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Original Article

Deep Venous Thrombosis in Elderly Inpatients with Pneumonia

Dong Wu, Zheng Wang, Hui Lin Liu, Fan Zhang *

Department of Geriatrics, Peking University Third Hospital, Beijing, China

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SUMMARY

Background: The occurrence of deep vein thrombosis (DVT) in COVID-19 pneumonia has raised wide concern recently, but few studies have reported the incidence of DVT in other types of pneumonia. We evaluate the prevalence, risk factors and treatment of DVT in the elderly inpatients with pneumonia.
Methods: A cohort of 550 elderly inpatients (≥ 75 years old) with pneumonia between 2017 and 2021 were reviewed. They were divided into DVT group and non-DVT groups on the basis of whether pneumonia was combined with new-found DVT. Clinical data were collected retrospectively. Patients with DVT were divided into anticoagulant group and non-anticoagulant groups on the basis of whether they received anticoagulant therapy.
Results: Ninety-seven patients were included in the DVT group; 453 in the non-DVT group. The incidence of DVT was 17.64%. Hospital stays were significantly longer for DVT patients than for non-DVT counterparts ($p = 0.005$). Coronary heart disease, heart failure, hyperlipidemia, bed rest, and elevated D-dimer were independent risk factors for DVT ($p < 0.05$). The rate of anticoagulant therapy in DVT group was 63.92% (62/97 cases). Follow-up showed that the continuous anticoagulant treatment rate was 48.39% (30/62 cases) at 3 months and 30.65% (19/62 cases) at 6 months.
Conclusion: Elderly inpatients with pneumonia are at high risk of DVT. The combination of DVT and pneumonia may lead to prolonged hospitalization. Coronary heart disease, heart failure, hyperlipidemia, bed rest and elevated D-dimer are independent risk factors for DVT in these patients. The rate of regular anticoagulant treatment is low because of the high risk of bleeding.

1. Introduction

Deep venous thrombosis (DVT) is one of the most common complications of inpatients in internal medicine. Infectious diseases, especially pulmonary infection, are the most important underlying diseases in patients with DVT.[1] Recently, many reports have found that DVT is common in patients with novel coronavirus disease 2019 (COVID-19). Meta-analysis showed that the incidence of DVT could be as high as 13% in these patients.[2] However, there are few reports on the occurrence of DVT in other common forms of pneumonia.

As age is an important influential factor for DVT formation and the risk of DVT increases with age, the incidence rate of DVT in patients older than 75 years of age is significantly higher than that in other age groups.[3] Studies have shown that being older than 75 is an independent risk factor for venous thrombosis.[4] Therefore, in this study we mainly focus on elderly inpatients (≥ 75 years old) with pneumonia, and explore the epidemiology, risk factors, clinical characteristics, treatment, and prognosis of DVT in these patients.

2. Materials and methods

2.1. Patient population

In this study, elderly inpatients with pneumonia treated in the Department of Geriatrics of our hospital between January 2017 and January 2021 were reviewed retrospectively. The inclusion criteria were: 1) patients who were diagnosed with pneumonia, 2) age ≥ 75 years; and 3) patients with complete clinical data. Exclusion criteria were: 1) patients with pneumonia who were admitted twice within 1 month; and 2) patients with hospitalization time < 24 h. The diagnosis of DVT was based on the results of deep venous Doppler ultrasound, and all DVTs were newly discovered during emergency before admission or hospitalization. The patients were divided into a DVT group and a non-DVT group on the basis of whether patients' pneumonia was combined with new DVT. The study was approved by the Peking University Third Hospital Medical Science Research Ethics Committee.

The clinical data of patients were collected by performing a retrospective survey of their electronic medical records, including sex, age, hypertension, hyperlipemia, coronary heart disease (CHD), diabetes, cerebral infarction, active malignant tumor, renal insufficiency, heart failure, respiratory failure, fracture or surgical immobilization in the previous 3 months, bed rest (completely bedridden or basically bedridden for at least 3 days), D-dimer, brain natriuretic peptide and albumin. The clinical characteristics of patients were analyzed to determine the risk factors of DVT.

