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Relationship between WIfI (wound, ischemia, foot infection) stage and quality of life at revascularization in the BEST-CLI (best endovascular versus best surgical therapy in patients with chronic limb threatening ischemia) trial Presented as an oral...

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Relationship between WIfI stage and quality of life at revascularization in the BEST-CLI trial

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ABSTRACT

Objective: The WIfI (Wound, Ischemia, foot Infection) stage measures the extent of wounds, ischemia, and foot infection in patients with chronic limb threatening ischemia (CLTI) and has been associated with the risk of major amputation. Patients with CLTI have impaired health-related quality of life (HRQoL), which can be multifactorial. We hypothesized that the severity of the limb threat (WIfI stage) would be associated with poor HRQoL among patients with CLTI presenting for revascularization.

Methods: The dataset of the BEST-CLI (best endovascular versus best surgical therapy in patients with CLTI) trial, a prospective, randomized trial comparing open and endovascular revascularization strategies, was queried for HRQoL assessments at patient enrollment. The HRQoL assessments included (1) Vascular Quality of Life; (2) 12-item short form survey (SF-12), containing the utility index score (short-form six-dimension R2 utility index, incorporating physical, emotional, and mental well-being) and mental and physical components; and (3) the EQ-5D. Multivariable regression analysis was used to identify the independent associations with the baseline HRQoL assessments.

Results: A total of 1568 patients with complete WIfI data were analyzed, of whom 71.5% were men. The WIfI distribution was 35.5% with stage 4, 29.6% with stage 3, 28.6% with stage 2, and 6.3% with stage 1. Patients presenting with WIfI stage 4, compared with stage 1 to 3, were more often men (74.9% vs 69.6%) and current smokers (25.4% vs. 17.6%), had had end-stage renal disease (13.3% vs 8.5%) and diabetes (83.6% vs 60.2%), were not independently ambulatory (56.8% vs 38.5%), and had had higher median morbidity scores (4 vs 3; $P < .05$ for all). On multivariable analysis, WIfI stage 4, compared with stage 1 to 3, was associated with lower SF-12 mental component scale scores (estimate, −2.43; 95% confidence interval, −3.73 to −1.13; $P < .001$) and short-form six-dimension R2 utility index scores (estimate, −0.02; 95% confidence interval, −0.03 to 0.001; $P = .04$). The WIfI stage was not independently associated with the baseline Vascular Quality of Life, SF-12 physical component scale, or EQ-5D assessments.

Conclusions: WIfI stage was independently associated with poorer quality of life because of mental, rather than physical, health for patients with CLTI. Clinicians should be aware of the burden of mental stress borne by those with the greatest limb impairment. (J Vasc Surg 2023;77:1099-106.)

Keywords: Limb ischemia; Quality of life; WIfI

The Society for Vascular Surgery's WIfI (Wound, Ischemia, foot Infection) staging system was developed to classify threatened limbs using factors that affect amputation risk and clinical management.[1] These include the extent of the wound, degree of ischemia, and severity of any foot infection. The system includes four stages using a combination of these factors, with stage 4 the most advanced.[1-3] An advanced WIfI stage on presentation has been correlated with a high risk of amputation, postrevascularization secondary interventions, and mortality.[2] However, limited evidence is available about the relationship between limb severity (WIfI) and health-related quality of life (HRQoL) for patients with chronic limb threatening ischemia (CLTI).

Patients with CLTI have been shown to have poor HRQoL on presentation for revascularization in three separate randomized trials.[4-6] However, these analyses did not incorporate details about the affected limb or had focused on postintervention changes in the HRQoL scores.[4-6] The HRQoL of patients with CLTI is worse than that of patients with most other chronic conditions.[4] An improved understanding of HRQoL considerations could better guide care for this complex and vulnerable patient population and enhance patient engagement for joint decision-making.

Our goal was to assess preoperative HRQoL and its relationship to the WIfI stage at presentation for patients with CLTI. We used data from the BEST-CLI (best endovascular versus best surgical therapy in patients with CLTI) trial, a multicenter, international, prospective, randomized, controlled trial comparing endovascular and open surgical revascularization for patients with CLTI.[7-9] The BEST-CLI trial collected prospectively obtained HRQoL information using multiple instruments, and we correlated the HRQoL findings with the baseline WIfI stages.

METHODS

The BEST-CLI trial was a multicenter, randomized, controlled trial comparing the best endovascular and open surgical revascularization for patients with CLTI due to infrainguinal peripheral arterial disease (PAD)

who were candidates for either revascularization strategy (ClinicalTrials.gov identifier NCT02060630). Details of the trial have been previously reported.[9] The institutional review board of each participating institution approved the protocol and the consent process. All the patients had provided written informed consent before study enrollment.

