

## ORIGINAL ARTICLE

# Potential predictors of quality of life in patients with venous leg ulcers: A cross-sectional study in Taiwan

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## Abstract

Internationally, the impact of venous leg ulcers (VLUs) on the quality of life is well recognised; however, in Taiwan, the focus is only on chronic wound management. This cross-sectional correlational study conducted at the cardiovascular and plastic surgery clinics of a regional teaching hospital between August 2019 and June 2020 investigates venous clinical severity, pain, fatigue, depression, sleep quality, quality of life, and related factors among 167 patients with VLUs. The potential predictors of the quality of life in terms of activities were venous clinical severity ( $P < 0.001$ ), pain ( $P = 0.004$ ), and fatigue ( $P < 0.001$ ) after adjusting for covariates. The potential predictors of the quality of life in terms of the psychological domain were marital status (single/divorced) ( $P = 0.016$ ), marital status (widowed) ( $P = 0.027$ ), venous clinical severity ( $P < 0.001$ ), pain ( $P = 0.001$ ), and fatigue ( $P = 0.002$ ). The potential predictors of the quality of life with regard to symptoms were venous clinical severity ( $P < 0.001$ ), pain ( $P < 0.001$ ), fatigue ( $P = 0.001$ ), and depression ( $P = 0.038$ ). These potential predictors can serve as the basis of interventions for patients with VLUs, such as those related to nutrition or training in wound dressing.

## KEYWORDS

depression, fatigue, quality of life sleep, venous clinical severity, venous leg ulcers

## Key Messages

- most medical professionals in Taiwan concentrate on wound care rather than comprehensive care, and there is a lack of research on the quality of life of patients with venous leg ulcers

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- venous clinical severity, pain, and fatigue were the common potential predictors of the quality of life related to activities, psychological well-being, and symptoms
- these predictors explained 40%, 34%, and 54% of variance in the data, respectively

## 1 | INTRODUCTION

Venous leg ulcers (VLUs) account for 60%-80% of all chronic recurring leg ulcers, lasting anywhere from a matter of weeks to more than 10 years; however, prevalence varies across settings – it tends to increase with age and ranges from 0.12% to 1.03% in patients aged 70 years and over.<sup>1,2</sup> Management of the multiple causes of VLUs is an interdisciplinary challenge with major socioeconomic significance.<sup>3,4</sup> Patients with VLUs concurrently experience various psychoneurological symptoms including leg swelling, skin irritation, itchiness, pain, depression, fatigue, anxiety, and sleep disturbance.<sup>5-8</sup> Psychoneurological symptoms and the long-term continuation of the condition not only affect patients' quality of life but also limit disease self-management, functional status, and work patterns; indeed, many patients resort to early retirement.<sup>8-11</sup>

The impact of direct and indirect personal, financial, and social burdens is profound. For example, in the US health care system, the direct financial cost of treating VLUs resulting from wound infections, recurrences, and complication-related hospitalisations was \$14.9 billion in 2012, and the concurrent psychological symptoms, such as depression, fatigue, anxiety, and sleep disturbance, associated with venous ulceration also involve high management costs.<sup>12</sup> However, such estimations of financial costs do not include patients' costs and the indirect societal costs that result from absence from work.<sup>13</sup> Moreover, it is important to recognise that VLUs and their related burdens lower the patient's quality of life. As a patient's mental health may affect their ability to manage their overall health, following up on patients with VLUs, including inquiries into their psychological state, is of the utmost importance to ensure wound healing and good quality of life.<sup>14</sup>

In Western countries, the quality of life of patients with VLUs is given precedence.<sup>5-7,9,15-18</sup> However, in Taiwan, most medical professionals concentrate on treating the leg ulcer in isolation rather than examining the multiple factors resulting in poor quality of life. To ensure that the care provided to patients with VLUs helps improve their general quality of life, an initial step is to identify the factors associated with health-related quality

of life. At present, there is a lack of research on the quality of life of patients with VLUs in Taiwan. Therefore, the purpose of this study was to explore the variables of venous clinical severity, pain, fatigue, depression, and sleep quality, as well as their relationships with quality of life, in patients with VLUs.

## 2 | METHODS

### 2.1 | Research design and participants

This cross-sectional correlational study was conducted between August 2019 and June 2020. Most patients with VLUs visit an outpatient clinic on a monthly basis and care for their wound with compression therapy (ie, a bandage or compression stocking) to reduce swelling and improve venous return. Therefore, we gathered a sample of individuals with VLUs who attended the cardiovascular and plastic surgery outpatient clinics of a regional teaching hospital in middle Taiwan. The inclusion criteria were as follows: (a) physician-diagnosed VLUs; (b) clinical classification of C6 according to the Clinical, Etiological, Anatomical, and Pathophysiological Classification of Chronic Venous Disorders; (c) at least 20 years of age; and (4) clear consciousness, ability to communicate, willingness to participate in the study, and completion of the consent form. Patients were excluded if they had been diagnosed with cognitive impairment or had an ulcerating malignant tumour. The sample size was computed with a prior power analysis using G\* Power version 3.1.9.2. With a power of 80%, alpha of 0.05, effect size of 0.15, and seven predictors, the required sample size was calculated as 103.

