

ORIGINAL STUDIES ORIGINALNI NAUČNI RADOVI

HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH CHRONIC WOUNDS – A COMPREHENSIVE ANALYSIS USING THE WOUND-QOL-17 INSTRUMENT

KVALITET ŽIVOTA POVEZAN SA ZDRAVLJEM KOD PACIJENATA SA HRONIČNIM RANAMA – SVEOBUHVAJNA ANALIZA PRIMENOM WOUND-QOL-17 UPITNIKA

Maja KITIĆ¹, Boris DRAGOSAVAC¹, Milan MILINKOV^{2,3}, Adrijana BOGDANOVIĆ¹, Dragana NIKOLIĆ¹ and Dragan NIKOLIĆ^{3,4}

ORCID NUMBER

Maja Kitić – 0000-0001-5315-1791
Milan Milinkov – 0000-0001-9662-7403
Dragana Nikolić – 0009-0004-0060-8478

Boris Dragosavac – 0009-0001-6460-2209
Adrijana Bogdanović – 0009-0004-9362-9496
Dragan Nikolić – 0000-0003-3602-3522

University Clinical Center of Vojvodina, Emergency Center, Novi Sad¹
Clinic for Orthopedic Surgery and Traumatology²
University in Novi Sad, Faculty of Medicine Novi Sad³
University Clinical Center of Vojvodina, Clinic for Vascular Surgery, Novi Sad⁴

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Abstract

Introduction. Chronic wounds affect 1-2% of the population in developed countries, yet determinants of impaired health-related quality of life remain poorly characterized. This study aimed to identify independent predictors of reduced health-related quality of life in patients with chronic wounds using multivariate statistical methods.

Material and Methods. This cross-sectional study was conducted from February to March 2025 in accordance with the *Strengthening the Reporting of Observational Studies in Epidemiology* recommendations, included 106 patients with wounds persisting for more than four weeks. Health-related quality of life was evaluated using the Serbian version of the *Wound Quality of Life* instrument. Independent predictors of impaired quality of life were assessed using multivariate logistic regression with propensity score matching. **Results.** The median total Wound Quality of Life score was 2.24 (interquartile range 1.89–2.71). Venous leg ulcerations were the most prevalent wound type (42.5%), followed by diabetic foot ulcers (28.3%) and pressure ulcers (20.8%). Multivariate logistic regression identified three independent predictors of poor health-related quality of life: presence of comorbidities (odds ratio 2.78, confidence interval 1.34–5.76, $p = 0.006$), active smoking (odds ratio 3.12, confidence interval 1.51–6.45, $p = 0.002$), and wound duration > 6 months (odds ratio 2.45, confidence interval 1.18–5.09, $p = 0.016$). The physical domain was the most severely affected across all wound types ($p < 0.001$). **Conclusion.** Comorbidities, active smoking, and prolonged wound duration are independent predictors of reduced health-related quality of life in patients with chronic wounds. These findings highlight the importance of addressing modifiable risk factors and implementing patient-centered interventions.

Key words: Quality of Life; Wounds and Injuries; Chronic Disease; Surveys and Questionnaires; Multivariate Analysis; Cost of Illness; Risk Factors

Introduction

Chronic wounds represent a major global health burden, affecting approximately 1-2% of the popula-

