

A Silent Threat: Deep Vein Thrombosis in Early-Stage Parkinson's Disease

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Introduction: The primary clinical manifestation of venous thrombosis is discomfort in the lower extremities. Some early Parkinson's disease (PD) patients feel discomfort in the lower limbs. Venous thrombosis can risk lives by causing pulmonary embolism. This study examines the incidence of DVT in early PD patients and its correlation with different clinical and lab features.

Methods: A cross-sectional study was conducted on 117 patients with early-stage PD. Ultrasonography was employed to detect the presence of DVT. Factors such as age, gender, body mass index, lifestyle habits (smoking and drinking), medical history (hypertension, diabetes, atrial fibrillation, and tumor), and other lab tests linked to thrombosis were analyzed.

Results: In 117 patients, 11 (9.4%) had DVT, while 106 (90.6%) did not. There were no significant differences in gender, BMI, habits, medical history, or other thrombosis-related tests between both groups. However, DVT patients were older with higher d-dimer levels. They also showed an increased right substantia nigra ultrasound echo area, higher HY grades, higher UPDRS 3 scores, less improvement in UPDRS 3 scores and levodopa response.

Discussion: The primary risk factors for lower extremity venous thrombosis were found to be age, d-dimer levels, and low-dose levodopa. Therefore, for elderly patients with early-stage PD, it is crucial to conduct d-dimer and lower extremity vascular ultrasound tests. The prevention of venous thrombosis in the lower extremities of early PD patients is of utmost importance.

Keywords: deep vein thrombosis, early-stage, Parkinson's disease, ultrasonography, risk

Background

Parkinson's Disease (PD) is a prevalent neurodegenerative condition among middle-aged and elderly individuals. The primary motor symptoms of PD encompass bradykinesia, muscle rigidity, resting tremor, and postural instability.¹ Most patients complain of bradykinesia, while a subset of newly diagnosed patients still complain of lower extremity swelling and pain.² The primary clinical symptoms of lower extremity venous thrombosis include leg swelling, discomfort, and superficial varicose veins.³ Although lower extremity deep vein thrombosis (DVT) is described as a disorder with abnormal clots of lower extremity venous thrombosis,⁴ a subset of patients is unable to recognize them as quickly as possible due to the lack of corresponding clinical signs and symptoms. Patients face significant risk if a thrombus dislodges and precipitates a pulmonary embolism.⁵ The incidence of DVT has been reported to be approximately 0.16% in the general population,⁶ while the incidence of DVT is notably higher in patients with Parkinson's Disease (PD) compared to the general population.⁷

Advanced PD patients with postural imbalance, especially during bedridden, are at significantly increased risk of venous thrombosis of the lower extremities.⁸ A series of abnormal muscle contractions caused by bradykinesia and increased muscle tone in early PD patients may also limit the pumping function in the lower extremity muscles, resulting

in impaired venous return.⁹ It has been documented that the contraction-relaxation cycle of the muscle pump promotes the return of venous blood. When the function of the muscle pump is compromised, stagnation of blood flow occurs between the venous valves and the blood vessel wall. This can subsequently lead to thrombosis. A significant increase in the probability of thrombosis and the rate of thrombus growth can be shown.⁹ In addition, a series of abnormal muscle contractions caused by increased muscle tone limits muscle pump function, attributing to impaired venous blood return and leading to the formation of venous blood clots. DVT can also develop into chronic pain, leg vein ulcers, and long-term disability with post-thrombotic syndrome.¹⁰ Abnormal blood flow can result in conditions such as paresthesia and pain, subsequently leading to a diminished quality of life. This phenomenon also plays a significant role in the manifestation of non-motor symptoms.

Moreover, DVT in the lower extremities may potentially lead to pulmonary embolism, a condition that escalates mortality rates among patients.¹¹ If early prophylaxis and intervention for lower extremity venous thrombosis are implemented, it could enhance the social functionality and quality of life in Parkinson's disease (PD) patients, while significantly reducing their mortality risk. Taken together, DVT is an important factor in the progression of PD, but there is insufficient reported evidence related to its risk factors.

This study aimed to evaluate the incidence of lower extremity venous thrombosis in early-stage PD, possible clinically relevant risk factors for developing DVT in patients with early PD (age, gender, years of onset, body mass index, smoking and alcohol habits, etc), test results (lipids, glucose, D-dimers, and platelets, etc), dyskinesia, and medication factors (on- and off-phase motor scores, Hoehn-Yahr (H-Y) staging, and improvement rate on the methyldopa loading test, etc). Notably, our study may contribute to compensating for the lack of research on risk factors for venous thrombosis in early PD. Additionally, our investigation may also improve the progression in PD patients through early prevention and treatment.