### 2.2 | Instruments

#### 2.2.1 | Demographics

The demographic characteristics explored included age, gender, employment status, marital status, educational level, history of venous surgery, body mass index, ankle-brachial pressure index, and Charlson Comorbidity Index.

## 2.2.2 | Venous clinical severity score

Studies have confirmed the relationship between wound severity and quality of life in patients with VLUs.<sup>3,5,7</sup> Venous clinical severity was measured via the venous clinical severity score (VCSS), calculated based on 10 clinical symptoms and conditions including pain, varicose veins, oedema, skin pigmentation, skin hardening, inflammation, and compressive therapy. The total score ranged from 0 to 30 points, with 0 signifying a healthy status and 30 signifying the most severe condition. Statistical correlation was used to assess the validity of the VCSS. A total VCSS that significantly, moderately, and positively correlates with the Clinical, Etiological, Anatomical, and Pathophysiological Classification ( $r = 0.49$ ,  $P < 0.001$ ); moderately correlates with the Chronic Venous Insufficiency Quality of Life Questionnaire score ( $r = 0.43$ ,  $P < 0.0001$ ); or slightly positively correlates with the overall venous ultrasound findings (reflux + obstruction) ( $r = 0.23$ ,  $P < .0001$ ) may reflect that the VCSS is a thorough evaluation in comparison with other assessment tools for VLUs.<sup>19</sup>

## 2.2.3 | Visual analogue scale

The relationship between pain and reduced the quality of life in patients with VLUs has been confirmed.<sup>5,18</sup> A 100-mm visual analogue scale (VAS) was used to evaluate wound pain status. Each millimetre specifies one point on the pain scale; the higher the score, the greater the pain. The test-retest reliability of the VAS using the intra-class correlation coefficient was 0.9. The good-to-excellent correlation between the VAS and NRS ( $r = 0.941$ ) was indicative of concurrent validity.<sup>20</sup>

## 2.2.4 | Fatigue

The Vitality Checklist, a subscale of the Medical Outcomes Study Short Form-36 (SF-36; Taiwanese version), was used to investigate energy and fatigue status. The checklist comprises four items, namely “how much of the time during the past four weeks did you have a lot of energy?”; “...did you feel full of life?”; “...did you feel burnt out?”; and “...did you feel tired?” A five-point Likert scale was used, ranging from one (none of the time) to five (all of the time). Lastly, raw scores were transformed into a score between 0 and 100, with lower scores indicating greater fatigue. The SF-36 has well-established psychometric properties,<sup>15,21</sup> and scores under 45 indicate clinically significant fatigue.<sup>22</sup>

## 2.2.5 | Geriatric Depression Scale Short Form

The Geriatric Depression Scale Short Form (GDS-SF), developed by Sheikh and Yesavage in 1986, is widely used to measure depressive symptoms over the last week for older adults and also shows good diagnostic sensitivity and specificity for adults aged 18 years and older.<sup>23</sup> There are 15 items in total, ranging from 0 to 15 points; the higher the score, the more severe the patient's depression. A total score of 0-4 indicates no depressive symptoms, 5-9 depicts mild depressive symptoms, and 10-15 confirms severe depressive symptoms.<sup>24</sup> In a previous study, according to the Diagnostic and Statistical Manual (4th edition) diagnostic criteria, the GDS-15 had a sensitivity of 84% and specificity of 89%.<sup>25</sup> Two other studies showed that for the Chinese version of the GDS-SF, Cronbach's  $\alpha$  was 0.78 and 0.80, test-retest reliability was 0.83 over 2 weeks, split-half reliability was 0.71, and inter-rater reliabilities were 0.94 (intra-class) and 0.99 (Cohen's kappa).<sup>26,27</sup> Finlayson et al<sup>28</sup> and Edwards et al<sup>11</sup> both used the GDS-SF to examine patients with VLUs who did not qualify as older adults.