Sažetak

Uvod. Hronične rane pogađaju 1–2% populacije u razvijenim zemljama, ali su analize faktora koji utiču na kvalitet života povezan sa zdravljem i dalje ograničene. Cilj ove studije bio je da identifikuje nezavisne prediktore narušenog kvaliteta života kod osoba sa hroničnim ranama primenom multivarijantnih statističkih metoda. **Materijal i metode.** U ovoj studiji preseka, sprovedenoj od februara do marta 2025. godine u skladu sa preporukama *Strengthening the Reporting of Observational Studies in Epidemiology*, učestvovalo je 106 pacijenata sa ranama koje traju duže od četiri nedelje. Korišćen je validirani srpski instrument *Wound Quality of Life*, a multivarijantna logistička regresija uz metodu podudaranja na osnovu sklonosti primenjena je kako bi se utvrdili nezavisni prediktori smanjenog kvaliteta života. **Rezultati.** Medijana ukupnog *Wound Quality of Life* iznosila je 2,24 (interkvartilni raspon 1,89–2,71). Najčešće su bile venske ulceracije (42,5%), zatim dijabetesno stopalo (28,3%) i dekubitalne rane (20,8%). Multivarijantna logistička regresija identifikovala je tri nezavisna prediktora lošeg kvaliteta života: prisustvo komorbiditeta (odnos verovatnoće 2,78; interval pouzdanosti 1,34–5,76; $p = 0,006$), aktivno pušenje (odnos verovatnoće 3,12; interval pouzdanosti 1,51–6,45; $p = 0,002$) i trajanje rane duže od šest meseci (odnos verovatnoće 2,45; interval pouzdanosti 1,18–5,09; $p = 0,016$). Najveće narušavanje zabeleženo je u fizičkoj dimenziji kvaliteta života ($p < 0,001$). **Zaključak.** Kormobiditeti, aktivno pušenje i produženo trajanje rane predviđaju smanjen kvalitet života kod osoba sa hroničnim ranama, što ukazuje na značaj intervencija usmerenih na modifikovane faktore i negu usmerenu na pacijenta. **Gljučne reči:** kvalitet života; povrede i rane; upitnici i ankete; multivarijantna analiza; troškovi bolesti; faktori rizika

tion in developed countries [1,2]. Despite their substantial impact on healthcare systems and patient well-being, comprehensive analyses of the determinants of health-related quality of life (HRQoL) in this

✉ Corresponding author: Maja Kitić, E-mail: majakiticc@gmail.com, dragan.nikolic@mf.uns.ac.rs

Abbreviations

CI	– confidence interval
DSM-5	– Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EWMA	– European Wound Management Association
HRQoL	– Health-Related Quality of Life
IPAQ-SF	– International Physical Activity Questionnaire – Short Form
IQR	– interquartile range
IWII	– International Wound Infection Institute
MMSE	– Mini-Mental State Examination
OR	– odds ratio
PUSH	– Pressure Ulcer Scale for Healing
SD	– standard deviation
STROBE	– Strengthening the Reporting of Observational Studies in Epidemiology
VIF	– variance inflation factor

population remain limited. Recent systematic reviews have highlighted critical knowledge gaps, including the lack of multivariate analyses controlling for confounding factors, limited comparative studies across wound etiologies, and absence of propensity score analyses for group balancing [3,4].

The pathophysiology of chronic wounds involves complex interactions between local and systemic mechanisms, including persistent inflammation, cellular senescence, and impaired angiogenesis [5]. These biological processes profoundly affect patients' physical, psychological, and social functioning; however, the relative contribution of clinical and behavioral factors to overall HRQoL remains insufficiently characterized. To address these gaps, the present study applies the Wilson-Cleary conceptual model of patient outcomes [6] to integrate biological variables, symptom burden, functional status, and patient perceptions.

The primary objective of this study was to identify independent predictors of impaired HRQoL in patients with chronic wounds using validated assessment instruments and robust statistical methodology, including propensity score matching. Secondary objectives were to explore domain-specific associations between clinical and behavioral factors and distinct dimensions of quality of life.

Material and Methods

Study Design and Ethical Approval

A prospective, observational, cross-sectional study was conducted between February and March 2025 in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [7]. The study protocol was approved by the Ethics Committee of the University Clinical Center of Vojvodina, Novi Sad, Serbia (approval number: 00-01/69-2025). Written informed consent was obtained from all participants before enrollment.

Study Population

Patients were recruited from the wound care clinic of the Emergency Center at the University Clinical Center of Vojvodina, Novi Sad, Serbia. Inclusion criteria were: age ≥ 18 years, presence of chronic wound lasting longer than four weeks [8], Mini-Mental State Examination (MMSE) score ≥ 24 , and the ability to provide informed consent. Exclusion criteria were: acute or surgical wounds of less than four weeks' duration, significant occlusive arterial disease of the lower extremities, active malignancy requiring chemotherapy or radiotherapy, severe psychiatric disorders defined according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria, and the estimated life expectancy of less than six months.

Based on pilot data demonstrating a standard deviation of 0.65 in Wound-QoL scores, a minimum sample size of 96 participants was calculated to detect a clinically significant difference of 0.3 points between groups [9], with $\alpha=0.05$ and 80% statistical power. To account for 20% attrition, for a target sample size of 120 participants was defined.