HRQoL was a prespecified secondary end point of the BEST-CLI trial. HRQoL was assessed by survey at the initial presentation and at designated follow-up points. Three well-validated survey instruments were used: the Vascular Quality of Life questionnaire (VascuQoL); 12-item short-form survey (SF-12), including the utility index score (SF6D-R2), mental composite scale (MCS), and physical composite scale (PCS); and EQ-5D.[10-14] The initial questionnaires were administered after the patients had provided written informed consent and had been enrolled but before revascularization. VascuQoL, a PAD-specific questionnaire, consists of 25 questions across five domains—activity, symptoms, pain, emotional, and social. The score ranges from 1 (worst) to 7 (best). The SF-12 includes 12 questions across eight domains—physical functioning, social functioning, role physical, role emotional, mental health, energy/vitality, bodily pain, and general health. It produces the summary scores—MCS, PCS, and SF6D-R2—which incorporate physical, emotional, and mental well-being. The MCS and PCS scores range from 0 (worst) to 100 (best) and the SF6D-R2 score ranges from 0.0 (worst) to 1.0 (best).

The WIfI stage is from 1 to 4 (worst) based on three components that are individually graded from 0 (best) to 3 (worst): wound, ischemia, and foot infection. The WIfI system was developed to standardize the reporting of the degree of CLTI in a limb. A more severe score has been associated with poor limb-associated outcomes.[1,2]

Statistical analysis. The baseline characteristics are summarized as the mean ± standard deviation and median (interquartile range [IQR]) for continuous variables and proportions for categorical variables. The analyzed variables included age ≥80 years, race, sex, heart failure, contralateral major amputation (above the ankle),

Table I. Demographics and comorbidities

Baseline characteristic	WIfI stage 4 (n = 557)	WIfI stage 1-3 (n = 1104)	P value
Age ≥80 years	53 (9.5)	97 (9.6)	.96
White race	384 (69.6)	748 (74.7)	.07
Black race	123 (22.3)	192 (19.2)	
All other races	45 (8.2)	61 (6.1)	
Male sex	417 (74.9)	704 (69.6)	**.03**
Heart failure	35 (6.3)	56 (5.5)	.53
Contralateral major amputation	45 (8.1)	60 (5.9)	.10
Bilateral CLTI	84 (15.1)	168 (16.6)	.43
COPD	79 (14.2)	166 (16.4)	.25
Smoking[a]			**<.001**
Current or within past year	211 (37.9)	500 (49.5)	
>1 Year previously	204 (36.7)	332 (32.9)	
Never	141 (25.4)	178 (17.6)	
ESRD	74 (13.3)	86 (8.5)	**.003**
Hyperlipidemia	418 (75.2)	759 (75.2)	.99
Hypertension	493 (88.7)	874 (86.5)	.22
Diabetes	465 (83.6)	608 (60.2)	**<.001**
Opiate use	133 (23.9)	241 (23.8)	.99
Ambulatory status[b]			**<.001**
Without assistance	240 (43.2)	621 (61.5)	
With assistance	223 (40.1)	277 (27.4)	
Nonambulatory	93 (16.7)	112 (11.1)	
Living at home	521 (93.9)	955 (94.6)	.58
Comorbidity score	4.00 (3.00-5.00)	3.00 (3.00-5.00)	**<.001**

CLTI, Chronic limb threatening ischemia; *COPD,* chronic obstructive pulmonary disease; *ESRD,* end-stage renal disease; *WIfI,* Wound, Ischemia, foot Infection.
Data presented as number (%) or median (interquartile range).
Boldface *P* values represent statistical significance.
[a]Those with current smoking or smoking within the previous year were significantly different from nonsmokers and those who had smoked >1 year before enrollment (*P* < .001).
[b]Ambulatory with assistance and nonambulatory patients were significantly different from patients who were ambulatory without assistance (*P* < .001).

ARTICLE HIGHLIGHTS

- **Type of Research:** Analysis of prospectively collected data from a randomized clinical trial
- **Key Findings:** Patients presenting with WIfI (Wound, Ischemia, foot Infection) stage 4 were more often current smokers, had had end-stage renal disease and diabetes, and were not independently ambulatory. WIfI stage 4, compared with WIfI stage 1 to 3, was associated with lower 12-item short-form survey mental component scale scores (estimate, −2.43; 95% confidence interval, −3.73 to −1.13; *P* < .001). The WIfI stage was not independently associated with the baseline Vascular Quality of Life questionnaire, 12-item short-form survey physical component scale, or EQ-5D assessments. The WIfI stage was independently associated with poorer quality of life owing to mental, rather than physical, health for patients with chronic limb threatening ischemia.
- **Take Home Message:** WIfI stage was independently associated with poorer quality of life because of mental, rather than physical, health for patients with chronic limb threatening ischemia.