## 2.2.6 | Chinese version of the Pittsburgh Sleep Quality Index

Sleep quality in the previous month was investigated using the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI), which consists of seven items, with each scored on a four-point Likert scale (0-3 points). The possible scores range between 0 and 21 points, with a total score of 5 or higher indicating poor sleep quality. In a previous study, the overall Cronbach's  $\alpha$  for the CPSQI was 0.83, and the test-retest reliability was 0.77-0.85.<sup>29</sup>

## 2.2.7 | VLU Quality of Life questionnaire

The VLU Quality of Life (VLU-QoL) questionnaire was used to investigate the quality of life in the previous 4 weeks. The VLU-QoL includes 34 symptoms classified into three domains: activities, psychological, and symptom distress. The total score for each domain is 0-100 points. The higher the score, the worse the patient's quality of life. Cronbach's  $\alpha$  for each domain was 0.85, 0.83, and 0.86, respectively.<sup>30</sup> Notably, Gu, Liu, and Xia translated the VLU-QoL questionnaire into simplified Chinese.<sup>31</sup> Cronbach's  $\alpha$  for this version was 0.94, inter-expert reliability was 0.84, and test-retest reliability was 0.83.<sup>31</sup> In this study, Cronbach's  $\alpha$  of the scale was 0.95, and the 21-day test-retest reliability was 0.98.

## 2.3 | Procedure

The institutional review board of the concerned hospital (IRB no. 2019048) approved this project. After receiving an explanation of the study's purpose and procedure, interested patients provided written informed consent. At the time of enrolment, participants' demographic data were obtained, and VCSS, pain status, fatigue, depressive symptoms, sleep quality, and quality of life were determined.

## 2.4 | Statistical analysis

Data were analysed using SPSS version 24.0 for Windows (IBM Corp., Armonk, NY, USA);  $P < 0.05$  was considered statistically significant. The descriptive statistics (ie, mean, standard deviation, frequency distribution, proportions) and inferential statistics (ie, independent sample  $t$ -tests, one-way analysis of variance, chi-squared tests, Pearson's product-moment correlation analysis, and multiple regression analysis) were used to scrutinise differences in measurement variables in terms of demography, assess the relationships between the measurement variables, and investigate the potential predictors of the quality of life.

# 3 | RESULTS

## 3.1 | Demographics and differences in the three VLU-QoL domains

Altogether, 167 patients with VLUs participated in this study; there was no refusal. The mean age of the participants was  $67.08 \pm 14.25$  years (31-99 years), 86 (51.5%) were women, 108 (64.7%) were unemployed, 107 (64.1%) were married, 61 (36.5%) had received only primary school education, and 124 (73.4%) had no history of venous surgery. The mean scores for the VCSS, pain VAS, SF-36 (fatigue), GDS-SF, and CPSQI were  $14.93 \pm 4.18$ ,  $41.74 \pm 29.14$ ,  $51.50 \pm 12.91$ ,  $2.76 \pm 3.48$ , and  $5.49 \pm 3.65$ , respectively. A majority of the participants (132, 79%) had no symptoms of depression (0-4 points), and more than half (84, 50.3%) reported good sleep quality. The scores for the three domains of the VLU-QoL were  $69.03 \pm 19.78$  for activities,  $63.03 \pm 19.43$  for psychological features, and  $47.08 \pm 21.50$  for symptom distress.

We initially inspected the patients' VLU-QoL scores for the activity domain. Unemployed patients scored higher than employed patients ( $t = 2.29$ ,  $P = 0.023$ ), clarifying that the quality of life in terms of unemployed

patients' activities was poorer. The score varied statistically across GDS-SF categories, and Scheffe's post hoc test indicated that the VLU-QoL (activities) score of patients with mild depressive symptoms was higher than that of those without depressive symptoms ( $F = 13.84$ ,  $P < 0.001$ ). Subsequently, we examined the VLU-QoL scores for the psychological domain. A statistically significant association with marital status was noticeable, which showed that single/divorced patients had higher scores than widowed patients ( $F = 4.80$ ,  $P = 0.009$ ) after Scheffe's post hoc test. Finally, we scrutinised the VLU-QoL scores for the symptom distress domain. The score was higher for men than women ( $t = 2.10$ ,  $P = 0.037$ ), indicating that the quality of life in terms of symptom distress was poorer for men. Table 1 presents the participants' demographic characteristics and differences in the three VLU-QoL domains.

## 3.2 | Correlations between demographics and the three VLU-QoL domains

### 3.2.1 | VLU-QoL: activities domain

There was a positive correlation between the activities score and the Charlson Comorbidity Index ( $P = 0.036$ ), VCSS ( $P < 0.001$ ), VAS ( $P < 0.001$ ), and CPSQI ( $P < 0.001$ ) scores, confirming that the more comorbidities patients had, the higher the venous clinical severity, the greater the pain experienced, and the poorer the sleep quality and quality of life. The activities score was negatively correlated with the SF-36 (fatigue) score ( $P < 0.001$ ), highlighting that patients with the most fatigue had the worst quality of life. Hence, the quality of life with respect to activities was poorer in patients with mild depressive symptoms.

### 3.2.2 | VLU-QoL: psychological domain

This correlation verified that the quality of life for the psychological domain was poorer for single/divorced patients compared with widowed patients. There was a positive correlation between the psychological domain score and the VCSS ( $P < 0.001$ ), VAS ( $P < 0.001$ ), and CPSQI ( $P = 0.005$ ) scores, demonstrating that the worse the venous clinical severity, the greater the pain felt by the patients, and the poorer the sleep quality and quality of life. The psychological domain score was negatively correlated with the SF-36 (fatigue) score ( $P < 0.001$ ), denoting that the more exhausted the patients, the worse their quality of life in terms of the psychological domain.