The risk factors of venous thromboembolism were assessed in accordance with Padua score standard, whereby a score of ≥ 4 points is considered to indicate a high risk of venous thrombosis.[5] The bleeding risk of DVT patients was assessed using the bleeding risk

* Corresponding author. Department of Geriatrics, Peking University Third Hospital, Beijing, China.
E-mail address: zfabcd2000@163.com (F. Zhang)

assessment table of hospitalized patients in internal medicine, whereby ≥ 2 items are considered to indicate a high risk of bleeding.[5] The clinical features of DVT, including symptoms, thrombus location, anticoagulant therapy, and prognosis, were collected. On the basis of whether anticoagulant therapy was administered, the DVT group was divided into an anticoagulant group and non-anticoagulant group.

2.2. Statistical analysis

Statistical analysis was carried out using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). The count data were expressed as rate (%), and the assessment of categorical variables was performed by chi-squared test between two groups. Continuous variables were tested for normal distribution using Kolmogorov-Smirnov statistics, the normal distribution data was represented by mean ± standard deviation, and the independent-samples *t*-test was used between two groups. Variables with statistically significant difference in univariate analysis ($p < 0.05$) were substituted into the logistic regression model of multivariate analysis. Multivariate logistic regression analysis was used to determine the independent risk factors for DVT. A *p* value of less than 0.05 was regarded as statistically significant.

3. Results

A total of 550 elderly inpatients (≥ 75 years old) with pneumonia were enrolled in this study. Of the 97 patients diagnosed with DVT group, 55 (56.7%) were male and 42 (43.3%) were female. The age range was 75–102 years with a median age of 86 years. Eleven patients (11.3%) were 75–79 years old, 65 (67.0%) were 80–89 years old, and 21 (21.6%) were ≥ 90 years old. The remaining 453 patients were included in the non-DVT group, 307 (67.8%) of whom were male and 146 (32.2%) female. Their age ranged from 75 to 95 years with a median age of 87 years. Forty-six patients (10.2%) were 75-79 years old, 257 (56.7%) were 80-89 years old, and 150 (33.1%) were ≥ 90 years old. The overall incidence rate of DVT was 17.64%.

The main symptoms of the patients with DVT involved edema of affected limbs; there were 38 cases (39.18%) of edema symptoms, with the other 59 patients (60.82%) having no obvious DVT symptoms. Sixteen cases (16.49%) involved the proximal deep vein (popliteal vein and above) and the other 81 cases (83.51%) involved only the distal deep vein. The affected veins included calf intermuscular vein (87 cases), superficial femoral vein (14 cases), posterior tibial vein (11 cases), popliteal vein (7 cases), fibular vein (7 cases), and iliac vein (3 cases).

The proportions of female sex, bed rest, elevated D-dimer, hyperlipidemia, CHD, and heart failure in the DVT group were significantly higher than those in non-DVT group ($p < 0.05$). There were no significant differences in age, active tumor, fracture, hypertension, diabetes, respiratory failure, renal insufficiency, dementia, and hospital mortality ($p > 0.05$, Table 1). Hospital stays for the DVT group were significantly longer than those for the non-DVT group ($p = 0.005$).

In multivariate analysis, the factors including coronary heart disease, heart failure, hyperlipidemia, bed rest and elevated D-dimer were independent risk factors for DVT ($p < 0.05$, Table 2).

There were 83 patients (85.57%) in the DVT group and 204 patients (45.03%) in the non-DVT group with a high risk-of-thrombus

Table 2
The independent risk factors for deep venous thrombosis.

Factors	OR (95% CI)	*p* value
Coronary heart disease	1.964 (1.203–3.207)	0.007*
Heart failure	1.867 (1.142–3.052)	0.013*
Bed rest	1.664 (1.028–2.695)	0.038*
Hyperlipidemia	1.853 (1.133–3.029)	0.014*
Elevated D-dimer (≥ 0.5 mg/L)	2.887 (1.701–4.899)	< 0.001*
Female	0.718 (0.446–1.154)	0.171

CI, confidence interval; OR, odds ratio.
* p < 0.05 by multivariable logistic regression analysis.

Table 1
Clinical characteristics of the DVT group and non-DVT group.