The association of the baseline characteristics and WIfI stage (4 vs 1-3) was tested using χ^2 statistics. Continuous variables were compared using the Student *t* test. A univariate liner regression model was fitted for each baseline characteristic and HRQoL score. Clinically, ambulatory status, tissue loss, and amputation of the non-index limb were expected to correlate highly with the WIfI stage. For each HRQoL score, a multipredictor linear regression model was fitted. Those with a missing predictor variable or HRQoL scores were excluded from the analyses. The parameter estimates with the 95% confidence intervals (CIs) are presented. For each analysis, *P* < .05 was considered statistically significant. SAS EG, version 8.3 (SAS Institute, Cary, NC), software was used to conduct the statistical analyses.

RESULTS

A total of 1830 patients were enrolled in the BEST-CLI trial. Those with missing WIfI components (n = 262) were excluded, leaving 1568 patients with complete WIfI data available for analysis. The WIfI distribution was 35.5% with stage 4, 29.6% with stage 3, 28.6% with stage 2, and 6.3% with stage 1. The patients presenting with WIfI stage 4, compared with stage 1 to 3, were more often men (74.9% vs 69.6%) and current smokers (25.4% vs. 17.6%), had had end-stage renal disease (13.3% vs 8.5%) and diabetes (83.6% vs 60.2%), were not independently ambulatory (56.5% vs 38.4%), and had had a higher median comorbidity index score of 4 (IQR, 3-5) vs 3 (IQR, 3-5; (*P* < .05 for all; Table I).

bilateral CLTI, chronic obstructive pulmonary disease, smoking (current or within the previous year, >1 year ago, never), end-stage renal disease, hyperlipidemia, diabetes, hypertension, opiate use before enrollment, comorbidity index (determined by the presence of diabetes, chronic obstructive pulmonary disease, congestive heart failure, previous myocardial infarction, contrary artery disease, hypertension, stroke, transient ischemic attack, PAD at baseline), ambulatory status (ambulatory without assistance, ambulatory with assistance, nonambulatory), living status before enrollment (living at home vs not), and WIfI stage.

Table II. Summary statistics of baseline quality of life scores stratified by WIfI (Wound, Ischemia, foot Infection) stage

| Quality of life assessment | Score | | | P value |
	Overall	WIfI stage 4	WIfI stage 1-3	
VascuQoL				.26
Mean ± SD	3.07 ± 1.26	3.00 ± 1.29	3.08 ± 1.23	
Median (IQR)	2.86 (2.08-3.96)	2.76 (2.04-3.84)	2.88 (2.16-3.96)	
Range	1.00-6.76	1.00-6.76	1.00-6.76	
SF6D-R2				.12
Mean ± SD	0.59 (0.13)	0.58 (0.14)	0.59 (0.13)	
Median (IQR)	0.57 (0.49-0.66)	0.57 (0.48-0.65)	0.58 (0.49-0.66)	
Range	0.35-1.00	0.35-1.00	0.35-1.00	
MCS				**.002**
Mean ± SD	46.45 (12.01)	45.07 (12.16)	47.10 (11.99)	
Median (IQR)	46.64 (38.07-55.77)	44.55 (36.49-53.92)	47.67 (38.85-56.37)	
Range	13.34-73.40	14.01-73.12	13.34-73.40	
PCS				.85
Mean ± SD	33.02 (8.54)	32.92 (8.89)	33.01 (8.37)	
Median (IQR)	32.16 (26.91-38.50)	31.51 (26.52-38.74)	32.33 (27.02-38.21)	
Range	10.43-61.20	10.43-55.91	12.63-61.20	
EQ-5D health status				.07
Mean ± SD	57.25 (21.77)	55.58 (21.82)	57.70 (22.09)	
Median (IQR)	60.00 (45.00-75.00)	55.00 (40.00-70.00)	60.00 (50.00-75.00)	
Range	0.00-100.00	0.00-100.00	0.00-100.00	

IQR, Interquartile range; *MCS*, mental component scale; *PCS*, physical component scale; *SD*, standard deviation; *SF6D-R2*, short-form six-dimension R2 utility index; *VascuQoL*, Vascular Quality of Life.
Boldface *P* values represent statistical significance.

The median MCS score for WIfI stage 4 was 44.55 (IQR, 36.49-53.92) vs 47.67 (IQR, 38.85-56.37) for WIfI stage 1 to 3 (*P* = .002). The median VascuQoL score for WIfI stage 4 was 2.76 (IQR, 2.04-3.84) vs 2.88 (IQR, 2.16-3.96) for WIfI stage 1 to 3 (*P* = .26). The median SF6D-R2 score for WIfI stage 4 was 0.57 (IQR, 0.48-0.65) vs 0.58 (IQR, 0.49-0.66) for WIfI stage 1 to 3 (*P* = .12). The median PCS score-for WIfI stage 4 was 31.51 (IQR, 26.52-38.74) vs 32.33 (IQR, 27.02-38.21) for WIfI stage 1 to 3 (*P* = .85). The median EQ-5D health status score for WIfI stage 4 was 55.00 (IQR, 40.00-70.00) vs 60.00 (IQR, 50.00-75.00) for WIfI stage 1 to 3 (*P* = .07; Table II). The results of the univariable analysis are presented in Supplementary Tables I-III (online only). The HRQoL assessments stratified by WIfI stage are listed in Supplementary Table IV (online only).