TABLE 1 Participant characteristics and differences in the three VLU-QoL domains

Variables	Participant	VLU-QoL		
	Characteristics Mean $\pm$ SD/n (%)	Activities Mean $\pm$ SD	Psychological Mean $\pm$ SD	Symptom distress Mean $\pm$ SD
Age	67.08 $\pm$ 14.25			
BMI	26.95 $\pm$ 6.37			
Charlson Comorbidity Index	1.14 $\pm$ 1.53			
ABI				
Right foot (n = 29)	.92 $\pm$ .29			
Left foot (n = 29)	.93 $\pm$ .20			
Gender				( <i>t</i> = 2.10, <i>P</i> = 0.037)*
Men	81 (48.50)	71.61 $\pm$ 19.62	64.59 $\pm$ 19.18	50.65 $\pm$ 22.42
Women	86 (51.50)	66.60 $\pm$ 19.74	61.56 $\pm$ 19.65	43.72 $\pm$ 20.16
Employed		( <i>t</i> = 2.29, <i>P</i> = 0.023)*		
No	108 (64.67)	71.59 $\pm$ 19.62	62.12 $\pm$ 19.08	46.99 $\pm$ 21.48
Yes	59 (35.33)	64.34 $\pm$ 19.37	64.69 $\pm$ 20.11	47.25 $\pm$ 21.72
Marital status			2 > 3**	
Married (1)	107 (64.07)	68.40 $\pm$ 18.88	63.03 $\pm$ 18.66	46.66 $\pm$ 20.75
Single/divorced (2)	25 (14.97)	73.59 $\pm$ 20.75	72.02 $\pm$ 18.91	51.90 $\pm$ 23.38
Widowed (3)	35 (20.96)	67.69 $\pm$ 21.85	56.61 $\pm$ 20.07	44.93 $\pm$ 22.51
Educational level				
Illiterate	35 (20.96)	71.85 $\pm$ 22.31	62.14 $\pm$ 21.23	50.50 $\pm$ 23.38
Primary school	61 (36.53)	68.04 $\pm$ 20.36	62.30 $\pm$ 20.21	48.24 $\pm$ 23.12
Middle/high school	57 (34.13)	68.06 $\pm$ 17.21	65.13 $\pm$ 17.41	45.39 $\pm$ 19.27
College and above	14 (8.38)	70.25 $\pm$ 21.76	59.84 $\pm$ 20.41	40.36 $\pm$ 17.57
Venous surgery				
No	124 (74.25)	68.97 $\pm$ 19.39	63.58 $\pm$ 19.46	46.07 $\pm$ 21.97
Yes	43 (25.75)	69.19 $\pm$ 21.12	61.44 $\pm$ 19.48	50.00 $\pm$ 20.05
GDS-SF	2.76 $\pm$ 3.48	2 > 1 (Scheffe's)***		2 > 1 (Scheffe's)*
0-4 (1)	132 (79.0)	65.20 $\pm$ 19.21	60.97 $\pm$ 19.13	45.00 $\pm$ 20.24
5-9 (2)	28 (16.8)	84.53 $\pm$ 13.43	70.54 $\pm$ 19.58	56.70 $\pm$ 25.02
10-15 (3)	7 (4.2)	79.19 $\pm$ 19.80	71.74 $\pm$ 16.80	47.86 $\pm$ 22.33
CPSQI	5.49 $\pm$ 3.65			
0-4 (1)	84 (50.3)	66.20 $\pm$ 20.14	42.53 $\pm$ 20.10	65.79 $\pm$ 18.40
5-21 (2)	83 (49.7)	60.30 $\pm$ 20.13	71.90 $\pm$ 19.10	51.69 $\pm$ 22.01
VCSS	14.93 $\pm$ 4.18			
VAS pain	41.74 $\pm$ 29.14			
SF-36 Fatigue	51.50 $\pm$ 12.91			
VLU-QoL				
Activities	69.03 $\pm$ 19.78			
Psychological	63.03 $\pm$ 19.43			
Symptom distress	47.08 $\pm$ 21.50			

Abbreviations: ABI, Ankle-brachial pressure index; BMI, body mass index; CPSQI, Chinese version of the Pittsburgh Sleep Quality Index; GDS-SF, Geriatric Depression Scale Short Form; SF-36, Medical Outcomes Study Short Form-36 (Taiwanese version); VAS, visual analogue scale; VCSS, venous clinical severity score; VLU-QoL, Venous Leg Ulcer Quality of Life questionnaire.

\**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001.

