

# Quality of Life Status and Influencing Factors Among Patients with Deep Vein Thrombosis

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**Objective:** The objective of the study was to describe the quality of life (QoL) status and investigate the influencing factors of QoL among patients with deep vein thrombosis (DVT).

**Methods:** A retrospective analysis at a single center was performed, and the clinical data of 161 patients with DVT admitted to West China Hospital of Sichuan University from June 2019 to June 2020 were collected with the Villalta scale, Hospital Anxiety and Depression Scale (HADS), and Chronic Venous Insufficiency Questionnaire (CIVIQ). The relationship between QoL and influencing factors, including characteristics, course of DVT, postthrombotic syndrome (PTS), psychological status, and behaviors, was analyzed by Student's *t*-test, analysis of variance and multiple linear regression.

**Results:** A total of 161 patients who completed all the questionnaires between 2019 and 2020 were included, and 110 patients (68%) were male. The mean QoL score acquired by the CIVIQ scale was  $74.18 \pm 8.44$ , and the results showed significant differences between patients of different ages, genders, behaviors and psychological statuses ( $P < 0.05$ ). Multiple regression analysis showed that age ( $P = 0.024$ ), negative mood ( $P < 0.001$ ), CCI index ( $P < 0.001$ ), PTS ( $P < 0.001$ ) and regular exercise ( $P = 0.002$ ) influenced the CIVIQ scale evaluation model, in which exercise regularly was a protective factor for QoL, and age, negative mood, CCI index and PTS were risk factors for QoL.

**Conclusion:** The QoL of DVT patients was impaired and associated with age, mood, CCI index and PTS. Regular exercise is beneficial for improving the quality of life of DVT patients.

**Keywords:** deep vein thrombosis, quality of life, influencing factors

## Introduction

DVT is the abnormal condensation of blood in a deep vein, typically in the lower leg,<sup>1</sup> which is known as VTE<sup>2</sup> combined with pulmonary embolism (PE). VTE is the main cause<sup>3</sup> of the global disease burden and is characterized by high morbidity and a high mortality rate. It can also cause bleeding, recurrent venous thrombosis, PTS, persistent breathing difficulties, pulmonary hypertension and other complications.<sup>4,5</sup> PTS develops in 40–60% of patients following a proximal DVT of the lower limb and results in chronic manifestations including pain, heaviness, swelling, itching, and ulcers.<sup>6</sup> While increasing the burden of medical expenses, the outcomes also have a substantial impact on the psychological and physical health, well-being, and daily functioning of patients, and threatens the life of patients following VTE.

Traditional measures of morbidity and mortality are limited in describe and quantify the impact of illness, particularly chronic illness, and various generic and disease-specific instruments have been constructed to assess the overall and multidimensional outcomes.<sup>7</sup> The increasing awareness of those chronic sequelae, together with an increased using of patient reported outcome measures to assess the impact of illness, has highlighted the utility of studying QoL in patients with DVT.<sup>8</sup>

According to the WHO, QoL is regarded as "... an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives, and in relation to his/her goals, expectations, standards and

concerns".<sup>9</sup> It is a broad-ranging concept, consists of individuals' physical health, social relationships, environmental, level of independence, psychological, and spiritual components, and used for the evaluation of patients' own health status and disease burden to reflect the clinical efficacy, disease prognosis and health economy. QoL is useful in medical decision making for ensuring improvement of the life domains who deems most important,<sup>10</sup> can fully and effectively reflect the patient's health status,<sup>11</sup> and also an outcome measure for chronic venous disease to allow for consistent reporting and comparison between studies.