Materials and Methods

Patients

This was a cross-sectional study involving a total of 197 cases. The study population comprised of patients diagnosed at Huzhou Central Hospital between November 2020 and July 2023, including 117 with PD and 80 without PD. The basic information of all participants was recorded, including age, gender, and past medical history. All enrolled patients and their families signed informed consent forms before the study. The inclusion criteria of this study included: (1) The patients' diagnoses met the standard of the 2015 International Clinical Diagnostic criteria for Parkinson's disease, and the patient who met the PD diagnosis was classified as H-Y 1–2.5 stage. (2) The patient signed an agreement to participate in the program. Conversely, the exclusion criteria were: the patients had (1) an active malignancy; (2) previous venous thromboembolism; (3) immobilization rest for more than 3 days due to physical reasons; (4) thrombophilia or blood system diseases; (5) acute myocardial infarction, heart failure; (6) acute cerebral infarction; (7) acute respiratory failure; (8) acute infection or rheumatic disease; (9) hormones application; (10) cognitive disorders.

Assessments

Patients were evaluated after admission, including laboratory tests, ultrasound, and scale assessment. For laboratory tests, SYSMEX XN-9000 Hematology Analyzer, and supporting reagents were used for routine blood testing. Abbott c16000 biochemical analyzer and matching reagents were used for biochemical tests. The coagulation function was measured by ACL TOP 750 LAS coagulation analyzer and matching reagents. Scales included the Hoehn-Yahr (H-Y) stage, the Unified Parkinson's Disease Rating Scale (UPDRS) 3 in off and open stage, the improvement rate in UPDRS 3 on treatment with levodopa, and daily levodopa equivalent dose (LED). Assessments were performed by physicians with uniform training criteria.

Ethics Approval and Consent to Participate

All research works were carried out by the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans and were approved by the Medical Ethics Committee of Huzhou Central Hospital

(number 20200907–01). All subjects signed informed consent forms and were fully informed of the details of the study, including their rights and possible benefits and risks.

Ultrasound Examination

All patients with lower limb vascular were ultrasound using Canon (Japan), and Toshiba Aplio i900 high-grade ultrasound machines (probe for i18LX5 linear array probe, the frequency of 8 to 12 MHz). Ultrasonic diagnostic criteria for DVT:³ deep vein in lower limb crus side tube cavity acoustic, visible hypoechoic or low echo mass packing, color Doppler ultrasound display tube cavity no blood flow signals or tube cavity filling defect. The midbrain substantia nigra ultrasound was performed using the phase-array probe i6sx1 of the instrument Japan Canon Aplio i900 ultrasound diagnostic instrument (2.6MHz, depth 14–16), dynamic range 45–55dB. The probes were placed in the left and right temporal Windows (off to the skin and parallel to the auricle-orbital line) in the left and right lateral decubitus position for sector scanning, and the standard section was obtained. The images were frozen and magnified to observe and measure each structure.

Statistical Analysis

Basic information on participants was presented as mean values (standard deviations) for continuous variables and as numbers (percentages) for categorical variables. Differences among these variables were assessed using the Chi-square test at 1 degree of freedom, as appropriate. The *t*-test was used for comparison between the two groups. In the cross-sectional study, simple linear regression analysis models were used to evaluate the associations between H-Y stage, improvement rate, scores of UPDRS3 off and UPDRS3 open, LED level, D-D Level and the course of age and duration in with DVT patients. In the cross-sectional study, multiple logistic regression models were used to evaluate the associations between H-Y stage, improvement rate, scores of UPDRS3 off and UPDRS3 open, LED level, D-D Level, age and duration for with DVT PD-early patients.

All data were analyzed using SPSS version 22.0 statistical software. A two-sided *p*-value < 0.05 was perceived as statistically significant. Results were presented as mean ± SEM.

Results

The Lower Extremity Deep Venous Thrombosis in DVT

Patients who complained of lower extremity swelling and pain were examined at the time of presentation for lower extremity arterial ultrasound to rule out thrombotic factors (*n*=197). Of note, the lower extremity arteriovenous ultrasound was detected in early PD patients with DVT (*n*=11, 9.4%) but not seen in early PD patients without DVT (*n*=106, 90.6%) (Figures 1 and 2). The results suggested the lower extremity deep venous thrombosis appears with DVT.

Significant Differences Between Early PD Patients with or without DVT

In a total of 117 cases of early-stage PD, 11 cases were detected with DVT and 106 cases without DVT. There were no differences between early PD patients with or without DVT in basic clinical features in terms of gender, years of experience, body mass index, alcohol and tobacco use, history of hypertension, diabetes, atrial fibrillation, or tumor. However, the comparison we observed showed that PD patients with concomitant DVT exhibited an age-correlated increase in D-dimer levels, a laboratory marker associated with thrombosis, whereas no significant differences were noted in other laboratory assays. Simultaneously, the nigrostriatal ultrasound revealed that the echo area of the right nigrostriatal region was significantly larger in patients diagnosed with DVT. There was no significant difference between the echo area of the left nigrostriatal ultrasound and the ultrasound width of the third ventricle. PD-related evaluation measures further indicated that patients with DVT were associated with a higher HY classification and elevated UPDRS 3 off-phase scores. However, the UPDRS 3 score in the open phase and the improvement rates in UPDRS 3 on treatment with levodopa were lower. The dose of levodopa used for treatment in patients with DVT was significantly reduced, which was summarized in Table 1. The difference is illustrated in Figure 3. The data indicated that early-stage PD patients are typically older, exhibit higher levels of d-dimer, and have significantly higher UPDRS 3 off-phase scores.