### 3.2.3 | VLU-QoL: symptom distress domain

A positive correlation was witnessed between the symptom distress score and the VCSS ( $P < 0.001$ ), VAS ( $P < 0.001$ ), and CPSQI ( $P < 0.01$ ) scores, suggesting that the worse the venous clinical severity and poorer the sleep quality, the lower the patient's quality of life. The symptom distress score was negatively correlated with the SF-36 (fatigue) score ( $P < 0.001$ ), validating that the more fatigued the patients, the worse their quality of life. Also, the score was lower for the group with good sleep quality than for the group with poor sleep quality with regard to the CPSQI ( $t = 2.81$ ,  $P = 0.006$ ), clarifying that patients who had better-quality sleep experienced a better quality of life. Table 2 presents the relationships between participants' demographic characteristics and the three VLU-QoL domains.

## 3.3 | Potential predictors of quality of life in three domains

The categorical variables associated with the potential predictive variables, such as marital status, were converted to dummy variables before statistical analysis; subsequently, regression analyses were performed with

the variables related to the three domains of the VLU-QoL, namely the activities, psychological, and symptom distress domains. Demographic variables were included in the regression model if there were significant differences in participants' demographic characteristics and significant correlations according to the three domains.

### 3.3.1 | Potential predictors of quality of life in the activities domain

The results were statistically significant with  $F_{7,159} = 17.04$ ,  $P < 0.001$ ,  $R^2 = 0.43$  (adjusted  $R^2 = 0.40$ ). With worsening venous clinical severity ( $B = 1.17$ ,  $P < 0.001$ ), patients experienced more pain ( $B = 0.14$ ,  $P = 0.004$ ) and greater fatigue ( $B = -0.58$ ,  $P < 0.001$ ), which was associated with poor self-perceived quality of life in the activities domain after adjusting for other covariates (Table 3).

### 3.3.2 | Potential predictors of quality of life in the psychological domain

The findings reached statistical significance with  $F_{7,159} = 13.12$ ,  $P < 0.001$ ,  $R^2 = 0.37$  (adjusted  $R^2 = 0.34$ ).

Variables	VLU-QoL		
	Activities	Psychological	Symptom distress
Age	0.14	-0.12	0.04
BMI	-0.05	-0.05	-0.11
ABI			
Right foot (n = 29)	-0.30	-0.05	-0.03
Left foot (n = 29)	-0.12	0.09	0.08
Charlson Comorbidity Index	0.16*	-0.02	0.07
VCSS	0.41***	0.39***	0.48***
VAS pain	0.37***	0.40***	0.63***
MOS SF-36 (Fatigue)	-0.54***	-0.38***	-0.37***
GDS-SF	-0.43***	0.22***	0.19*
CPSQI	0.27***	0.22**	0.33**
VLU-QoL			
Activities	—		
Psychological	0.59***	—	
Symptom distress	0.54***	0.68**	—

TABLE 2 Correlations between participant characteristics and the three VLU-QoL domains

Abbreviations: ABI, Ankle-brachial pressure index; BMI, body mass index; CPSQI, Chinese version of the Pittsburgh Sleep Quality Index; GDS-SF, Geriatric Depression Scale Short Form; MOS SF-36, Medical Outcomes Study Short Form-36 (Taiwanese version); VAS, visual analogue scale; VCSS, venous clinical severity score; VLU-QoL, Venous Leg Ulcer Quality of Life questionnaire.

\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

TABLE 3 Potential predictors of quality of life in three domains (N = 167)

Variables	Activities		Psychological		Symptom distress	
	B	P	B	P	B	P
Intercept	75.99		60.33		32.30	
Gender						
Men <sup>a</sup>						
Women					-3.65	0.123
Employment status						
No <sup>a</sup>						
Yes	-4.53	0.080				
Marital status						
Married <sup>a</sup>						
Single/divorced			8.58	0.016		
Widowed			-7.05	0.027		
Charlson Comorbidity Index	-0.80	0.343				
VCSS	1.17	<0.001	1.20	<0.001	1.61	<0.001
VAS pain	0.14	0.004	0.17	0.001	0.33	<0.001
MOS SF-36 (fatigue)	-0.58	<0.001	-0.45	0.002	-0.44	0.001
GDS-SF	0.46	0.367	-0.60	0.257	-1.02	0.038
CPSQI	0.11	0.771	0.49	0.237	0.72	0.058
Total R <sup>2</sup>	0.43		0.37		0.56	
Adjusted R <sup>2</sup>	0.40		0.34		0.54	

Abbreviations: B, unstandardised coefficients; CPSQI, Chinese version of the Pittsburgh Sleep Quality Index; GDS-SF, Geriatric Depression Scale Short Form; SF-36, Medical Outcomes Study Short Form-36 (Taiwanese version); VAS, visual analogue scale; VCSS, venous clinical severity score; VLU-QoL, Venous Leg Ulcer Quality of Life questionnaire.

<sup>a</sup>Reference group.