Factors	Total (n = 550)	DVT (n = 97)	Non-DVT (n = 453)	*p* value
Female (n, %)	188 (34.2)	42 (43.3)	146 (32.2)	0.045*
Respiratory failure (n, %)	116 (21.1)	26 (26.8)	90 (19.9)	0.133
Diabetes (n, %)	215 (39.1)	40 (41.3)	175 (38.6)	0.648
Hypertension (n, %)	399 (72.5)	67 (69.1)	332 (73.3)	0.452
Hyperlipidemia (n, %)	167 (30.4)	40 (41.2)	127 (28.0)	0.015*
Renal insufficiency (n, %)	144 (26.2)	31 (31.9)	113 (24.9)	0.163
Dementia (n, %)	105 (19.1)	25 (25.8)	80 (17.7)	0.087
Bed rest ≥ 3 days (n, %)	219 (39.8)	53 (54.6)	166 (36.6)	0.001*
Coronary heart disease (n, %)	199 (36.2)	52 (54.6)	147 (32.5)	< 0.001*
Heart failure (n, %)	167 (30.4)	47 (48.5)	120 (26.5)	< 0.001*
Heart failure (NTHA III/IV) (n, %)	83 (15.1)	12 (12.4)	71 (15.7))	0.532
Cerebral infarction (n, %)	209 (38.0)	45 (46.4)	164 (36.2)	0.066
Active tumor (n, %)	96 (17.5)	21 (21.6)	75 (16.6)	0.240
Fracture or surgical (n, %)	86 (15.6)	19 (19.6)	67 (14.8)	0.280
Elevated D-dimer (≥ 0.5 mg/L) (n, %)	304 (55.3)	73 (75.3)	231 (50.1)	< 0.001*
BNP (n, %)				0.155
< 1000 ng/L	276 (50.2)	40 (41.2)	236 (52.1)	
1000–2999 ng/L	150 (27.3)	35 (36.1)	115 (25.4)	
3000–4999 ng/L	52 (9.5)	9 (9.3)	43 (44.3)	
≥ 5000 ng/L	72 (13.1)	13 (13.4)	59 (13.0)	
Albumine (< 30 g/L) (n, %)	111 (20.2)	22 (22.7)	89 (19.6)	0.489
High risk of thrombosis score (n, %)	287 (52.2)	83 (85.6)	204 (45.0)	< 0.001*
hospital mortality (n, %)	82 (14.9)	18 (18.6)	64 (14.1)	0.273
Hospital stay (days)	19.29 ± 10.43	22.31 ± 10.95	18.68 ± 10.22	0.005*

BNP: brain natriuretic peptide, DVT: deep venous thrombosis, NTHA: New York heart association class.
The normal distribution data was represented as mean ± standard deviation (SD) and analyzed by the independent samples t test. The count data was represented as number (%) and analyzed by the chi-squaretest.* p < 0.05 was considered statistically significant.

score, the difference was statistically significant ($p < 0.05$). Sixty-three patients (64.95%) in the DVT group had a high risk-of-bleeding score.

Sixty-two patients in the DVT group received anticoagulant therapy and were included in the anticoagulant group, while the remaining 35 patients were included in the non-anticoagulant group because of active bleeding or high risk of bleeding. The rate of anticoagulant therapy was 63.92%. The rates of gastrointestinal bleeding, malignant tumor, high risk of bleeding score, and all-cause mortality in the non-anticoagulant group were significantly higher than those in the anticoagulant group ($p < 0.05$). After discharge, the re-examination rate of DVT by lower extremity venous ultrasound in the anticoagulation group was significantly higher than that in the non-anticoagulation group ($p < 0.05$) (Table 3). The rate of continuous anticoagulant treatment was 48.39% (30 of 62 cases) at 3 months and only 30.65% (19 of 62 cases) at 6 months during the follow-up. There patients stopped anticoagulant therapy because of bleeding (one case due to hematuria and two cases due to gastrointestinal bleeding, which occurred at 2 days, 3 months, and 5 months, respectively after anticoagulation). No fatal bleeding occurred.