The tools currently used to assess QoL among VTE patients include generic and disease-specific instruments. Studies before involving QoL assessment of DVT patients mostly adopt generic instruments such as the Medical Outcome Survey Short-Form 36 items (SF-36) and the Medical Outcome Survey Short-Form 12 items (SF-12),<sup>12</sup> which can be used irrespective of illness but may lack the sensitivity to capture disease specific aspects and to detect clinically-relevant changes over time. Therefore, disease-specific QoL measures is recommended in clinical trials.<sup>13,14</sup>

Studies have shown that scores of QoL in patients following DVT was significant lower comparing to population norms or matched controls with no history of DVT,<sup>15-17</sup> and QoL in patients with DVT for four months was impaired and comparable to patients suffering from chronic diseases of the heart, lung, or joints.<sup>18</sup> What's worse, compared to other patients with chronic vascular diseases (CVD), DVT patients seem to have poorer QoL.<sup>19,20</sup> However, a meta-analysis of patients with a history of DVT showed that QoL scores were comparable to population norms one year after an episode of DVT,<sup>21</sup> and a longitudinal study showed that QoL in patients following DVT improved over time.<sup>22</sup> Many studies have shown that PTS damages the QoL of patients following acute DVT.<sup>16,17,22,23</sup> Factors have been found to be associated with impaired QoL such as the course of disease, age, obesity, comorbidity, location and extent of the thrombus, and socioeconomic status, have been assessed to a limited extent and their association with impaired QoL has been inconsistent across studies.<sup>17,22,24,25</sup>

Due to cultural differences between homelands and abroad and because the assessment results of quality of life with the same tool may be different in different regions,<sup>26</sup> foreign research results cannot reflect the status in China. Therefore, the aim of this review is to present the status of QoL and associated factors among DVT patients in China. The results may contribute to design of a better management system for those patients and improve their QoL.

## Methods

### Participants

This cross-sectional study recruited DVT patients treated at West China Hospital, Sichuan University from June 2019 to June 2020. The inclusion criteria met the DVT diagnostic standards of standards for the diagnosis and efficacy of clinical diseases, and patients could be communicated with. The exclusion criteria were patients with mental disorders, cognitive disorders or incomplete medical records in the hospital information system.

### Sample Size

Based on the rule of thumb suggested by Harrell,<sup>27</sup> at least 10 subjects per variable in the linear regression model. With the Consideration of a 10% rate of invalid questionnaires, the sample size was estimated as 150.

### Data Collection

The data were collected after patient discharge from the hospital for 3 to 6 months. We collected age, gender, marital status, culture, occupation, family income, course of disease, and comorbidity through the hospital information system and investigated smoking history, exercise habits, Villalta scale, psychological status and quality of life through telephone interviews. Before telephone interviews, unified training should be conducted to standardize the language of the investigator, and then the investigator should explain the items of the Villalta scale and other questionnaires. The investigator should check whether the patient has corresponding symptoms and guide the patients to choose the options that accord with their own situation.

The definition of the criterion was as follows: smoking history refers to the existence of continuous smoking of cigarettes for 6 months or more.<sup>28</sup> Regular physical exercise was defined as 30 min of moderate exercise 3 times/wk.<sup>29</sup>

## Instruments

### Charlson Comorbidity Index (CCI)

The score standard refers to the CCI score of Roffman in 2016<sup>30</sup>, which involves 17 diseases.

### Villalta Scale

The Villalta scale was developed for the diagnosis, grading, prediction, and follow-up of postthrombotic syndrome (PTS),<sup>31</sup> which consists of five patient-rated venous symptoms (pain, cramps, heaviness, paresthesia, pruritus) and six clinician-rated physical signs (pretibial edema, skin induration, hyperpigmentation, pain during calf compression, venous ectasia, redness). The signs on the Villalta scale are scored from 0 (=absent) to 3 (=severe) and are summed for the total score (range 0–33). A total score <5 indicates no PTS, 5–9 points indicates mild PTS, 10–14 points indicates moderate PTS, and  $\geq 15$  points is classified as severe PTS.