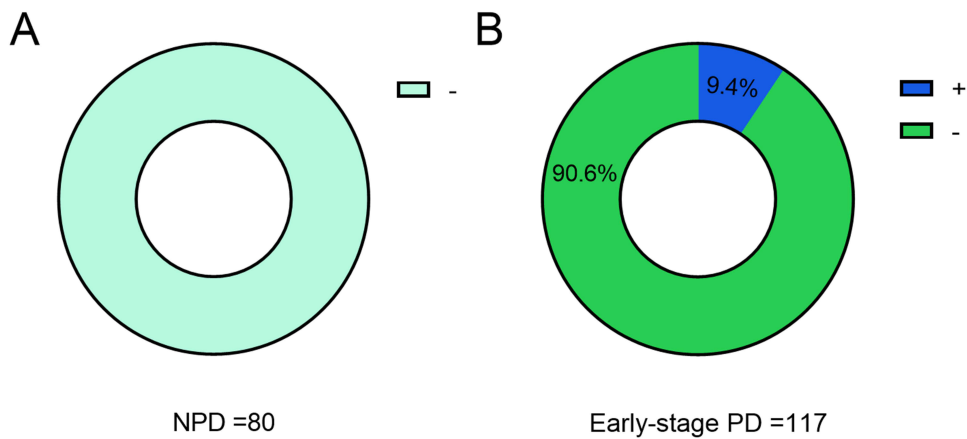


Figure 1 The incidence of DVT in early-stage PD. (A) Patients without PD (80 cases) did not see DVT; (B) In patients with early-stage PD (117 cases), DVT was visible in 11 cases.

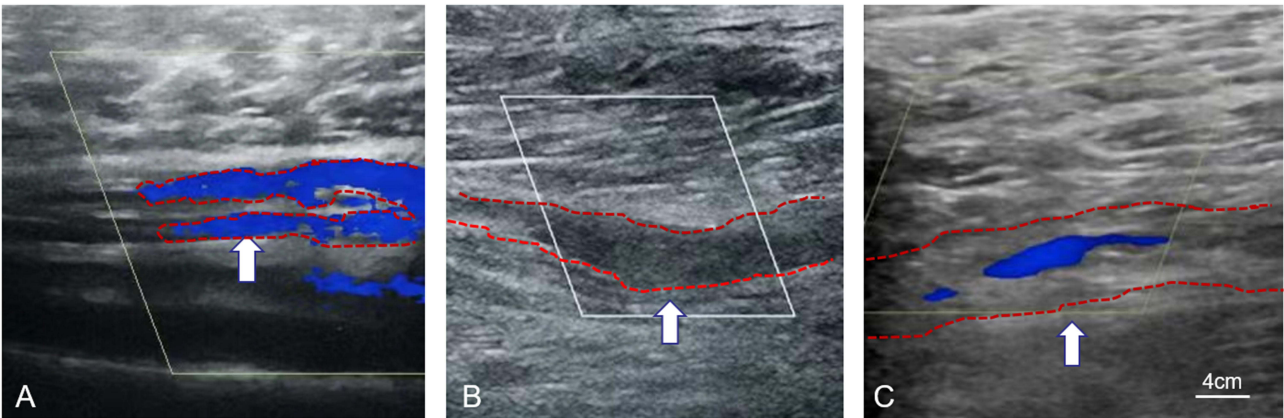


Figure 2 Representative diagrams of color Doppler ultrasound (CDFI). (A) Normal picture, color CDFI lower limb calf lateral deep vein lumen filled with blood flow signal; (B) DVT diagram, hypo echo-phore filling was seen in the lumen of the deep vein on the lower leg side, and no obvious blood flow signal was seen in CDFI; (C) DVT diagram, the echo-phore attached to the tube wall was seen in the deep vein of the lower leg side, and the blood flow filling defect was seen in the CDFI lumen. The white arrows indicate the color Doppler sampling frame we selected. The red areas represent intermuscular veins running. The scaler bar is 4 cm.