4. Discussion

Elderly inpatients with infectious diseases such as pneumonia represent a population at high risk of DVT. The risk of DVT increases with age. Previous studies have shown that 67.25% of 5036 DVT inpatients were over 75 years old.[3] Here we focused on elderly patients (≥ 75 years old) with pneumonia. We retrospectively analyzed 550 elderly inpatients with pneumonia over the most recent 4 years. Among them, 97 patients were diagnosed with DVT, with the incidence of DVT as high as 17.64%. Our research confirmed that elderly patients with pneumonia have a higher risk of DVT. Aging patients often suffer from a variety of diseases, which may lead to a higher risk of DVT.[6] In our cohort, the incidence of CHD (36.2%), heart failure (30.4%), hypertension (72.5%), cerebrovascular disease (38.0%), and other diseases were high, which may be one of the reasons for the significant increase of the incidence of DVT in this population. In addition, elderly patients often need to stay in bed during hospitalization, resulting in less activity, slower blood flow, and venous thrombosis in the lower extremity. Moreover, infectious diseases are inducing factors of DVT. Inflammation caused by infection may trigger DVT by activating coagulation and fibrinolysis processes related to thrombosis.[7,8]

Our results showed that heart failure, CHD, and hyperlipidemia were independent risk factors for DVT in elderly patients with pneumonia. The pathophysiological mechanisms of DVT in patients with heart failure include: lower extremity venous congestion caused by decreased systolic or diastolic function; endothelial dysfunction and hypercoagulability; and decreased exercise tolerance, which further increases the risk of DVT.[9] Previous studies have reported that heart failure, including acute heart failure and stable heart failure, is related to DVT.[10] Our results confirm that heart failure may play an important role in DVT in the elderly inpatients with pneumonia. CHD is not a recognized predisposing factor for DVT, but our results show that the risk of DVT in elderly pneumonia patients with CHD is 1.964 times higher than that in non-CHD patients. Some studies have shown a potential link between venous thromboembolism and atherosclerosis, with the risk factors of CHD and DVT overlapping.[11] A study involving 1.1 million participants showed that some cardiovascular risk factors, including age, smoking and obesity, were also significantly associated with venous thromboembolism.[12] A meta-analysis also showed that hypertension, dyslipidemia, obesity, and other major risk factors for CHD were associated with increased risk of DVT.[13] In the present study, we also found that the incidence of hyperlipidemia in the DVT group was significantly higher than that in the non-DVT group, suggesting that more attention should be paid to the risk of DVT in elderly inpatients with pneumonia and CHD.

Bed rest is a strong inducing factor of DVT.[5] Our results suggest that the risk of DVT in bedridden patients is 1.664 times higher than that in non-bedridden patients. Bed rest may play an important role in the process of DVT in the elderly patients with pneumonia. Additionally, elevated D-dimer is a strong predictor of DVT. Although the sensitivity of D-dimer in elderly patients is reduced,[14] we still found that it is an independent predictor of DVT in elderly patients with pneumonia.

Table 3
Clinical characteristics of the anticoagulant group and non-anticoagulant group.

Factors	Anticoagulant (n = 62)	Non-anticoagulant (n = 35)	*p* value
Female (n, %)	24 (38.7)	18 (51.4)	0.287
Age (years)	85.68 (4.66 ± 0.59)	85.71 (5.61 ± 0.95)	0.286
Hospital mortality (n, %)	6 (9.7)	12 (34.3)	0.005*
Reexamination (n, %)	25 (40.3)	3 (8.6)	0.001*
Edema (n, %)	22 (35.5)	16 (45.7)	0.388
Respiratory failure (n, %)	16 (25.8)	10 (28.6)	0.814
Heart failure (n, %)	26 (41.9)	21 (60.0)	0.096
Coronary heart disease (n, %)	32 (51.6)	20 (57.1)	0.674
Pulmonary embolism (n, %)	10 (16.1)	0 (0.0)	0.012*
Atrial fibrillation (n, %)	15 (24.2)	7 (20.0)	0.802
Renal insufficiency (n, %)	16 (25.8)	15 (42.9)	0.113
Diabetes (n, %)	26 (41.9)	14 (40.0)	1.000
Hypertension (n, %)	43 (69.4)	24 (68.6)	1.000
Active tumor (n, %)	9 (14.5)	12 (34.3)	0.038*
Fracture (n, %)	14 (22.6)	5 (14.3)	0.428
Cerebral infarction (n, %)	25 (40.3)	20 (57.1)	0.139
Dementia (n, %)	15 (24.2)	10 (28.6)	0.638
Bed rest ≥ 3 days (n, %)	31 (50.0)	21 (60.0)	0.400
Gastrointestinal bleeding (n, %)	3 (4.8)	14 (40.0)	< 0.001*
High risk of bleeding score (n, %)	35 (56.5)	28 (80.0)	0.026*

