimal cut-off point and its sensitivity, specificity, negative predictive value, positive predictive value. All statistical analyses were conducted with SPSS (Version 18; SPSS, Central South University,Hunan, China), A P-value of < 0.05 (two-tailed) was considered to be significant.

The study was approved by the ethics committee of Xiangya Hospital of Central South University and was conducted according to the Helsinki Declaration of Ethical Principles for Medical Research involving Human Subjects.

Results

1. Relationship between PICC and LEDVT
In this study, 3452 patients who were admitted to 7 wards of Neurology Department of Xiangya Hospital of Central South University from 1 April 2017 to 1 April 2020 were included in the study. 270 patients (7.82%) were diagnosed with LEDVT by ultrasound.This includes 104 patients with PICC,43 patients(41.35%) were diagnosed with LEDVT by ultrasound. Univariate logistic regression analysis showed that malignant tumor, PICC, recent surgery and diabetes were associated with LEDVT and the presence of PICC increased the risk of LEDVT by 9 times(OR = 9.692 [95%CI: 6.414−14.646],P = 0.000);After adjusting for gender, age and other factors, multivariate logistic regression analysis found that age,PICC and recent surgery were associated with the LEDVT and the presence of PICC increased the risk of LEDVT by 7 times (OR = 7.048 [95% CI: 4.486−11.074], P = 0.000).(Table 1)

Table 1 Logistic regression analysis of related factors of LEDVT

Factors	LEDVT	NO LEDVT	Univariate		Multivariate	
	(n=270)	(n=3182)	OR （95%CI)	P	OR （95%CI)	P
Age(year, $\overline{X}\pm s$)	61.27±12.63	61.57±13.71	0.998(0.989-1.007)	0.724	1.013(1.003-1.023)	0.010
Male	156	1941	0.875(0.680-1.125)	0.298	1.056(0.802-1.390)	0.698
Malignant tumor	48	79	8.493(5.787-12.464)	0.000	1.237(0.705-2.170)	0.458
Recent surgery	80	160	7.593(5.857-10.797)	0.000	4.375(2.768-6.913)	0.000
PICC	43	61	9.692(6.414-14.646)	0.000	7.048(4.486-11.074)	0.000
Diabetes	14	616	0.228(0.132-0.393)	0.000	0.834(0.458-1.517)	0.551
Abnormal liver function	4	61	0.769(0.278-2.132)	0.614	1.220(0.404-3.686)	0.725
Renal dysfunction	5	72	0.815(0.326-2.035)	0.661	2.393(0.831-6.887)	0.106

2.Relationship between PICC and D-dimer

In this study, 1360 patients with D-dimer value recorded within 7 days before the diagnosis of ultrasound, 597 patients (43.90%) had D-dimer > 0.5 mg/L.This includes 101 patients with PICC,80 patients(79.21%) had D-dimer > 0.5 mg/L. Univariate logistic regression analysis showed that age,male, malignant tumor, PICC, recent surgery and diabetes were associated with LEDVT and the presence of PICC promoted the increase of D-dimer value by 5 times(OR = 5.467 [95%CI: 3.338−8.956],P = 0.000);After adjusting gender, age and other factors, multivariate logistic regression analysis found that age,PICC, recent surgery and renal dysfunction were associated with the LEDVT and the presence of PICC promoted the increase of D-dimer value by 5 times (OR = 5.133 [95% CI: 3.072−8.575], P = 0.000). (Table 2)

Table 2 Logistic regression analysis of related factors of D-dimer

Factors	D-dimer > 0.5mg/L	D-dimer≤0.5mg/L	Univariate		Multivariate	
	(n=597)	(n=763)	OR (95%CI)	P	OR (95%CI)	P
Age(year, $\overline{X}$±s)	61.91±15.50	60.17±14.46	1.008(1.001-1.015)	0.033	1.020(1.011-1.028)	0.000
Male	339	486	0.749(0.602-0.932)	0.010	0.827(0.648-1.056)	0.128
Malignant tumor	85	38	3.167(2.126-4.720)	0.000	0.670(0.367-1.223)	0.192
Recent surgery	158	64	3.931(2.872-5.381)	0.000	4.947(3.034-8.067)	0.000
PICC	80	21	5.467(3.338-8.956)	0.000	5.133(3.072-8.575)	0.000
Diabetes	52	133	0.452(0.322-0.635)	0.000	0.720(0.476-1.088)	0.119
Abnormal liver function	21	14	1.951(0.983-3.869)	0.056	1.692(0.767-3.734)	0.193
Renal dysfunction	20	18	1.435(0.752-2.737)	0.274	2.222(1.063-4.644)	0.034