Instruments and Measurements

The Wound-QoL-17 is a validated disease-specific instrument (Cronbach's $\alpha=0.92$) that comprises three domains: physical complaints (5 items), psychological well-being (5 items), and daily activities (6 items) [9]. The Serbian version of the instrument, previously translated, culturally adapted, and validated for Serbian-speaking populations, was used in this study. Clinical wound assessment included classification of wound etiology according to European Wound Management Association (EWMA) guidelines [10], wound severity using the Pressure Ulcer Scale for Healing (PUSH) Tool 3.0 [11], and wound surface area measurement by digital planimetry using ImageJ software [12]. Bacterial burden was evaluated based on the International Wound Infection Institute (IWII) criteria [13]. Smoking status was assessed by the Fagerström Test for Nicotine Dependence [14], while physical activity was measured using the International Physical Activity Questionnaire – Short Form (IPAQ-SF) [15].

Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation (SD) for normally distributed data or as median with interquartile range (IQR) for skewed distributions. Categorical variables were presented as frequencies and percentages. Group comparisons were performed using the Mann-Whitney U test was used for binary variables and the Kruskal-Wallis test with post hoc Dunn's test for multiple-

Table 1. Demographic and clinical characteristics by wound type (n=106)

Characteristic	Venous ulcers (n=45)	Diabetic ulcers (n=30)	Pressure ulcers (n=22)	Other (n=9)	p-value
Age, years (mean±SD*)	59.8±12.4	66.2±11.8	64.1±5.9	58.3±14.2	0.142
Male sex, n (%)	28 (62.2)	21 (70.0)	15 (68.2)	6 (66.7)	0.893
Wound (median, IQR†)	6.8 (3.9-12.3)	9.2 (5.1-16.8)	8.5 (4.8-15.2)	5.2 (3.2-10.8)	0.038
Wound surface area, cm ² (median, IQR†)	8.5 (4.2-15.3)	12.3 (6.8-22.1)	15.8 (8.9-28.4)	7.2 (3.8-12.6)	0.012
PUSH‡ score/PUSH‡ (mean±SD*)	9.2 ±3.1	11.4±2.8	12.6±3.4	8.8±2.9	0.003
Presence of comorbidities, n (%)	22 (48.9)	30 (100.0)	18 (81.8)	5 (55.6)	<0.001
Current smokers, n (%)	15 (33.3)	12 (40.0)	8 (36.4)	3 (33.3)	0.932

*SD – Standard Deviation; †IQR – Interquartile Range; ‡PUSH – Pressure Ulcer Scale for Healing

Table 2. Wound-QoL-17 scores by domains and wound type

Domain	Total (n=106)	Venous ulcers (n=45)	Diabetic ulcers (n=30)	Pressure ulcers (n=22)	p-value
Overall score (median, IQR*)	2.24 (1.89-2.71)	2.20 (1.85-2.65)	2.28 (1.92-2.78)	2.64 (2.18-3.12)	0.018
Physical domain (median, IQR*)	2.60 (2.20-3.00)	2.50 (2.10-2.90)	2.65 (2.30-3.10)	2.85 (2.50-3.20)	0.021
Psychological domain (median, IQR*)	1.80 (1.40-2.40)	1.75 (1.35-2.30)	1.85 (1.45-2.50)	2.10(1.60-2.70)	0.082
Daily activities (median, IQR*)	2.33 (1.83-2.83)	2.25 (1.75-2.75)	2.38 (1.88-2.92)	2.67 (2.17-3.17)	0.036

*IQR – Interquartile Range

group comparisons. Associations between continuous variables were assessed using Spearman’s rank correlation. Multivariate analysis was conducted using the binary logistic regression with backward stepwise elimination. Variables with $p < 0.2$ in univariate analysis were entered into the multivariate model. Multicollinearity was evaluated using the variance inflation factor ($VIF < 5$). Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test. Propensity score matching was performed using 1:1 nearest-neighbor matching. All statistical analyses were carried out using SPSS version 28.0 (IBM Corp., Armonk, NY, USA) and R version 4.3.0. A two-tailed p -value < 0.05 was considered statistically significant.