Risk Factors Associated with DVT in Early-Stage PD Patients

A binary logistic regression analysis was performed to analyze the risk factors associated with DVT in patients with early-stage PD. The analysis revealed clinical basic characteristics including gender, years of disease, body mass index,

Table 1 Over All Clinical Findings in the LEVT-Positive and Negative Early-Stage PD Patients

	LEVT (+)	LEVT (-)	P value
Case Numbers	11	106	
Age(year)	75.09 ± 1.124	66.36 ± 0.74	0.001*
Gender (F:M)	2.67	0.8	0.073
BMI	23.34 ± 1.01	23.54 ± 0.25	0.812
Duration(year)	3.86 ± 0.86	2.8 ± 0.29	0.267
H-Yahr stage	2.36 ± 0.07	1.82 ± 0.05	0.002*
LED (mg/day)	246.6 ± 42.44	299.8 ± 15.07	0.274
History of Hypertension (HTN)	7(63.3%)	50(47.17%)	0.298
History of Diabetes Mellitus (DM)	2(18.2%)	13(12.26%)	0.576

(Continued)

Table 1 (Continued).

	LEVT (+)	LEVT (-)	P value
History of atrial fibrillation	0	3(2.8%)	0.572
History of smoke	1(9.09%)	13(12.26%)	0.758
History of wine	0	14(13.21%)	0.199
History of cancer	1(9.09%)	2(1.89%)	0.15
Triglyceride (TG, mmol/L)	1.1 ± 0.12	1.37 ± 0.09	0.308
Cholesterol(mmol/L)	4.27 ± 0.22	7.06 ± 2.83	0.729
Blood platelet (PLT, 10 ⁹ /L)	181.9 ± 17.46	183.0 ± 5.77	0.638
D-dimer (DD, mg/L)	1.41 ± 0.6	0.49 ± 0.06	0.001*
Activated partial thromboplastin time (APTT, s)	30.08 ± 0.56	29.02 ± 0.26	0.183
Substantia nigra echo area left (cm ²)	0.12 ± 0.05	0.12 ± 0.02	0.74
Substantia nigra echo area right (cm ²)	0.20 ± 0.06	0.1 ± 0.01	0.048*
Diacele echo length (cm)	0.95 ± 0.51	0.49 ± 0.03	0.344
UPDRS3(close)	53.09 ± 5.08	34.58 ± 1.8	0.002*
UPDRS3(open)	40.91 ± 4.53	23.08 ± 1.45	<0.001*
Improvement rate (%)	22.6 ± 3.73	35.63 ± 1.66	0.015*

Notes: Data are presented as the mean ± SEM. *P < 0.05.

tobacco and alcohol addiction, hypertension, diabetes, atrial fibrillation, and tumor were not risk factors for lower limb venous thrombosis, except for age. Older patients were associated with a higher risk of DVT (Table 2). There was a significant difference in the content of d-d dimer, and higher levels of d-d dimer were associated with a higher risk of