On multivariable analysis, WIfI stage 4 had VascuQoL scores comparable to those of WIfI stage 1 to 3 (−0.12; 95% CI, −0.25 to 0.02; *P* = .09). However, female sex, current smoking, and preoperative opioid use were associated with lower VascuQoL scores (Table III). WIfI stage 4 was associated with a worse or lower SF6D utility index score (−0.02; 95% CI, −0.03 to 0.001; *P* = .04), as were female sex, current smoking, and preoperative opioid use. WIfI stage 4 was associated with a worse or lower SF-12 MCS score (−2.43; 95% CI, −3.73 to −1.13; *P* < .001), as were female sex, current smoking, and

preoperative opioid use. However, WIfI stage 4 was not associated with a worse or lower SF-12 PCS score (0.04; 95% CI, −0.89 to 0.97; *P* = .93) but current smoking, not living at home, non-Black race, and preoperative opioid use were associated with lower scores (Table IV). WIfI stage 4 was not associated with a worse or lower EQ-5D score (−1.85; 95% CI, −4.22 to 0.52; *P* = .13; Table V).

DISCUSSION

Patients presenting with CLTI in the BEST-CLI trial with an advanced WIfI stage had had worse or lower HRQoL assessments related to their mental health, as demonstrated by the SF-12 MCS and SF6D utility index scores. The HRQoL assessments with a greater focus on physical health (ie, VascuQoL, SF-12 PCS, and EQ-5D) did not show a correlation with an advanced WIfI stage. Patients with CLTI who were currently smoking had worse HRQoL shown by all the assessments. The present analysis has provided a perspective on the HRQoL of patients with CLTI before revascularization and can help the surgeon and supporting team to maximize multidisciplinary support and treatment. Although previous studies have analyzed the HRQoL of patients with PAD, these studies had been limited by not assessing the relationship to the severity of limb threat as measured by the WIfI stage.[4-6]

Table III. Multivariable analysis of overall Vascular Quality of Life (VascuQoL) and short-form six-dimension R2 utility index (SF6D-R2) scores[a]

Covariate	VascuQoL			SF6D-R2		
	Estimate	95% CI	P value	Estimate	95% CI	P value
Age ≥80 years	0.05	−0.17 to 0.27	.66	0.01	−0.01 to 0.03	.42
Race			**<.001**			**.02**
Black	0.11	−0.05 to 0.27	.16	0.01	−0.01 to 0.03	.17
All other	−0.44	−0.69 to −0.20	**<.001**	−0.03	−0.06 to −0.00	**.03**
White	Ref			Ref		
Male sex	0.21	0.07 to 0.35	**.003**	0.03	0.02 to 0.05	**<.001**
Heart failure	0.04	−0.25 to 0.32	.79	0.01	−0.02 to 0.04	.68
Bilateral CLTI	−0.15	−0.32 to 0.02	.08	−0.01	−0.03 to 0.01	.29
COPD	−0.09	−0.29 to 0.10	.35	−0.01	−0.03 to 0.01	.41
Smoking			**<.001**			**<.001**
Current or within past year	−0.61	−0.79 to −0.43	**<.001**	−0.05	−0.07 to −0.03	**<.001**
>1 year ago	−0.18	−0.36 to 0.00	**.05**	−0.01	−0.03 to 0.01	.37
Never	Ref			Ref		
ESRD	0.03	−0.19 to 0.24	.80	0.01	−0.02 to 0.03	.51
Hyperlipidemia	0.06	−0.09 to 0.21	.45	0.01	−0.00 to 0.03	.16
Diabetes	−0.15	−0.32 to 0.01	.07	−0.01	−0.03 to 0.01	.37
Hypertension	−0.15	−0.36 to 0.07	.18	0.00	−0.03 to 0.02	.75
Opiate use	−0.35	−0.50 to −0.20	**<.001**	−0.04	−0.05 to −0.02	**<.001**
Comorbidity index	−0.02	−0.08 to 0.05	.65	−0.01	−0.01 to 0.00	.16
Living at home	0.09	−0.18 to 0.36	.52	0.02	−0.00 to 0.05	.10
WIfI stage (4 vs 1-3)	−0.12	−0.25 to 0.02	.09	−0.02	−0.03 to −0.001	**.04**

CI, Confidence interval; *CLTI,* chronic limb threatening ischemia; *COPD,* chronic obstructive pulmonary disease; *ESRD,* end-stage renal disease; *Ref,* reference; *WIfI,* Wound, Ischemia, foot Infection.
Boldface *P* values represent statistical significance.
[a]Parameter estimates >0 indicate higher VascuQoL scores and SF6D-R2 scores.