A single/divorced ( $B = 8.58$ ,  $P = .016$ ) or widowed status ( $B = -7.05$ ,  $P = 0.027$ ), with worse venous clinical severity ( $B = 1.20$ ,  $P < 0.001$ ), resulted in patients feeling more pain ( $B = 0.17$ ,  $P = 0.001$ ) and more fatigue ( $B = -0.45$ ,  $P = 0.002$ ), which were associated with poor self-perceived quality of life in the psychological domain after adjusting for other covariates (Table 3).

### 3.3.3 | Potential predictors of quality of life in the symptom distress domain

Our data demonstrated statistical significance with  $F_{7,159} = 33.57$ ,  $P < 0.001$ ,  $R^2 = 0.56$  (adjusted  $R^2 = 0.54$ ). As venous clinical severity increased ( $B = 1.61$ ,  $P < 0.001$ ), patients experienced more pain ( $B = 0.33$ ,  $P < 0.001$ ), greater fatigue ( $B = -0.44$ ,  $P = 0.001$ ), and higher depressive symptoms ( $B = -1.02$ ,  $P = 0.038$ ), all of which were associated with poor self-perceived quality of life in the symptom distress domain after adjusting for other covariates (Table 3). Table 3 shows the potential predictive variables for quality of life in the three domains.

## 4 | DISCUSSION

### 4.1 | Demographics and differences in the three VLU-QoL domains

#### 4.1.1 | Demographics

The participants' characteristics were consistent with the common high-risk groups for venous ulcers in the literature: older adults ( $67.08 \pm 14.25$  years), women (51.5%), and obese individuals (body mass index  $>25$  kg/m<sup>2</sup>).<sup>1,2,32,33</sup> Nearly two-thirds (64.7%) of the participants were unemployed, which could be attributed to their wounds because they could not stand for prolonged periods. The leakage of exudate might also have affected their working time.<sup>7</sup> More than half (64.1%) of the participants were married, highlighting that a family support system was established to a certain extent. Studies reveal that more than 60% of patients rely on themselves or family support for wound care.<sup>11,28</sup> In this study, 74.3% of the patients did not have a history of venous surgery owing to the

lack of insurance coverage and the high risk of surgery for older adults.

However, the patients in this study had a relatively low disease burden, with a mean VCSS of  $14.93 \pm 4.18$ , which was lower than the scores reported by Abreu et al<sup>34</sup> and Tracz et al<sup>16</sup> (ie,  $18.64 \pm 3.03$  and  $18.73 \pm 4.18$ , respectively). The VAS pain score of  $41.74 \pm 29.14$  was higher than that the score ( $38.17 \pm 22.93$ ) reported by Finlayson et al.<sup>28</sup> Besides, this study is the first to use the vitality domain of the SF-36 to measure fatigue (ie, a mean score of  $51.50 \pm 12.91$ ) in patients with VLUs, which was slightly higher than the normal population. Many participants (79%) had no depressive symptoms, with a mean score of  $2.76 \pm 3.48$ , and the mean GDS-SF score was lower than the scores reported by Finlayson et al<sup>28</sup> ( $4.3 \pm 3.6$ ) and Edwards et al<sup>11</sup> ( $4.29 \pm 3.63$ ). Around half of the participants (50.3%) had poor sleep quality (CPSQI >5), which is consistent with the findings of Salomé et al<sup>35</sup> using the PSQI (ie, 64% of their patients indicated that they had poor sleep quality).

The scores of the activities domain ( $69.03 \pm 19.78$ ) and the psychological domain ( $63.03 \pm 19.43$ ) were higher than those reported by Hareendran et al<sup>30</sup>:  $29.49 \pm 22.85$  and  $32.08 \pm 21.49$ , respectively; however, the symptom distress domain score ( $47.08 \pm 21.50$ ) was lower than that in Hareendran et al,<sup>30</sup> which was  $58.8 \pm 20.0$ .

#### 4.1.2 | Demographic differences in the three VLU-QoL domains

The quality of life in terms of the activities of unemployed patients was poor ( $t = 2.29$ ,  $P = 0.023$ ), which can be attributed to a lack of income, making it difficult to afford wound dressings, pressure therapy, and nutritional supplements.<sup>14</sup> This situation would affect wound healing and quality of life with respect to activities. More than 60% of patients with VLUs depend on family support for wound care.<sup>11</sup> We found that single/divorced patients had poorer quality of life in relation to the psychological domain ( $F = 4.80$ ,  $P = 0.009$ ) than widowed patients, which may be because of a weaker support network of family and friends. Our data suggest that the quality of life of male patients was worse than that of women with respect to symptoms ( $t = 2.10$ ,  $P = 0.037$ ). Numerous studies affirm that symptoms of and treatments for VLUs affect patients' physiology, emotions, and psychological health, harming their quality of life<sup>12,14,36</sup>; however, these studies report that quality of life tends to decrease more strongly for female patients,<sup>18</sup> which is inconsistent with our findings.