### Hospital Anxiety and Depression Scale, HADS

The HADS is a 14-question instrument that measures anxiety and depression.<sup>32</sup> Each item is scored between 0 (no impairment) and 3 (severe impairment), with a maximum score of 21. A total score of anxiety/depression subscale  $\geq 8$  means that the patient has anxiety and depression, and total score of HADS  $\geq 9$  means that the patient is combined with bad emotions.

### The Chronic Venous Insufficiency Questionnaire, CIVIQ

The CIVIQ<sup>33</sup> contains 20 items, including four dimensions: level of pain (pain in ankle or legs, limitation in work or daily activities because of leg problem, sleep bad because of leg problem, the limitation because of leg problem in work or daily activities while standing for a long time), physical (the limitation because of leg problem in work or daily activities while climbing stairs, kneeling, walking briskly, and doing housework), social impairment (the limitation because of leg problem in work or daily activities while travel by car, bus or plane, going to discos, weddings, parties, cocktails, and doing exercises) and psychological (feeling nervous, tired, irritable, being a burden to others, embarrassed to show legs, difficult to get going in the morning, hard for long standing or stretching, limp, unwilling to go out). Each item is scored between 1 (most serious) and 5 (lightest), with a maximum score of 100. Higher scores represent higher QoL due to DVT, and a total score  $\geq 80$  is divided into groups with satisfactory QoL.

### Ethical Issues

All patients provided written informed consent, and the study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This study was approved by the research ethics committee of the hospital [2018-WCE10326].

### Data Analysis

SPSS ver. 24.0 (SPSS Inc., Chicago, IL, USA) was used, continuous variables were presented using the mean and standard deviation (SD) or median and interquartile range (IQR), while frequencies and percentages were summarized for categorical variables. Differences between groups were analyzed using Student's *t*-test or analysis of variance. Multiple linear regression was used to identify the predictive factors for the quality of life of patients with DVT, and a two-tailed *P* value of  $< 0.05$  was considered statistically significant for all analyses.

## Results

### Characteristics, Behaviors and Emotions of Participants

Of the 161 initially enrolled patients, 161 VTE patients, including 110 males and 51 females, completed the telephone evaluation, with a mean age of  $58.70 \pm 8.61$  years.

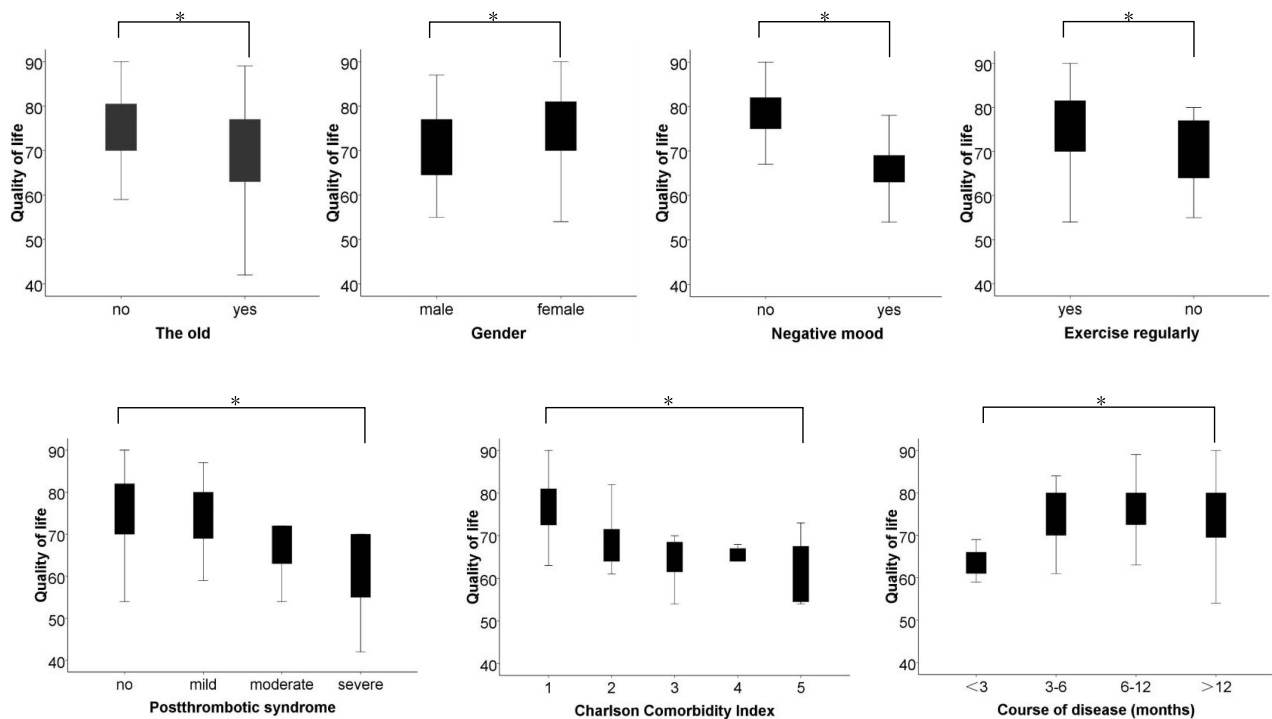
The average CIVIQ score was  $74.12 \pm 8.43$  among the patients (Table 1). Comparing the CIVIQ scores in patients with different degrees of education, marriage, complications, relapse, compliance, and smoking, there were no significant differences ( $p > 0.05$ ). Female patients had a higher CIVIQ score than male patients ( $p = 0.002$ ). Patients with severe