3.The relationship between D-dimer value in patients with PICC and those without PICC

For patients were diagnosed LEDVT, there was no significant difference in D-dimer between patients with PICC and patients without PICC; for patients were diagnosed not LEDVT, the level of D-dimer in patients with PICC were higher than that patients without PICC, the difference was statistically significant (P < 0.05). (Table 3)

Table 3
Comparison of D-dimer value in patients with PICC and those without PICC

	The level of D-dimer in patients with PICC	The level of D-dimer in patients without PICC	t	P
LEDVT	2.05 ± 1.69	1.99 ± 1.87	0.21	0.836
NO LEDVT	1.31 ± 1.26	0.69 ± 1.19	3.82	0.000

4.Comparison of D-dimer before and after PICC insertion

The level of D-dimer after PICC insertion was significantly higher than that before PICC insertion (P < 0.05)

(Table 4.)

Table 4
Comparison of D-dimer before and after PICC insertion

	N	D-dimer	*t*	*P*
Before PICC insertion	92	0.86 ± 0.84	-7.07	0.00
After PICC insertion	92	1.78 ± 1.45		

5. Analysis of the predictive value of D-dimer in patients with PICC and patients without PICC to LEDVT

The results of ROC curve analysis showed that the AUC value of D-dimer in the diagnosis of LEDVT in patients with PICC was 0.657 (95% CI: 0.549-0.765), P < 0.05, Youden index was 0.3433, the optimal critical value of D-dimer in the diagnosis of LEDVT in patients with PICC was 0.675 mg / L, the sensitivity was 48.28%, specificity was 86.05%, respectively the positive predictive value was 55.22%, and the negative predictive value was 82.35%.

The AUC value of D-dimer in the diagnosis of LEDVT in patients without PICC was 0.800（95%CI：0.769-0.830），P<0.05，Youden index was 0.479, the optimal critical value of D-dimer in the diagnosis of LEDVT in patients without PICC was 0.665mg/L, the sensitivity was 72.01%, specificity was 75.89%, respectively the positive predictive value was 36.82%, and the negative predictive value was 93.25%.(Table 5, Figures 1 and 2)

Table 5 Analysis of the predictive value of D-dimer to LEDVT

	The optimal critical value	Sensitivity	Specificity	Positive predictive value	negative predictive value	Area under ROC curve	95% confidence interval
The level of D-dimer in patients with PICC	0.675	48.28%	86.05%	55.22%	82.35%	0.657	0.549-0.765
The level of D-dimer in patients without PICC	0.665	72.01%	75.89%	36.82%	93.25%	0.800	0.769-0.830

Discussion

Foreign body in vascular system is the most important independent risk factor of upper extremities deep vein thrombosis (UEDVT)[27−30]. CVC increased the risk of UEDVT by 7 times (odd ratio [or] 7.3, 95% confidence interval [5.79, 9.21]; P < 0.0001) [29]. PICC is placed in a much smaller vein than in CVC, and the risk of DVT in PICC is 2.5 times higher than that in CVC [31], of which 33−60% were asymptomatic [32]. It is easy to understand that PICC is the most important risk factor for UEDVT[33, 34], but the presence of PICC in this study increased the risk of LEDVT by 7 times (or = 7.048 [95% CI: 0.05] .It has

been speculated that endothelial injury, vascular reactivity and coagulation promotion may lead to PICC related deep venous thrombosis, which extends beyond the vascular bed of PICC itself, but lacks systemic coagulation indicators to confirm this association.

D-dimer is a fibrin degradation product, which can be determined in the blood after the blood clot is degraded by the fibrinolysis process [35]. The formation and decomposition of blood clot is a dynamic process, and D-dimer can be elevated in various situations such as trauma and inflammation. Therefore, this study included the D-dimer values of these patients 7 days before the diagnosis of LEDVT after PICC insertion. It was found that the increase of D-dimer value was closely related to PICC insertion.In order to further understand the relationship between PICC and D-dimer value and LEDVT, we compared the D-dimer values of patients with PICC and patients without PICC under thrombus or non thrombus state, and found that the D-dimer value of patients with PICC in non thrombus group was higher than that in patients without PICC, and the difference was statistically significant. Considering that there are many and complex factors affecting the formation of LEDVT, it is difficult to judge whether the D-dimer values of patients with PICC is higher than that patients without PICC in the non thrombus group, because the PICC insertion population is more inclined to hypercoagulable patients or the influence of PICC itself. Therefore, in this study, D-dimer values within 7 days before and 7 days after PICC insertion were included in the analysis. It was found that the D-dimer value after PICC insertion was significantly higher than that before PICC insertion,which supported the view that PICC led to the increase of D-dimer.