## 4.2 | Correlations with demographics and three domains of the VLU-QoL

### 4.2.1 | VLU-QoL: activities domain

The more comorbidities the patients had, the worse their quality of life ( $\gamma = 0.16$ ,  $P = 0.036$ ) because combined comorbidities may have synergistic effects. Furthermore, the higher the venous clinical severity, the lower the quality of life with respect to activities ( $\gamma = 0.41$ ,  $P < 0.001$ ), the psychological domain ( $\gamma = 0.39$ ,  $P < 0.001$ ), and symptom distress ( $\gamma = 0.48$ ,  $P < 0.001$ ). This outcome is consistent with the findings of several other studies that found a significant correlation between the number and area of ulcers, pain, emotions, and quality of life.<sup>6,17,18</sup>

### 4.2.2 | VLU-QoL: psychological domain

Fatigue is a complex phenomenon whereby patients experience unpleasant internal and subjective feelings, including general tiredness, discomfort, a lack of vitality, negative perceptions of health, and feelings of exhaustion. This phenomenon occurs at the physical, psychological, and emotional levels.<sup>37</sup> We noticed that the more tired the participants were, the worse their quality of life with respect to activities ( $\gamma = -0.54$ ,  $P < 0.001$ ), the psychological domain ( $\gamma = -0.38$ ,  $P < 0.001$ ), and symptom distress ( $\gamma = -0.37$ ,  $P < 0.001$ ). Despite the use of a single vitality item by Finlayson et al<sup>28</sup> in the SF-12 to measure fatigue, few studies consider it a single symptom in patients with VLUs. Interestingly, 59% of patients with VLUs were fatigued.<sup>28</sup> Another study used the vitality item from the SF-12 to measure fatigue in patients.<sup>11</sup> The authors reported that 66% of patients with VLUs were fatigued, which negatively impacted their quality of life.<sup>11</sup>

Patients with VLUs have a higher incidence of depressive symptoms compared with healthy people. This connection may be owing to the pain of the wound, the worry that other people can smell the odour of the wound exudate, and the stress associated with a chronic non-healing wound.<sup>38-40</sup> We observed an association between mild depressive symptoms in our patients with poorer quality of life with respect to activities ( $F = 13.84$ ,  $P < 0.001$ ) and symptom distress ( $F = 3.53$ ,  $P = 0.032$ ), which was not present in those without depressive symptoms. This may be attributed to the sensitivity and itchiness of the skin surrounding the wound, the embarrassment associated with the odour of the wound exudate, which affects social activities, and frustration and loss of control in the long term, which would further develop into symptoms of depression.<sup>8,11</sup>



### 4.2.3 | VLU-QoL: symptom distress domain

A meta-analysis reported that the prevalence of pain in people with VLUs ranged from 46.3% to 100%, with a pooled estimated proportion of 80% (95% confidence interval 0.65-0.92) and a mean pain intensity score of 4 (95% confidence interval 3.4-4.5).<sup>41</sup> Biopsychosocial factors, especially inflammatory cytokines, play a crucial role in brain function, which may influence pain perception and play a role in the development of sickness behaviours such as fatigue, sleep disturbance, and cognitive changes.<sup>8,42</sup> Numerous studies have reported that pain associated with VLUs is often inadequately assessed or managed and is related to diminished quality of life and delays in wound healing.<sup>8-11,43</sup> We found that the more painful the ulcers, the poorer the patients' quality of life with respect to the domains of activities ( $\gamma = 0.37$ ,  $P < 0.001$ ), psychology ( $\gamma = 0.40$ ,  $P < 0.001$ ), and symptom distress ( $\gamma = 0.63$ ,  $P < 0.001$ ). This result is consistent with the typical pain evolution of VLUs described in the literature. This pain can evolve to become intractable chronic pain if left unresolved at this stage,<sup>44</sup> affecting sleep quality and activities; inducing various psychosocial burdens, such as social isolation, depression, loss of control, and helplessness; and significantly harming quality of life.<sup>43,45</sup>

Patients who had poor sleep quality also had poorer quality of life with respect to symptoms ( $t = 2.81$ ,  $P = 0.009$ ) than those who had better sleep quality. Furthermore, the poorer the sleep quality, the lower the patients' quality of life with respect to the domains of activities ( $\gamma = 0.27$ ,  $P < 0.001$ ), psychology ( $\gamma = 0.22$ ,  $P = 0.005$ ), and symptom distress ( $\gamma = 0.33$ ,  $P < 0.001$ ). This finding is consistent with the results of Hellström et al,<sup>6</sup> who showed that sleep quality and quality of life were significantly correlated.