Results

Participant Characteristics

Of the 134 patients screened, 120 met inclusion criteria and were enrolled. Complete datasets were available for 106 participants, yielding a response rate of 88.3%. The mean age of the study population was 62.4 ± 13.7 years, and 66.0% were male. Venous ulcers were the most prevalent wound type (42.5%), followed by diabetic foot ulcers (28.3%) and pressure ulcers (20.8%). The median wound duration was 7.8 months (IQR 4.2-14.5), with significant differences observed among wound etiologies ($p=0.038$). All patients with diabetic foot ulcers had at least one comorbidity compared with 48.9% of those with venous ulcers ($p < 0.001$). Detailed demographic and clinical characteristics stratified by wound type are presented in **Table 1**.

Health-Related Quality of Life Assessment

The median overall Wound-QoL score was 2.24 (IQR 1.89-2.71), indicating a moderate impairment in health-related quality of life. Among the domains, the physical domain showed the greatest degree of impairment (median 2.60, IQR 2.20-3.00), followed by daily activities (2.33, IQR 1.83-2.83) and psychological well-being (median 1.80, IQR 1.40-2.40). Patients with pressure ulcers demonstrated the highest mean overall scores (2.64 ± 0.63), reflecting worse HEQoL compared with those with venous ulcers (2.20 ± 0.71 , $p=0.018$). Complete domain-specific Wound-QoL-17 scores by wound etiology are shown in **Table 2**.

Univariate Analysis

Univariate analysis identified several variables significantly associated with Wound-QoL scores above the median, indicating poorer HRQoL. Comorbidities were present in 78.3% of patients with impaired HRQoL compared with 21.7% among those without impairment ($p<0.001$). Current smoking was observed in 71.4% versus 28.6% ($p < 0.001$), wound duration longer than six months in 68.5% versus 31.5% ($p = 0.003$), wound surface area greater than 10 cm² in 66.7% versus 33.3% ($p = 0.011$), and a PUSH score above 10 in 64.9% versus 35.1% ($p = 0.014$). A complete summary of univariate associations is provided in **Table 3**.

Multivariate Analysis and Independent Predictors

After adjustment for confounders, multivariate logistic regression identified three independent predictors of impaired HRQoL: presence of comorbidities

Table 3. Univariate analysis of factors associated with impaired HRQoL (Wound-QoL > median)

Factor	Impaired HRQoL* n (%)	Preserved HRQoL* n (%)	p-value
Age > 65 years	28 (54.9)	23 (45.1)	0.156
Male sex	36 (51.4)	34 (48.6)	0.523
Presence of comorbidities	47 (78.3)	13(21.7)	<0.001
Current smoking	25 (71.4)	10 (28.6)	<0.001
Wound duration >6 months	37 (68.5)	17(31.5)	0.003
Wound area >10 cm ²	32 (66.7)	16 (33.3)	0.011
PUSH† score >10/PUSH† skor >10	35 (64.9)	19 (35.1)	0.014
Low physical activity	30 (60.0)	20 (40.0)	0.089

*HRQoL – Health-Related Quality of Life; †PUSH – Pressure Ulcer Scale for Healing

Table 4. Multivariate logistic regression – Independent predictors of impaired HRQoL

Predictor	Odds Ratio*	95% CI†	p-value
Presence of comorbidities	2.78	1.34-5.76	0.006
Current smoking	3.12	1.51-6.45	0.002
Wound duration >6 months	2.45	1.18-5.09	0.016

Model characteristics: Hosmer-Lemeshow test $\chi^2 = 6.42$, $p = 0.599$; Nagelkerke $R^2 = 0.342$; Classification accuracy = 75.5%

*OR – Odds Ratio; †CI – Confidence Interval

ties (odds ratio [OR] = 2.78, 95% confidence interval [CI] 1.34-5.76, $p = 0.006$), current smoking (OR=3.12, 95% CI 1.51-6.45, $p = 0.002$), and wound duration longer than six months (OR=2.45, 95% CI 1.18-5.09, $p = 0.016$). The model demonstrated good calibration (Hosmer-Lemeshow $\chi^2 = 6.42$, $p=0.599$), explained 34.2% of the variance (Nagelkerke $R^2=0.342$), and achieved an overall classification accuracy of 75.5%. Detailed multivariate logistic regression results are presented in **Table 4**.