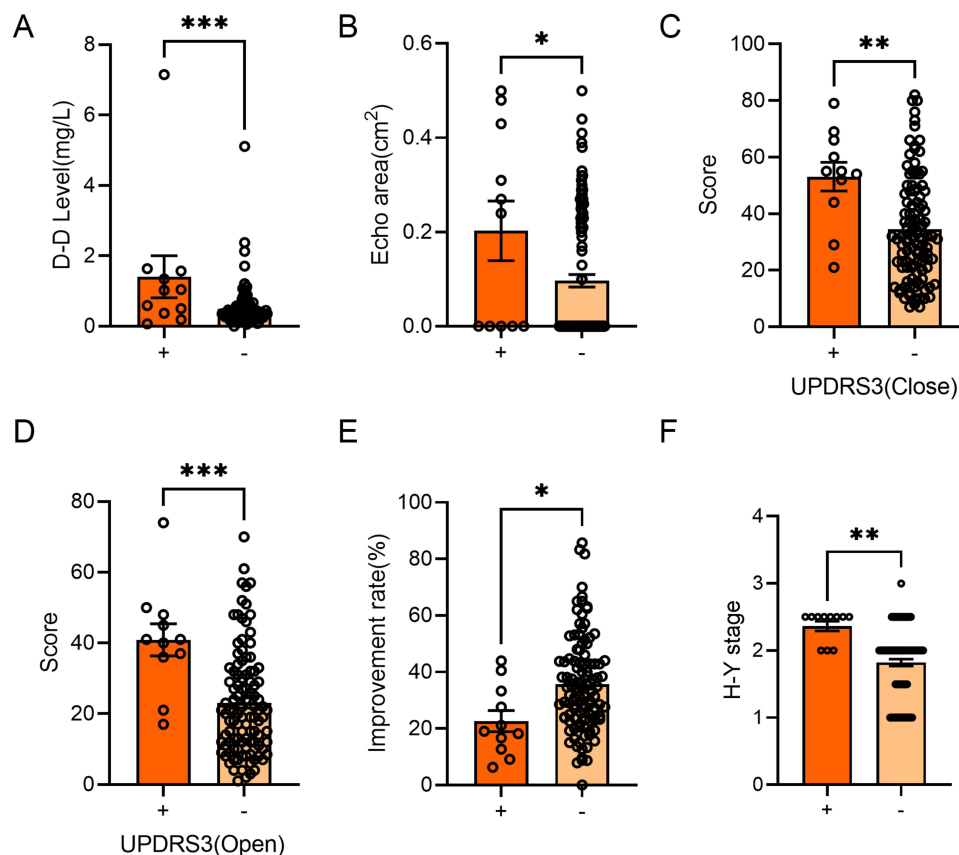


Figure 3 Clinical findings in the DVT positive and negative early-stage PD patients. D-D Level (A), SNR echo area (B), scores of UPDRS3 off (C) and UPDRS3 open (D), improvement rate (E), and H-Y stage (F) was a significant change in DVT positive early-stage PD patients. +, DVT positive early-stage PD patients, 11 cases; -, DVT negative early-stage PD patients, 106 cases. Data are presented as the mean ± SEM. *P < 0.05; **P < 0.01, ***P < 0.001.

Table 2 Binary Logistic Regression Analysis in Relation to LEVT About History

	Odds Ratio	95% CI	P value
Age(year)	1.393	1.122–1.728	0.003*
Gender	0.391	0.065–2.333	0.303
BMI	1.115	0.849–1.464	0.433
History of HBP	0.464	0.088–2.438	0.364
History of DM	0.584	0.056–6.078	0.653
History of atrial fibrillation	61876825.7	0	0.999
History of smoke	0.514	0.018–14.608	0.697
History of wine	66128790.47	0	0.998
History of cancer	0.055	0–7.669	0.25

Notes: Data are presented as the mean $\pm$ SEM. *P < 0.05.

DVT. Other laboratory assessments, including nigrostriatal ultrasound (Table 3), HY staging, UPDRS “on-off” phase scores, and the rate of improvement in UPDRS 3 with levodopa therapy, showed no significant differences between patients with or without DVT. Therefore, these factors were not considered as risk factors in the Parkinson’s disease-related assessment metrics. While HY grading showed an indicative trend for the risk of DVT, the concentration of levodopa used in treatment in our study was a risk factor for DVT (Table 4). Therefore, the results suggested that both age and d-d dimer content levodopa dosage are the essential risk factors for DVT.

Correlation of disease duration, age, d-d dimer content, scale evaluation, and LED concentration in early-stage PD patients

In patients with early PD, disease duration was positively correlated with HY grading, UPDRS switching phase score, and LED dose, and was not significantly correlated with d-d dimer levels and improvement rates on the medroxyprogesterone test

Table 3 Binary Logistic Regression Analysis in Relation to LEVT About Examinations

	Odds ratio	95% CI	P value
TG (mmol/L)	0.591	0.182–1.923	0.382
Cholesterol(mmol/L)	1.001	0.882–1.136	0.986
PLT (10 ⁹ /L)	1.001	0.990–1.013	0.831
D-D(mg/L)	1.936	1.005–3.729	0.048*
APTT(s)	1.237	0.919–1.667	0.161
Substantia nigra echo area left (cm ²)	0.229	0.002–29.810	0.553
Substantia nigra echo area right (cm ²)	41.252	0.466–3653.656	0.104
Diacele echo length (cm)	0.31	0.028–3.422	0.339

Notes: Data are presented as the mean $\pm$ SEM. *P < 0.05.

Table 4 Binary Logistic Regression Analysis in Relation to LEVT About Drugs and Its Efficacy

	Odds Ratio	95% CI	P value
Duration(year)	1.056	0.831–1.343	0.656
H-Yahr stage	10.6	0.956–117.552	0.054
LED (mg/day)	0.993	0.987–0.999	0.031*
UPDRS3(close)	1.203	0.893–1.621	0.224
UPDRS3(open)	0.817	0.560–1.192	0.294
Improvement rate (%)	0.853	0.686–1.062	0.156

Notes: Data are presented as the mean $\pm$ SEM. *P < 0.05.