Thrombosis is a natural process, which is activated by internal and external pathways. Both pathways contain a stimulating event, which starts a series of coagulation in the body and eventually forms fibrin rich thrombus. Endothelial injury is often an inciting event for our body's natural coalescence cascade to be activated. In order to maintain balance, the body starts appropriate fibrinolysis or blood clot formation destruction mechanism. DVT is formed when the mechanism that makes the body easy to coagulate is not hindered, or when the mechanism of decomposing blood clots is overloaded [36]. On the other hand, PICC occupies nearly half of the inner diameter of the vein, resulting in local blood flow slowing down, which can produce micro venous thrombosis, activate the coagulation system in the process of reflux, so as to produce a larger range of deep venous thrombosis [36]. We have reason to believe that the operation of PICC insertion itself or the existence of PICC leads to the general increase of D-dimer value. Under the joint action of other factors, some patients eventually form deep venous thrombosis beyond the PICC vascular bed.

At the same time, we compared the predictive value of D-dimer in the diagnosis of LEDVT in patients with PICC and without PICC. The results showed that when the patients with PICC,the AUC value of D-dimer in the diagnosis of LEDVT was 0.657 (95% CI: 0.549–0.765), and the negative predictive value was 82.35%

.when the patients without PICC, the AUC value of D-dimer in the diagnosis of LEDVT was 0.800 (95% CI: 0.769–0.830), and the negative predictive value was 93.25%. It is suggested that the D-dimer value of patients with PICC is not suitable to be used as a key index to exclude LEDVT.

Our study has important limitations. First of all, we did not conduct UEDVT screening, which may have missed a lot of asymptomatic UEDVT data. Therefore, we can not explain whether PICC as an important risk factor causes UEDVT first and then the LEDVT, or that compared with the upper limb, the lower extremity venous valves are more and fragile, and the blood flow rate is slower, which only causes the LEDVT. Secondly, this study is limited to neurology patients, and there may be specific bias of the disease itself. Finally, this is a retrospective study,the D-dimer values were collected within 7 days before and after PICC insertion,during this period, other events that could affect the increase of D-dimer were not excluded.

These limitations notwithstanding, our study has important strengths:1.The study shows that PICC in upper extremities could be a risk for LEDVT in Neurology department,suggesting that we should not only pay attention to the complications of PICC side limbs, but also pay attention to the compound risks after PICC insertion, especially the possibility of LEDVT. For patients with high risk of thrombosis, it is necessary for specialized nursing team to weigh the risks and benefits of PICC, and to consider alternative vascular access schemes for high-risk patients; 2. For the first time, the systemic coagulation index D-dimer was used to preliminarily explain the possible relationship between PICC in upper extremities and LEDVT. It can be considered try to use prophylactic anticoagulant regimen when patients at high risk of thrombosis need PICC insertion;3.It was found that the predictive value of D-dimer in patients with PICC is lower than that in patients without PICC,It is suggested D-dimer value is not suitable to rule out PICC associated LEDVT, so as to avoid missed diagnosis of PICC related LEDVT, which may cause adverse sequences or even life threading

Conclusion

PICC insertion may increase the value of D-dimer and become an important risk factor of LEDVT;The predictive value of D-dimer in patients with PICC is lower than that in patients without PICC,D-dimer may not be suitable for routine examination in patients with PICC to exclude LEDVT.

Abbreviations

PICC
Peripherally Inserted Central venous Catheter; LEDVT:lower extremity deep venous thrombosis; UEDVT:upper extremity deep venous thrombosis

Declarations

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

Wanli Liu participated in data acquisition and management of the study, analyzed and interpreted the data, and drafted and revised the manuscript. Lianxiang He and Wenjing Zeng and Liqing Yue participated in data interpretation, and revision of the manuscript. Jie Wei and Shuangshuang Zeng participated in protocol drafting, study management. Zhicheng Gong was trial manager, designed, initiated and managed the study, participated in data acquisition and interpretation, and revised the manuscript.All authors read and approved the final manuscript.