Overall, the MCS and PCS scores were poor for all patients in our analysis, regardless of the WIfI stage. The mean and median MCS and PCS scores were well below the values reported for the general population.[4] The SF-12 questionnaire, with three subscales—the SF6D utility index, MCS, and PCS—provides focused assessments for mental health, physical health, and a focused short-form assessment. An advanced WIfI stage was associated with worse, statistically and clinically, HRQoL as assessed by the MCS. The presence of concurrent mental stress is important in patients with CLTI and has most likely been undertreated.[15-19] Patients with PAD have been shown to have higher rates of depression, especially those with CLTI.[20] The Nottingham Health Profile analyzed HRQoL of patients with PAD and demonstrated that CLTI patients had significant difficulty with work, housework, family life, social life, hobbies, and travel compared with the healthy control patients, emphasizing the interplay between mental health and PAD.[16]

The SF-12 and its subscales, MCS and PCS, have been examined for both chronic disease states and cardiovascular conditions.[21-24] An analysis of 10 patients with chronic disease examined the effects of age on HRQoL and showed that the PCS score worsened with age but that the MCS score remained relatively stable.[21] An analysis of hemodialysis patients showed that the PCS score was negatively affected by hypoalbuminemia and the severity of cardiac and pulmonary disease and that the MCS score was most affected by living alone.[22] An analysis of patients with chronic obstructive pulmonary disease showed similar factors were associated with lower PCS and MCS scores, with underweight patients, patients with frequent exacerbations, and patients with short walking distances performing fairly poorly for both.[23] The MCS and PCS have also been longitudinally followed up for patients after interventions. An analysis of HRQoL at 12 months after percutaneous coronary intervention and coronary artery bypass grafting showed a greater PCS improvement for those who had undergone coronary artery bypass grafting compared with those who had undergone percutaneous coronary intervention.[24] No differences were found in the MCS score when stratified by procedure type. Future analysis of the BEST-CLI data will involve the short- and long-term postoperative changes in HRQoL at the follow-up intervals.

Table IV. Multivariable analysis of 12-item short-form survey (SF-12) mental component scale (MCS) and physical component scale (PCS) scores[a]

Covariate	MCS			PCS		
	Estimate	95% CI	*P* value	Estimate	95% CI	*P* value
Age ≥80 years	2.69	0.55 to 4.83	**.01**	−0.51	−2.03 to 1.02	.52
Race			.08			**.02**
Black	−0.08	−1.63 to 1.46	.91	1.21	0.11 to 2.31	**.03**
All other	−2.72	−5.12 to −0.31	**.03**	−1.28	−3.00 to 0.44	.14
White	Ref			Ref		
Male sex	3.18	1.82 to 4.54	**<.001**	0.61	−0.36 to 1.58	.22
Heart failure	0.70	−2.05 to 3.45	.62	−0.05	−2.01 to 1.91	.96
Bilateral CLTI	−1.56	−3.20 to 0.07	.06	−0.36	−1.52 to 0.81	.55
COPD	−0.57	−2.44 to 1.31	.55	−0.56	−1.89 to 0.78	.41
Smoking			**.003**			**<.001**
Current or within past year	−3.02	−4.78 to −1.26	**<.001**	−2.00	−3.26 to −0.74	**.002**
>1 Year ago	−1.41	−3.14 to 0.33	.11	0.55	−0.69 to 1.79	.39
Never	Ref			Ref		
ESRD	0.93	−1.15 to 3.01	.38	−0.79	−2.27 to 0.70	.30
Hyperlipidemia	0.87	−0.61 to 2.35	.25	0.20	−0.86 to 1.25	.72
Diabetes	−0.07	−1.68 to 1.54	.93	−1.13	−2.28 to 0.02	**.05**
Hypertension	−0.94	−3.04 to 1.17	.38	−0.17	−1.67 to 1.32	.82
Opiate use	−2.59	−4.00 to −1.17	**<.001**	−1.53	−2.55 to −0.52	**.003**
Comorbidity index	−0.33	−0.99 to 0.33	.32	−0.45	−0.92 to 0.02	.06
Living at home	1.32	−1.30 to 3.94	.32	1.97	0.09 to 3.85	**.04**
WIfI stage (4 vs 1-3)	−2.43	−3.73 to −1.13	**<.001**	0.04	−0.89 to 0.97	.93

CI, Confidence interval; *CLTI*, chronic limb threatening ischemia; *COPD*, chronic obstructive pulmonary disease; *ESRD*, end-stage renal disease; *Ref*, reference; *WIfI*, Wound, Ischemia, foot Infection.
Boldface *P* values represent statistical significance.
[a]Parameter estimates >0 indicate higher MCS and PCS scores.