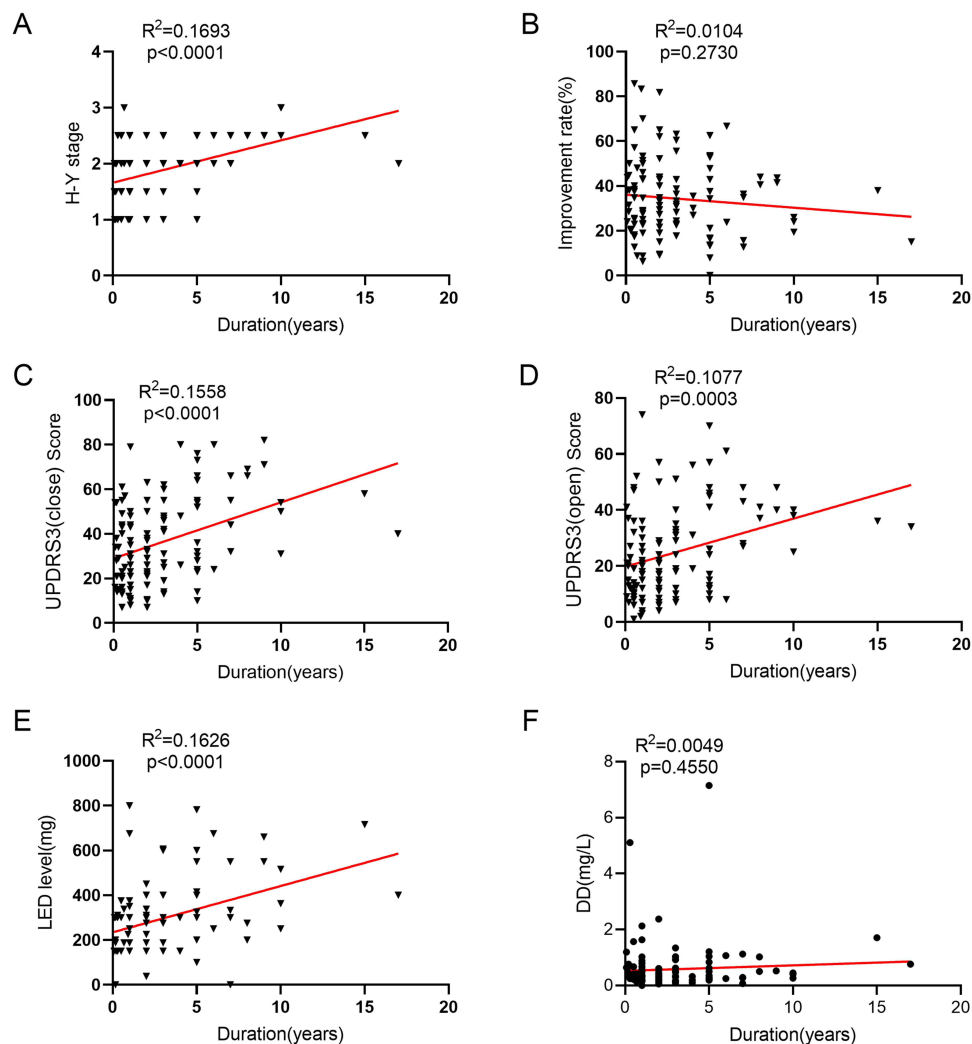


Figure 4 Early PD patients in the course of duration and H-Y stage (A), improvement rate (B), scores of UPDRS3 off (C) and UPDRS3 open (D), LED level (E), and D-D Level (F) of relevance. The red line represents the trend line. The ordinate represents the corresponding index. The abscissa is duration. N=117. P value and the correlation coefficient in the top left corner of the picture.

(Figure 4). Differently, age was positively correlated with d-d dimer content, HY grading, and UPDRS switching period scores, but negatively correlated with the improvement rate in UPDRS 3 on treatment with levodopa in early-stage PD patients. Interestingly, there was no significant correlation between age and LED concentration (Figure 5). Taken together, it is clear that the dosage of LED does not have a significant effect on the duration of the disease. When the earlier PD is detected, the earlier treatment has a more significant effect on drug improvement.

Discussion

Deep vein thrombosis (DVT) is often predisposed to by advanced age, fractures, breaking, pregnancy, malignancy, and use of oral contraceptives. It has been reported that the common disease of peripheral blood vessels is caused by abnormal blood clotting blocking the deep vein vascular lumen, resulting in venous return obstruction.¹² Thus, acute stroke has a high risk of DVT, in which limb weakness, immobility, and even bed ridden ness are risk factors for the development of lower extremity deep vein thrombosis in neurological diseases.⁸ The incidence of DVT in acute stroke patients is 45%, and the incidence of DVT in severe hemiplegia patients is as high as 60%~75%.¹³ It is important to note that patients with advanced PD may be at risk of developing DVT because balance disorders can drastically reduce their