Ethical Approval and Consent to participate

The study was approved by the ethics committee of Xiangya Hospital of Central South University(202004327) and was conducted according to the Helsinki Declaration of Ethical Principles for Medical Research involving Human Subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Commission NHAF. Technical operation specifications for intravenous therapy nursing. China nursing management. 2014;1(14):1–4.

2. Song L, et al. Malposition of peripherally inserted central catheter: experience from 3012 cancer patients. Int J Nurs Pract. 2014;20(4):446–9.

3. Nifong TP, McDevitt TJ. The effect of catheter to vein ratio on blood flow rates in a simulated model of peripherally inserted central venous catheters. Chest. 2011;140(1):48–53.

4. Chopra V, et al. Peripherally inserted central catheter-related deep vein thrombosis: contemporary patterns and predictors. J Thromb Haemost. 2014;12(6):847–54.

5. Dubois J, et al. Incidence of deep vein thrombosis related to peripherally inserted central catheters in children and adolescents. Can Med Assoc J. 2007;177(10):1185–90.

6. Chopra V. G.M.B.S., The Association between Upper and Lower Extremity Deep Vein Thrombosis and Peripherally Inserted Central Catheters: Think Below the Waist Annual Scientific Conference Abstract. Society of Hospital Medicine, 2014(Las Vegas, NV.).

7. Liu Y, et al. Peripherally inserted central catheter thrombosis incidence and risk factors in cancer patients: a double-center prospective investigation. Ther Clin Risk Manag. 2015;11(29):153–60.

8. Itkin M, et al. Peripherally inserted central catheter thrombosis–reverse tapered versus nontapered catheters: a randomized controlled study. J Vasc Interv Radiol. 2014;25(1):85–91.e1.

9. Sriskandarajah P, et al. Retrospective cohort analysis comparing the incidence of deep vein thromboses between peripherally-inserted and long-term skin tunneled venous catheters in hemato-oncology patients. Thrombosis Journal. 2015;13(21):1–7.

10. Aw A, et al. Incidence and predictive factors of symptomatic thrombosis related to peripherally inserted central catheters in chemotherapy patients. Thromb Res. 2012;130(3):323–6.

11. Chemaly RF, et al. Venous thrombosis associated with peripherally inserted central catheters: a retrospective analysis of the Cleveland Clinic experience. Clin Infect Dis. 2002;34(9):1179–83.

12. King MM, et al. Peripherally inserted central venous catheter-associated thrombosis: retrospective analysis of clinical risk factors in adult patients. South Med J. 2006;99(10):1073–7.

13. Liem TK, et al. Peripherally inserted central catheter usage patterns and associated symptomatic upper extremity venous thrombosis. J Vasc Surg. 2012;55(3):761–7.

14. Olson JD. D-dimer: An Overview of Hemostasis and Fibrinolysis, Assays, and Clinical Applications. Adv Clin Chem. 2015;69(2):1–46.

15. Easaw JC, et al. Canadian consensus recommendations on the management of venous thromboembolism in patients with cancer. Part 2: treatment. Curr Oncol. 2015;22(2):144–55.

16. Greene MT, et al. The Association Between PICC Use and Venous Thromboembolism in Upper and Lower Extremities. The American Journal of Medicine. 2015;128(9):986–93.e1.

17. Al-Asadi O, Almusarhed M, Eldeeb H. Predictive risk factors of venous thromboembolism (VTE) associated with peripherally inserted central catheters (PICC) in ambulant solid cancer patients: retrospective single Centre cohort study. Thrombosis Journal. 2019;17(2):1–7.

18. Chopra V, et al. Peripherally inserted central catheter-related deep vein thrombosis: contemporary patterns and predictors. J Thromb Haemost. 2014;12(6):847–54.

19. van der Straaten Mark Roest Fred Haas Philip. De Groot Rob G, Fijnheer FHJH. Elevated levels of D-dimer and fragment 1 + 2 upon central venous catheter insertion and factor V Leiden predict subclavian vein thrombosis. the hematology journal, 2005. 4(90): 499–504.

20. Chen Q, Z.Z.D.H. and Zhi ZFAZ. Perioperative Venous Thromboembolism (VTE) Prophylaxis in Thoracic Cancer Patients: Chinese Experts Consensus - Interpretation of Clinical Significance of D-dimer. Zhongguo Fei Ai Za Zhi. 2019;12(22):761–6.

21. Zhang D, et al. Diagnostic accuracy of biomarker D-dimer in patients after stroke suspected from venous thromboembolism: A diagnostic meta-analysis. Clin Biochem. 2019;63(2):126–34.