Unlike mental health assessments, the physical assessments were not worse with an advanced WIfI stage, although the scores were low for all the patients, as shown by the VascuQoL, SF-12 PCS, and EQ-5D scores. The PCS is focused on physical aspects and the VascuQoL and EQ-5D have a high focus on physical health components. One possibility is that the physical impairment associated with all stages of CLTI is advanced, and thus, any differences between stages will be much less pronounced. The interactions of CLTI with pain and neuropathy could also affect the physical disability component of CLTI, with patients with small or no wounds having worse physical quality of life than might patients with neuropathy and an advanced wound.

The present study had several limitations. The location and site of survey administration, whether in the clinic or preoperative area, could have influenced the patients' responses. The patients were administered the questionnaire after they had been told they had a limb threatening problem and after trial enrollment. This could have affected their perceptions and responses. The incomplete capture of baseline WIfI data in the BEST-CLI trial was a potential source of bias. Also, these instruments have not been validated for CLTI, which was why multiple questionnaires were used. The development of CLTI-specific instruments to evaluate HRQoL are needed.

CONCLUSIONS

We found that WIfI stage is independently associated with poorer quality of life because of mental, rather than physical, health for patients with CLTI. Clinicians should be aware of the burden of mental stress borne by those with a more advanced limb threat.

AUTHOR CONTRIBUTIONS

Conception and design: JS, VR, MM, KR, AF
Analysis and interpretation: JS, VR, MM, KR, MC, RP, LC, KG, TH, MV, MC, CW, MS, AF
Data collection: JS, MM, KR, LC, KG, MS, AF
Writing the article: JS, VR, AF
Critical revision of the article: JS, MM, KR, MC, RP, LC, TH, MV, MC, CW, MS, AF
Final approval of the article: JS, VR, MM, KR, MC, RP, LC, KG, TH, MV, MC, CW, MS, AF

Table V. Multivariable analysis of EQ-5D health status[a]

Covariate	Estimate	95% CI	P value
Age ≥80 years	2.45	−1.47 to 6.37	.22
Race			**.03**
Black	2.37	−0.44 to 5.18	.10
All other	−3.88	−8.26 to 0.50	.08
White	Ref		
Male sex	1.26	−1.22 to 3.74	.32
Heart failure	−2.59	−7.59 to 2.41	.31
Bilateral CLTI	−5.26	−8.24 to −2.27	**<.001**
COPD	−2.74	−6.15 to 0.68	.12
Smoking			**.004**
Current or within past year	−2.71	−5.92 to 0.51	.100
>1 Year ago	1.78	−1.39 to 4.94	.27
Never	Ref		
ESRD	−3.72	−7.51 to 0.07	**.05**
Hyperlipidemia	0.43	−2.28 to 3.13	.76
Diabetes	−1.40	−4.34 to 1.53	.35
Hypertension	0.54	−3.28 to 4.36	.78
Opiate use	−1.88	−4.46 to 0.71	.15
Comorbidity index	−1.38	−2.58 to −0.19	**.02**
Living at home	5.00	0.21 to 9.79	**.04**
WIfI stage (4 vs 1-3)	−1.85	−4.22 to 0.52	.13

CI, Confidence interval; CLTI, chronic limb threatening ischemia; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; Ref, reference; WIfI, Wound, Ischemia, foot Infection.
Boldface P values represent statistical significance.
[a]*Parameter estimates >0 indicate higher EQ-5D scores.*

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Supplementary Table I (online only). Univariate regression of overall Vascular Quality of Life (VascuQoL) and short-form six-dimension R2 utility index (SF6D-R2)[a]