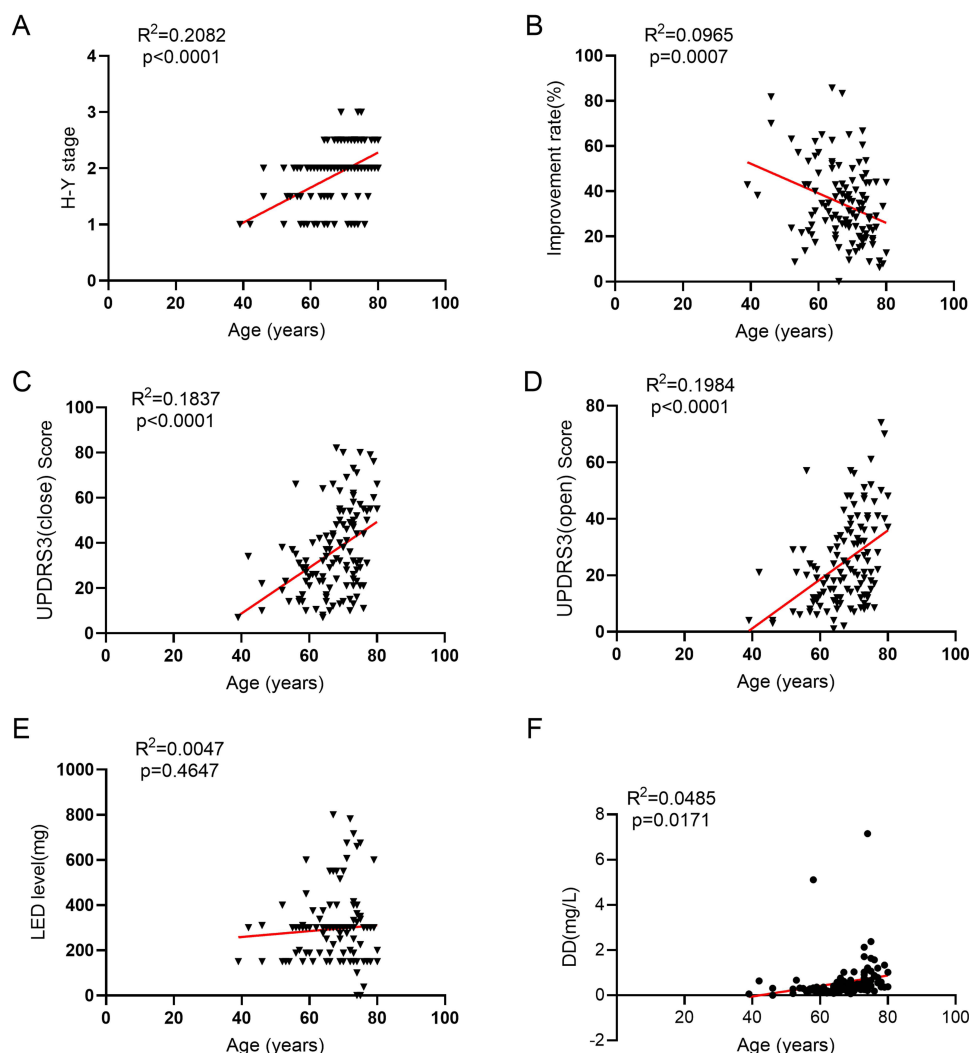


Figure 5 Early PD patients in the course of age and H-Y stage (A), improvement rate(B), scores of UPDRS3 off (C) and UPDRS3 open (D), LED level(E), and D-D Level(F) of relevance. The red line represents the trend line. The ordinate represents the corresponding index. The abscissa is age. N=117. P value and the correlation coefficient in the top left corner of the picture.

mobility and may even require wheelchairs or even bed rest.⁷ However, early-stage PD patients with DVT are now rarely reported. Therefore, our study aims to analyze risk factors for early-stage PD with DVT.

We have discovered that the incidence of DVT was as high as 9.4% in patients with early PD, while no DVT occurred in patients without PD. Older adults were more likely to develop DVT, while gender, age of onset, body mass index, tobacco and alcohol addiction, hypertension, diabetes, atrial fibrillation, and tumors were not associated with the development of DVT. These results suggested that patients with lower-extremity venous thrombosis had higher levels of d-d dimer, with no differences in other laboratory tests associated with thrombosis. The earlier PD is detected and treated, the more dramatic the improvement of the medication. Similarly, we found that the right nigrostriatal ultrasound echo region was significantly higher in patients with lower extremity venous thrombosis, whereas the left nigrostriatal ultrasound echo region was not significantly different from the third ventricle ultrasound width. Patients with lower extremity venous thrombosis have a higher HY stage, higher UPDRS 3 off-phase scores, lower open-phase UPDRS 3 scores, and the improvement rate in UPDRS 3 on treatment with levodopa, suggesting the worse the motor function, the greater the likelihood of developing DVT. The dosage of levodopa (LED) used in therapy is significantly lower in patients with lower extremity venous thrombosis. A dichotomous logistic regression analysis was performed to analyze the associated risk factors in this study. The results showed that age, content of d-d dimer, and low levodopa dosage are

the main risk factors for lower extremity venous thrombosis. The results of linear correlation analysis suggested that the dosage of LED has no significant effects on the duration of the disease. The earlier PD is detected and treated, the more dramatic the improvement of the medication.

Patients with cancer have a 4~7-fold increased risk of DVT compared to healthy individuals.¹⁴ In this study, the presence of cancer in the early stages of PD did not show any significant difference in the occurrence of DVT. While most epidemiological studies suggest an inverse relationship between the risk of developing neurodegenerative diseases and cancer, there is growing evidence indicating a positive correlation between specific types of cancer and PD.¹⁵ Out of the 28 genetic variants associated with Parkinsonism, six were also linked to cancer.¹⁶ The association between DVT and tumors in early PD patients requires further exploration.