**Table 1** Characteristics of Study Subjects (n = 161)

Patient Characteristics	Median (IQR) <sup>a</sup> /Frequency (%)	CIVIQ Mean(SD)	t/F	P-value
<b>Age, years</b>	58.7(31.0–79.0)		4.738	< 0.001
<65 years	119	75.87±6.92		
≥65 years	42	69.14±10.25		
<b>Gender</b>			3.227	0.002
Male	110(68.3)	75.54±8.33		
Female	51(31.7)	71.06±7.88		
<b>Degree of education</b>			1.615	0.202
Primary school and below	68(42.2)	72.90±9.73		
Junior high school - High school (Technical high school)	67(41.6)	75.48±7.67		
Undergraduate degree and above	26(16.1)	73.81±6.05		
<b>Marital status</b>			0.412	0.689
Married	151(93.8)	74.19±8.42		
Unmarried	10(6.2)	73.00±8.88		
<b>PTS</b>			12.509	< 0.001
No	84(52.2)	75.85±8.24		
Light	59(36.6)	74.78±6.38		
Middle	10(6.2)	65.10±6.67		
Severe	8(5.0)	62.38±10.51		
<b>CCI index</b>			14.817	< 0.001
1	123(76.4)	76.51±6.84		
2	17(10.6)	67.18±9.28		
3	11(6.8)	67.45±9.56		
4	6(3.7)	65.67±1.63		
5	4(2.5)	61.00±8.43		
<b>Recurrence</b>			1.736	0.114
Yes	10(6.2)	69.20±11.30		
No	151(93.8)	74.51±8.10		
<b>Compliance</b>			0.129	0.869
Fine	77(47.8)	74.21±6.23		
Bad	84(52.2)	74.04±9.56		
<b>Smoke</b>			1.142	0.255
Yes	23(14.3)	72.26±9.44		
No	138(85.7)	74.43±8.24		
<b>Regular exercise</b>			3.437	0.001
Yes	42(26.1)	70.33±8.38		
No	119(73.9)	75.45±8.06		
<b>Course of disease</b>			7.384	< 0.001
<3 months	12(7.5)	63.92±9.97		
3–6 months	37(23.0)	74.32±7.44		
6–12 months	24(14.9)	76.25±7.96		
>12 months	88(54.7)	74.84±7.89		
<b>Negative emotions</b>			10.213	< 0.001
Yes	49(30.4)	66.12±6.29		
No	112(69.6)	77.62±6.89		
<b>CIVIQ</b>	74.1(42.0–90.0)			

**Notes:** Continuous variables are expressed as median with interquartile ranges. Discrete variables are expressed as number (%).