Covariate	VascuQoL			SF6D-R2		
	Estimate	95% CI	P value	Estimate	95% CI	P value
Age ≥80 years	0.30	0.10 to 0.50	**.003**	0.03	0.00 to 0.05	**.02**
Race			**.003**			.07
Black	0.10	−0.05 to 0.25	.18	0.01	−0.01 to 0.03	.21
All other	−0.33	−0.56 to −0.11	**.004**	−0.02	−0.04 to 0.00	.08
White	Ref			Ref		
Male sex	0.16	0.03 to 0.29	**.02**	0.02	0.01 to 0.04	**<.001**
Heart failure	−0.03	−0.29 to 0.22	.81	−0.01	−0.04 to 0.01	.33
Contralateral major amputation	0.10	−0.13 to 0.34	.39	0.00	−0.02 to 0.03	.85
Bilateral CLTI	−0.19	−0.35 to −0.03	**.02**	−0.02	−0.03 to 0.00	**.05**
COPD	−0.27	−0.43 to −0.10	**.001**	−0.03	−0.05 to −0.01	**.001**
Smoking			**<.001**			**<.001**
Current or within past year	−0.48	−0.64 to −0.33	**<.001**	−0.04	−0.05 to −0.02	**<.001**
>1 Year ago	−0.09	−0.25 to 0.07	.29	0.00	−0.02 to 0.02	.93
Never	Ref			Ref		
ESRD	0.05	−0.14 to 0.25	.59	0.01	−0.01 to 0.03	.51
Hyperlipidemia	0.05	−0.09 to 0.18	.51	0.01	−0.01 to 0.02	.30
Diabetes	−0.02	−0.15 to 0.11	.74	0.00	−0.01 to 0.02	.83
Hypertension	−0.04	−0.22 to 0.13	.63	0.00	−0.02 to 0.02	.88
Tissue loss	0.01	−0.13 to 0.16	.85	0.01	−0.01 to 0.02	.47
Opiate use	−0.36	−0.50 to −0.23	**<.001**	−0.04	−0.06 to −0.03	**<.001**
Comorbidity index	−0.02	−0.07 to 0.02	.27	−0.00	−0.01 to 0.00	.13
Ambulatory status			**<.001**			**<.001**
Nonambulatory	−0.52	−0.70 to −0.33	**<.001**	−0.07	−0.09 to −0.05	**<.001**
With assistance	−0.37	−0.50 to −0.24	**<.001**	−0.04	−0.06 to −0.03	**<.001**
Without assistance	Ref			Ref		
Living at home	−0.04	−0.29 to 0.21	.78	0.02	−0.01 to 0.04	.21
WIfI stage (4 vs 1-3)	−0.08	−0.21 to 0.06	.26	−0.01	−0.03 to 0.003	.12

CI, Confidence interval; *CLTI*, chronic limb threatening ischemia; *COPD*, chronic obstructive pulmonary disease; *ESRD*, end-stage renal disease; *Ref*, reference; *WIfI*, Wound, Ischemia, foot Infection.
Boldface *P* values represent statistical significance.
[a]Parameter estimates >0 indicate higher VascuQoL scores and SF6D-R2 scores.

Supplementary Table II (online only). Univariate regression of SF-12 mental component scale (MCS) and physical component scale (PCS) scores[a]

Covariate	MCS			PCS		
	Estimate	95% CI	P value	Estimate	95% CI	P value
Age ≥80 years	3.34	1.44 to 5.24	**<.001**	0.55	−0.81 to 1.90	.43
Race			.19			.07
Black	−0.31	−1.73 to 1.11	.67	1.06	0.05 to 2.08	**.04**
All other	−1.98	−4.12 to 0.15	.07	−0.52	−2.04 to 1.00	.50
White	Ref			Ref		
Male sex	2.77	1.52 to 4.01	**<.001**	0.24	−0.64 to 1.13	.59
Heart failure	−0.73	−3.14 to 1.67	.55	−1.69	−3.40 to 0.02	**.05**
Contralateral major amputation	0.27	−1.95 to 2.49	.81	−1.02	−2.60 to 0.56	.20
Bilateral CLTI	−1.64	−3.17 to −0.10	**.04**	−0.93	−2.02 to 0.17	.10
COPD	−1.75	−3.31 to −0.19	**.03**	−1.93	−3.04 to −0.82	**<.001**
Smoking			**.001**			**<.001**
Current or within past year	−2.08	−3.55 to −0.60	**.01**	−1.69	−2.73 to −0.64	**.002**
>1 Year ago	0.07	−1.47 to 1.61	.93	0.09	−1.01 to 1.18	.87
Never	Ref			Ref		
ESRD	0.36	−1.48 to 2.20	.70	−0.83	−2.14 to 0.48	.21
Hyperlipidemia	0.52	−0.76 to 1.81	.42	−0.33	−1.24 to 0.59	.48
Diabetes	0.12	−1.10 to 1.34	.85	−0.91	−1.78 to −0.04	**.04**
Hypertension	−0.79	−2.48 to 0.91	.36	−0.62	−1.83 to 0.58	.31
Tissue loss	−0.11	−1.47 to 1.24	.87	0.01	−0.95 to 0.98	.98
Opiate use	−3.34	−4.64 to −2.05	**<.001**	−1.55	−2.48 to −0.62	**.001**
Comorbidity index	−0.27	−0.68 to 0.14	.20	−0.60	−0.88 to −0.31	**<.001**
Ambulatory status			**<.001**			**<.001**
Nonambulatory	−3.73	−5.45 to −2.01	**<.001**	−4.26	−5.48 to −3.05	**<.001**
With assistance	−2.53	−3.76 to −1.29	**<.001**	−2.99	−3.86 to −2.12	**<.001**
Without assistance	Ref			Ref		
Living at home	0.86	−1.54 to 3.25	.48	2.01	0.30 to 3.72	**.02**
WIfI Stage (4 vs 1-3)	−2.03	−3.30 to −0.76	**.002**	−0.09	−0.99 to 0.81	.85

CI, Confidence interval; *CLTI*, chronic limb threatening ischemia; *COPD*, chronic obstructive pulmonary disease; *ESRD*, end-stage renal disease; *Ref*, reference; *WIfI*, Wound, Ischemia, foot Infection.
Boldface *P* values represent statistical significance.
[a]Parameter estimates >0 indicate higher MCS and PCS scores.