22. Jeffrey I, Weitz MABC. A Test in Context: D-Dimer. JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, 2017. 70(19): p. 2411–2419.

23. Lim W, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. Blood Adv. 2018;2(22):3226–56.

24. Chopra V, et al. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. Lancet. 2013;382(9889):311–25.

25. Kanno Y, et al. Elevation of plasma D-dimer is closely associated with venous thrombosis produced by double-lumen catheter in pre-dialysis patients. Nephrology Dialysis Transplantation. 2007;22(4):1224–7.

26. Greene MT, et al. The Association Between PICC Use and Venous Thromboembolism in Upper and Lower Extremities. The American Journal of Medicine. 2015;128(9):986–93.e1.

27. Frolova AI, et al. Complications of peripherally inserted central catheters in pregnancy: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2020. https://doi.org/10.1080/14767058.2020.1769591.

28. Jiang M, et al. Risk of venous thromboembolism associated with totally implantable venous access ports in cancer patients: a systematic review and meta-analysis. J Thromb Haemost. 2020. https://doi.org/10.1111/jth.14930.

29. Joffe HV, et al. Upper-extremity deep vein thrombosis: a prospective registry of 592 patients. Circulation. 2004;110(12):1605–11.

30. Heil J, et al. Deep Vein Thrombosis of the Upper Extremity. Dtsch Arztebl Int. 2017;114(14):244–9.

31. Chopra V, et al. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. Lancet. 2013;382(9889):311–25.

32. Sajid MS, et al. Upper limb deep vein thrombosis: a literature review to streamline the protocol for management. Acta Haematol. 2007;118(1):10–8.

33. Al-Asadi O, Almusarhed M, Eldeeb H. Predictive risk factors of venous thromboembolism (VTE) associated with peripherally inserted central catheters (PICC) in ambulant solid cancer patients: retrospective single Centre cohort study. Thrombosis Journal. 2019;17(2):1–7.

34. Jones D, et al. The risk of venous thromboembolism associated with peripherally inserted central catheters in ambulant cancer patients. Thrombosis Journal. 2017;15(25):1–7.

35. Wells PS, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med. 2003;349(13):1227–35.

36. Hattab Y, et al. Deep Venous Thrombosis of the Upper and Lower Extremity. Crit Care Nurs Q. 2017;40(3):230–6.

Figures
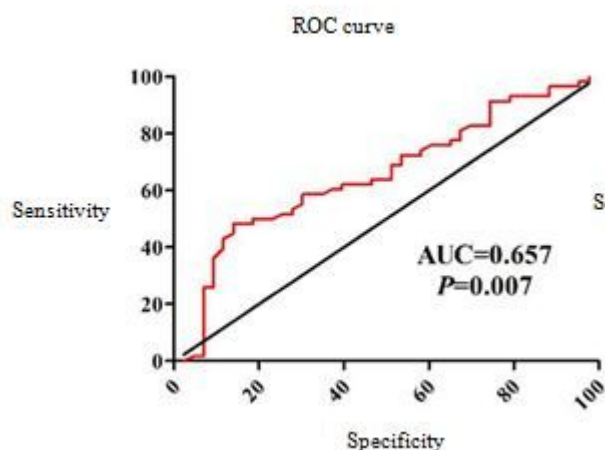
Figure 1

Area under ROC curve of D-dimer in the diagnosis of LEDVT in patients with PICC
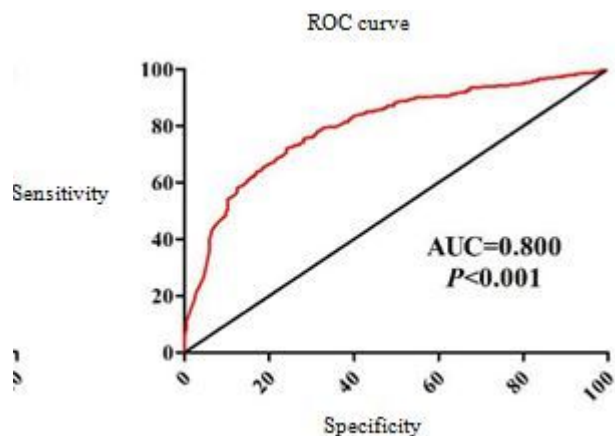
Figure 2

Area under ROC curve of D-dimer in the diagnosis of LEDVT in patients without PICC