**Abbreviations:** PTS, post-thrombotic syndrome; CCI, Charlson comorbidity index; CIVIQ, the chronic venous insufficiency questionnaire; IQR, interquartile range<sup>a</sup>.



**Figure 1** Characteristics, behaviors and emotions of participants.

**Note:** \*Statistical significance ( $P < 0.01$ ) when comparing quality of life among patients with different characteristics, behaviors and emotion status.

PTS, alcohol intake, anxiety, depression, negative mood and without regular exercise had a lower CIVIQ score ( $p < 0.05$ , Figure 1).

## Influencing Factors of QoL in DVT Patients in Multivariable Analysis

Age, sex, PTS score, smoking history, irregular exercise, CCI index, course of disease and adverse mood conditions were used as independent variables, and the CIVIQ score was used as the dependent variable. The multivariate model indicated that age, negative mood, PTS degree, CCI index and regular exercise had significant associations with the QoL of DVT patients. Age had a negative effect on the CIVIQ score ( $\beta = 0.119$ ,  $P = 0.024$ ). Patients with negative mood ( $\beta = -7.776$ ,  $P < 0.001$ ), higher PTS degree ( $\beta = -3.316$ ,  $P < 0.001$ ), higher score of CCI index ( $\beta = -2.199$ ,  $P < 0.001$ ), longer course of DVT ( $\beta = 1.046$ ,  $P = 0.016$ ) and without regular exercise ( $\beta = -3.340$ ,  $P = 0.002$ ) were more likely to have worse quality of life (Table 2).

## Discussion

In line with other studies,<sup>34,35</sup> our results demonstrate significant impairment in QoL, and the mean CIVIQ score of 161 patients following DVT was  $74.12 \pm 8.43$ . A survey<sup>34</sup> including 100 DVT patients showed that the mean CIVIQ score of patients was 71.52 to 78.65. The mean CIVIQ score was 71.8–77.0 among 278 patients with acute DVT.<sup>35</sup> Female patients had a higher CIVIQ score than male patients, but sex was not a factor affecting quality of life. Giustozzi<sup>36</sup> and Utne<sup>17</sup> found a connection between QoL and sex in DVT patients with the EQ-5D and the Venous Insufficiency Epidemiological and Economic Studies - the quality of life/symptom (the VEINES-QoL/sym) questionnaire, respectively. We ascribe this disparity to the gender difference of the study populations.

Our results showed no connection between recurrence, marital status, educational level and QoL. Previous study<sup>37</sup> also indicated that recurrence is not related to the QoL of DVT patients, but some study<sup>26</sup> showed that recurrence is a predictor of QoL among VTE patients, which may be related to the different baseline data of these studies. Only 9 recurrent patients in this study were not able to indicate the relationship between recurrence and QoL. Wik<sup>25</sup> investigated 131 female patients with DVT using the VEINES-QoL/sym and found that education level and marital status were

**Table 2** Multiple Linear Regression for Influencing Factors of Quality of Life

Characteristics	$\beta$	SE	Beta	t	P	$\beta$ [95% CI]
Constant	88.421	4.158		21.267	< 0.001	80.206 to 96.635
Age	-0.119	0.052	-0.122	-2.279	0.024	-0.222 to -0.016
Negative mood	-7.776	1.090	-0.426	-7.132	< 0.001	-9.930 to -5.622
PTS	-3.316	0.557	-0.319	-5.952	< 0.001	-4.417 to -2.215
CCI index	-2.199	0.517	-0.249	-4.252	< 0.001	-3.221 to -1.177
Regular exercise	-3.340	1.058	-0.175	-3.158	0.002	-5.430 to -1.250
Course of DVT (years)	1.046	0.429	0.127	2.440	0.016	0.199 to 1.893
Gender	-1.056	1.036	-0.058	-1.019	0.310	-3.103 to -0.016

**Notes:** Gender (female=1, male=2), PTS (no=1, mild=2, moderate=3, severe=4); Course of DVT (within 3 months=1, 3–6 months=2, 6–12 months=3, longer than 12 months=4), Regular exercise (no=1, yes=2), Negative mood (no=1, yes=2),  $R^2=0.616$ ,  $F=26.891$ ,  $P<0.01$ .