Supplementary Table III (online only). Univariate regression of EQ-5D health status[a]

Covariate	Estimate	95% CI	P value
Age ≥80 years	3.16	−0.30 to 6.63	.07
Race			.31
Black	1.43	−1.14 to 4.01	.27
All other	−1.76	−5.62 to 2.10	.37
White	Ref		
Male sex	0.74	−1.53 to 3.01	.52
Heart failure	−6.50	−10.85 to −2.14	**.003**
Contralateral above the ankle amputation	−0.05	−4.06 to 3.96	.98
Bilateral CLTI	−5.00	−7.79 to −2.21	**<.001**
COPD	−4.55	−7.39 to −1.71	**.002**
Smoking			.06
Current or within past year	−1.62	−4.30 to 1.07	.24
>1 Year ago	1.15	−1.66 to 3.95	.42
Never	Ref		
ESRD	−4.35	−7.69 to −1.00	**.01**
Hyperlipidemia	−0.40	−2.73 to 1.93	.74
Diabetes	−2.86	−5.07 to −0.64	**.01**
Hypertension	−2.57	−5.64 to 0.50	.10
Tissue loss	−1.47	−3.92 to 0.98	.24
Opiate use	−3.15	−5.53 to −0.78	**.01**
Comorbidity index	−1.87	−2.61 to −1.14	**<.001**
Ambulatory status			**<.001**
Nonambulatory	−6.84	−9.96 to −3.71	**<.001**
With assistance	−3.66	−5.91 to −1.41	**.001**
Without assistance	Ref		
Living at home	5.51	1.16 to 9.86	**.01**
WIfI stage (4 vs 1-3)	−2.12	−4.44 to 0.19	.07

CI, Confidence interval; *CLTI*, chronic limb threatening ischemia; *COPD*, chronic obstructive pulmonary disease; *ESRD*, end-stage renal disease; *Ref*, reference; *WIfI*, Wound, Ischemia, foot Infection.
Boldface *P* values represent statistical significance.
[a]Parameter estimates >0 indicate higher EQ-5D scores.

Supplementary Table IV (online only). Health-related quality of life (HRQoL) scores stratified by WIfI (Wound, Ischemia, foot Infection) stage

HRQoL assessment	WIfI stage				P value
	1	2	3	4	
VascuQoL					.45
Mean ± SD	3.22 ± 1.29	3.07 ± 1.18	3.06 ± 1.27	3.00 ± 1.29	
Median (IQR)	3.12 (2.24-3.88)	2.88 (2.12-3.96)	2.84 (2.12-3.94)	2.76 (2.04-3.84)	
SF6D-R2					.38
Mean ± SD	0.60 ± 0.14	0.59 ± 0.13	0.59 ± 0.13	0.58 ± 0.14	
Median (IQR)	0.60 (0.51-0.67)	0.58 (0.49-0.66)	0.57 (0.50-0.66)	0.57 (0.48-0.65)	
MCS					**.02**
Mean ± SD	46.50 (11.84)	47.21 (12.19)	47.13 (11.86)	45.07 (12.16)	
Median (IQR)	47.47 (39.63-54.69)	48.23 (38.81-56.79)	47.20 (38.62-55.92)	44.55 (36.49-53.92)	
PCS					.64
Mean ± SD	33.96 (8.28)	33.08 (8.12)	32.74 (8.61)	32.92 (8.89)	
Median (IQR)	32.74 (27.75-39.86)	32.41 (27.04-38.50)	32.18 (26.60-37.79)	31.51 (26.52-38.74)	
EQ-5D					.15
Mean ± SD	59.98 (21.57)	58.18 (21.80)	56.75 (22.48)	55.58 (21.82)	
Median (IQR)	60.00 (50.00-75.00)	60.00 (49.00-75.00)	60.00 (50.00-73.00)	55.00 (40.00-70.00)	

IQR, Interquartile range; *MCS*, mental component scale; *PCS*, physical component scale; *SD*, standard deviation; *SF6D-R2*, short-form six-dimension R2 utility index; *VascuQoL*, Vascular Quality of Life.
Boldface *P* values represent statistical significance.