### 4.3 | Potential predictors of quality of life in patients with VLUs among the three domains

Our multiple regression analysis demonstrated that the potential predictors of quality of life with respect to patients' activities were venous clinical severity ( $P < 0.001$ ), pain ( $P = 0.004$ ), and fatigue ( $P < 0.001$ ). The potential predictors of quality of life with respect to the psychological domain were marital status (single/divorced,  $P = 0.016$ ; widowed,  $P = 0.027$ ), venous clinical severity ( $P < 0.001$ ), pain ( $P = 0.001$ ), and fatigue ( $P = 0.002$ ). Finally, the potential predictors of quality of life in terms of symptoms were venous clinical severity

( $P < 0.001$ ), pain ( $P < 0.001$ ), fatigue ( $P = 0.001$ ), and depression ( $P = 0.038$ ).

Thus, venous clinical severity was identified as a potential predictor of quality of life across all three domains. The deterioration of clinical venous lesions is because of the existence of chronic venous insufficiency. Enhancing our understanding of the symptoms and formulating individual interventions may help improve the conditions of patients' lower limb venous return and promote VLU healing. Moreover, pain was a potential predictor of quality of life in all three domains. Unresolved pain may have a cumulative impact on quality of life, restricting activities and increasing dependence on family or friends.<sup>46</sup> This reliance can cause interpersonal tension in relationships.<sup>47</sup> Fatigue was also a predictor of all three domains of quality of life. Many patients with VLUs have had persistent ulcers for decades, affecting their activities, work, and sleep and reducing their vitality, motivation, and mental capacity. Associated symptoms include amnesia, irritability, muscle weakness, and headaches. Even with sufficient sleep, patients may still feel unbearable fatigue, which impacts their quality of life.<sup>37</sup> Marital status was a potential predictor of the psychological aspects of quality of life. Providing patients with mental support would increase their confidence in wound care. Depression is a symptom-oriented predictor of quality of life that may be caused by long-term stress associated with the wound. In our study, only 21% of the participants reported mild to severe depressive symptoms; this may be because Asian cultures value more reserved emotional styles than Western countries and because older adults do not often feel comfortable discussing their depression with their family for fear of burdening them. In the future, strategies for ameliorating these problems should be further explored.

## 5 | CONCLUSION

This study investigated the potential predictors of quality of life in 167 patients with VLUs. We found that being male, unemployed, single/divorced, and widowed place individuals at particularly high risk of poor quality of life. Being single/divorced or widowed was associated with quality of life in the psychological domain. The three common potential predictors – venous clinical severity, pain, and fatigue – were associated with reduced quality of life in all three domains of the VLU-QoL. Depressive symptoms were the fourth potential predictor of quality of life in the symptom domain. The identified potential predictors in these three domains of the VLU-QoL explained 34%-54% of the variance in the quality of life of patients with VLUs in Taiwan.

## 5.1 | Limitations and future recommendations

A limitation of this study was its cross-sectional correlational design, which hindered our understanding of how patient demographics, venous clinical severity, pain, fatigue, depressive symptoms, sleep quality, and quality of life changed over time and in different stages of the condition. The common symptoms of VLU were individually examined; hence, the effects of symptom clusters and the sequences of symptom occurrence were not assessed. In addition, we only did not stipulate that patients had to undergo any specific treatments for their wounds (eg, surgery, wound dressings, compression therapy, or physical therapy) or the period for which they had to receive medical treatment. Therefore, changes or differences in venous clinical severity, pain, fatigue, depressive symptoms, sleep quality, or quality of life over time that might be associated with specific treatments or the duration of medical treatment were not assessed. Furthermore, owing to time, labour, resource, and ethical constraints, we did not investigate any blood biochemical attributes that could impact venous clinical severity and our investigated cluster symptom variables.

A longitudinal follow-up study would be useful as it would enable researchers to comprehend the changes in venous clinical severity, pain, fatigue, depressive symptoms, sleep quality, and quality of life at different stages of wound development and care. New strategies need to be developed to treat these patients, including plans to mitigate the effects of the wounds and to prevent recurrence and new wounds. With a growing number of individuals living with VLUs, we must enhance the understanding of the biological underpinnings of these symptom clusters to develop more targeted and effective symptom management strategies regarding the brain and the immune system. These research directions may open opportunities for researchers to examine interdependent and possibly synergistic interactions between biological and behavioural factors, symptom clusters, and outcomes in VLUs.

## 5.2 | Implications for clinical practice

It is imperative to provide patients with holistic care, and not limit treatment to wound care. Maintaining a good nurse–patient relationship, with continuous and friendly communication, would help comfort patients and make them feel supported so that they can participate more in their wound management. Our study demonstrated that marital status, venous clinical severity, pain, fatigue, and depressive symptoms are potential predictors of quality of life in patients with VLUs. These results can serve as the

basis of intervention measures, such as those related to nutritional advice and training in wound dressing, and help enhance the quality of VLU care in Taiwan.

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### CONFLICT OF INTEREST

The authors declare no conflicts of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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