**Abbreviations:** PTS, post-thrombotic syndrome; CCI, Charlson comorbidity index; CI, confidence interval.

independent predictors of decreased QoL. This may be associated with the inclusion of few women in this study, and further studies with larger sample sizes are recommended to analyze the correlation between sex, recurrence, marital status and education level and QoL.

Age is a factor that affects quality of life, which is consistent with previous studies. Monreal<sup>37</sup> also confirmed that age was associated with the QoL of DVT patients. In addition to the effects of aging of body functions, older people are more likely to suffer from comorbidities. The second factor affecting the QoL of DVT patients is depression, anxiety or negative mood. This is consistent with previous studies.<sup>38</sup> For patients, DVT is not only a life-threatening disease that may lead to pulmonary embolism (PE) but also may affect future work and life and increase the psychological burden of patients. Therefore, dynamic assessment of psychological status, early identification and intervention are needed, and comprehensive guidance and full health education are recommended to improve the psychological status of patients.<sup>39</sup>

Our data suggest that patients with severe PTS at have worse QoL scores, which is consistent with previous studies. There was a significant reduction in QoL with increased severity of PTS.<sup>26</sup> Utne<sup>17</sup> found that DVT patients with PTS have significantly lower QoL than those with no PTS and that PTS was a predictor of decreased quality of life with acute DVT. More often pain-, skin-, and psychiatric problems, and were more often on sick-leave were reported in cases who developed PTS, resulting in reduced physical tolerance for a day's work. PTS negatively affects patients' QoL and causes a significant burden on the healthcare system. These findings highlight the importance of early intervention and prevention of disease progression. In the other hand, DVT patient management should be graded in clinical practice, especially in the continuous management of patients. We should focus on patients with PTS and provide individualized health guidance to improve QoL.

Regular exercise was a predictor of QoL in DVT patients in our study, and the QoL was better among DVT patients with regular exercise. Regular exercise can improve patients' sports endurance and optimize brain-derived neurotrophic factor (BDNF), which has been implicated in individual emotions.<sup>40</sup> Participating in physical activities regularly can release stress, improve sleep conditions and eliminate negative moods, thus improving QoL.<sup>41</sup> Physical activity and exercise are inversely associated with depression levels, and increasing physical activity can improve QoL, so physical activity should be promoted more actively within clinical practice. We recommend aerobic exercise, such as walking and jogging, and encourage patients to exercise leg muscle strength, especially calf muscle strength.<sup>42</sup>

There are several limitations to this study. First, 68.3% of the patients were male and 6.2% of patients were unmarried, denoting a rather homogenous study population, which limited our ability to determine the potential effects of gender/spouse/recurrence characteristics in our analyses. In addition, patients were only sampled from Southwest China, which limits its external validity. Due to a lack of data in other areas, the sample may not be representative of general DVT patients in China. Despite this, our research has provided valuable new data on the relationships among the Villalta scale, emotion status, comorbidities, regular exercise and QoL measures, and the results may still be generalizable to patients from the areas mentioned above.

## Conclusion

The QoL of DVT patients is impaired. Age, negative emotions, PTS, CCI index and regular exercise were related to physical status. Early management, including health education, self-management in the whole course, psychological assessment at follow-up and personalized intervention aiming to improve the cognitive level of patients, could be enhanced to improve the QoL of DVT patients.

## Disclosure

All authors declare no competing interests in this work.

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