Reexamination: DVT was examined by lower extremity venous ultrasound after discharge.
The normal distribution data was represented as mean ± standard deviation (SD) and analyzed by the independent samples t test. The count data was represented as number (%) and analyzed by the chi-squaretest.* p < 0.05 was considered statistically significant.

Active tumor is a confirmed risk factor for DVT.[15] In our cohort, we found 97 cases of active tumors, with a combined rate of 17.5%, including lung cancer (34 cases), colon cancer (10 cases), prostate cancer (22 cases), breast cancer (4 cases), lymphocytic tumor (8 cases), gastric cancer (3 cases), pancreatic cancer (3 cases), esophageal cancer (2 cases), kidney cancer (3 cases), rectal cancer (3 cases), bladder cancer (2 cases), liver cancer (1 case), and ovarian cancer (1 case). The high rate of tumor may be another reason for the high incidence of DVT in this group, but we found no significant difference between the DVT and non-DVT groups. This may be related to the small sample size of this single-center study, or to the complex clinical status of elderly patients with more complications.

In our study, hospital stays for patients in the DVT group were significantly longer than those for the non-DVT group (p = 0.005). DVT can lead to pulmonary embolism, which is life-threatening. Once the diagnosis of DVT is clear, effective treatment should be initiated, anticoagulant therapy being the main therapeutic option for DVT. Our study showed that the improvement rate and hospital mortality rate in the anticoagulant group were better than those in the non-anticoagulant group. However, only 62 patients (63.92%) with DVT received anticoagulant treatment, the rate of which was low, mainly related to the higher risk of bleeding in elderly patients. Sixty-three patients (64.95%) in the DVT group had a high risk of bleeding, including 17 patients with gastrointestinal bleeding, and these patients often cannot accept regular anticoagulation treatment. Gastrointestinal bleeding and high bleeding risk score in the non-anticoagulant group was significantly higher than that in the anticoagulant group. Another reason may be that 81 cases (83.51%) only involved the distal deep vein while 59 (60.82%) had no obvious DVT symptoms. This may lead to insufficient attention to the treatment of DVT by doctors and patients. It is easier for DVT patients with pulmonary embolism to accept regular anticoagulant therapy, and to a statistically significant extent. All ten patients with pulmonary embolism in our study received regular anticoagulant therapy.

During follow-up, the rate of continuous anticoagulant treatment was 48.39% at 3 months and only 30.65% at 6 months. Our results suggest that the proportion of pneumonia patients older than 75 years with DVT receiving regular anticoagulant therapy is very low because of the high risk of bleeding. Moreover, both the anticoagulant and non-anticoagulant groups had lower re-examination rates. This suggests that elderly patients with pneumonia/DVT and their families did not pay sufficient attention to the treatment of DVT, possibly because DVT is asymptomatic or mild in the elderly population. Clinicians may thus need to improve the management of elderly patients with DVT.

To summarize, elderly inpatients with pneumonia are at high risk of DVT. Additionally, we found that CHD, heart failure, hyperlipidemia, bed rest, and elevated D-dimer were independent risk factors for DVT. However, owing to the high risk of anticoagulant bleeding, the proportion of elderly inpatients with pneumonia and DVT receiving regular anticoagulant therapy is low.

5. Limitations of the study

First, the study was performed retrospectively. A prospective study may be better in deciding the risk factors for DVT in elderly inpatients with pneumonia. Second, although the clinical data of patients were included as far as possible, there were still other possible risk factors for DVT, such as smoking and obesity, which were not included in the study. Hence we suggest that a multi-center, large-scale, clinical study of similar design should be performed in the future.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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