Patients with early-stage PD do not have balance disorders, but bradykinesia, myotonia, and increased muscle tone in the limbs are the core symptoms.¹⁷ Myotonia is a bidirectional resistance throughout the entire range of motion and may involve simultaneous contraction of both active and antagonistic muscles. A series of abnormal muscle contractions caused by increased muscle tone limits muscle pump function, leading to impaired venous blood return, resulting in the formation of venous blood clots.¹⁸ Motor retardation encompasses muscle weakness, rigidity, tremor, motor variability, and slowed cognition. Physiological differences in EMG activity between patients and healthy subjects suggest that the dynamics of voluntary contraction may be organized differently than usual.¹⁹ The differences manifested in the contractile function of their muscle pumps were also affected.⁹ Consequently, bradykinesia contributes to an elevated risk of thrombosis. Accordingly, our research implies a pathophysiological foundation for the development of lower extremity venous thrombosis in patients with early-stage PD.

At the same time, we have found that all DVT in patients with early PD is distal DVT below the knee. Distal deep vein thrombosis is a thrombosis isolated to the veins of the lower leg.²⁰ In contrast, the manifestations of deep vein thrombosis in the distal extremity are asymptomatic.²¹ In addition, it can be easily overlooked and requires early screening, detection, diagnosis, and treatment to avoid the possibility of dislodged blood clots leading to pulmonary embolism. Our study has also found that age is a risk factor for the development of DVT in patients with early-stage PD. The risk of lower extremity venous thrombosis escalates with patient age, despite previous studies not consistently supporting this correlation.⁷ It may be related to the stage of the disease course of the PD patients included in the target population. While the previous study included PD patients with whole H-Y stages, our study only included early-stage PD patients.

D-dimer is the most commonly used and simple biomarker for the evaluation of systemic venous thrombosis.³ Our study found that D-dimer was significantly higher in the DVT-positive group than in the DVT-negative group. D-dimer may also serve as a risk factor for the development of DVT in patients with early-stage PD, and it is therefore necessary to screen such patients for D-dimer. Yamane et al have reported results suggesting that D-dimer is not meaningful. D-dimer may be more important in predicting DVT in patients with early-stage PD. In the middle and late stages of PD, the pathological damage is wider and deeper, and the confounding factors are more complex, which may not be suggestive. We have also found that transcranial sonography in the DVT-positive group shows a large area of hyper-echogenicity in the substantia nigra on the right side. The reports and evidence of its correlation are not sufficient, and the reasons cannot be explained at present. It is necessary to increase the sample size to find more positive patients for analysis. However, this phenomenon suggested that we can perform transcranial ultrasound at an early stage and find that the substantia nigra echo is helpful to screen patients with positive DVT. In addition, although the binary logistics regression analysis in the H-Y stage was not statistically significant, there was a risk factor trend ($P=0.054$). The comparison between the DVT positive group and the DVT negative group suggests that the stage of the positive group was more advanced. Yamane et al⁷ reported that there was no significant correlation between the H-Y stage and DVT ($P=0.15$). It may be related to the fact that the patients he enrolled were in whole HY stages, while our study was in stages 1–2.5. The sample sizes of our two studies were different, but both were small and needed to be confirmed by more samples.

The UPDRS-3 scores in both the on and off phases do not suggest an association with DVT. The regression analysis of the correlation between drug treatment and DVT does not suggest that the UPDRS-3 scores are a risk factor. The results of linear correlation analysis suggested that the dose of LED has no significant effect on the duration of the disease. For earlier PD, the earlier treatment has a more significant effect on the improvement of drugs. At the same time, the levodopa equivalent dose is lower in the DVT-positive group, suggesting that higher doses of therapeutic drugs are

needed to improve motor symptoms and reduce the incidence of DVT. At present, thrombolysis,²² anticoagulation,²⁰ and intravascular therapy¹² are the main treatments for thrombosis. There is insufficient evidence about whether dopaminergic drugs reduce or treat DVT in early PD patients. There are also some limitations. The overall number of cases, especially the number of DVT-positive cases, is not enough. There is no classification of lower extremity deep vein thrombosis, which may have different risk factors in different types of thrombosis. Assessment of improvement in patients with post-treatment thrombosis is lacking. These aspects could be improved to get more objective results in the future. Oxidative stress and Wnt/ β signaling pathway play an important role in the formation of neurodegenerative diseases and thrombosis.^{23,24} To further explore the pathogenesis, pathology, and molecular mechanism behind DVT by using the relevant model of Parkinson's disease, to provide some basis for subsequent intervention.²⁵

Conclusion

In summary, we suggest that for early-stage PD, D-dimer test and lower extremity vascular ultrasonography are necessary for older patients. Early screening, early detection, early diagnosis, and early treatment are extremely important for early-stage PD patients to prevent the development of lower extremity venous thrombosis, which may avoid the occurrence of malignant events.

Data Sharing Statement

The data in this study are available upon request from the corresponding author.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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