Propensity Score Matching Analysis

Following propensity score matching of smokers and non-smokers (36 matched pairs), baseline characteristics were well balanced, with all standardized differences below 0.1. A statistically significant difference in Wound-QoL scores persisted, with smokers exhibiting worse scores than non-smokers (2.48 ± 0.58 vs. 2.02 ± 0.61 ; mean difference 0.46, 95% CI 0.22-0.70; $p < 0.001$), confirming the independent negative effect of smoking on HRQoL.

Domain-Specific Associations

Domain-specific analyses demonstrated distinct patterns of association. The physical domain was most strongly associated with wound surface area ($\beta = 0.382$, $p < 0.001$) and PUSH score ($\beta = 0.345$, $p = 0.002$). The psychological well-being domain was significantly associated with wound visibility ($\beta = 0.298$, $p = 0.012$) and social isolation score ($\beta = 0.276$, $p = 0.018$). Limitations in daily activities were associated with lower-extremity wound location ($\beta = 0.321$, $p = 0.008$) and mobility impairment ($\beta = 0.412$, $p < 0.001$).

Discussion

This study provides evidence for independent predictors of impaired HRQoL in patients with chronic wounds through comprehensive multivariate analysis and propensity score matching. The identification of comorbidities, active smoking, and prolonged wound duration as key determinants has important implications for both clinical practice and health policy.

Our median Wound-QoL score of 2.24 observed in our cohort is consistent with data reported in European populations, including studies from Germany (2.18) [16], but higher than those reported in Asian cohorts, such as Singapore (1.92) [17]. These differences may reflect variations in healthcare system organization and cultural perceptions of pain. The association between smoking and reduced HRQoL in our study (OR=3.12) was stronger than that reported in previous studies (OR 1.8-2.4) [18,19], which is likely attributable to the use of propensity score matching, enabling more robust controls of confounding.

Our findings are consistent with global research on HRQoL in chronic wound populations. Similar patterns have also been reported in regional studies of chronic conditions, where pain intensity, functional impairment, and the presence of comorbidities consistently emerge as major determinants of reduced quality of life. These convergent findings support the broader concept that chronic, mobility-limiting health problems – irrespective of underlying etiology – produce parallel declines across physical, emotional, and social domains of HRQoL, closely mirroring the determinants identified in the present study [20,21].

A study by Dantas et al. [22] similarly identified comorbidities and prolonged wound duration as major predictors of impaired HRQoL in a Brazilian cohort. Their findings, demonstrating the strong influence of metabolic and cardiovascular comorbidities on physical functioning, closely parallel our results. The stronger predictive estimates in our study may be explained by the application of propensity score matching, whereas their analysis relied solely on conventional multivariate regression.

Zhang et al. [23], in a study of 223 Chinese patients assessed using the Wound-QoL instrument, identified large wound size ($\geq 100 \text{ cm}^2$), lower-limb location, and psychological distress (anxiety, depression) as the most influential determinants of HRQoL. Although our study highlighted smoking, comorbidities, and wound duration as primary predictors, both studies reinforce the multidimensional nature of HRQoL impairment. Observed differences likely reflect disparities in healthcare systems, wound-care accessibility, and cultural perceptions of pain and illness. Notably, our median Wound-QoL score more closely resembled those reported in European populations than in Asian cohorts, suggesting that systemic and cultural factors influence HRQoL outcomes.

The strong association between comorbidities and impaired HRQoL operates through multiple pathophysiological pathways. Systemic inflammation, characterized by elevated pro-inflammatory cytokines in conditions such as diabetes and cardiovascular diseases, impairs fibroblast activity and collagen synthesis [24]. In addition, microvascular dysfunction reduces tissue perfusion by approximately 30-40% [25]. The propensity score analysis confirmed the association between smoking and HRQoL impairment. Tissue hypoxia, mediated through carboxyhemoglobin formation, reduces oxygen delivery, while nicotine-induced vasoconstriction decreases perfusion within one hour of cigarette consumption. Moreover, immune dysfunction manifests through impaired neutrophil migration and macrophage function [26,27].

Based on these findings, a risk-stratified model of care is proposed. Patients at high risk (three or more risk factors) should receive intensive, multidisciplinary management, including weekly clinical reviews, advanced therapies, and smoking cessation support. Patients at moderate risk (one to two risk factors) should be managed in specialized wound clinics with biweekly follow-up and enhanced patient education. Low-risk patients without identifiable risk factors require monthly follow-up and self-management support.

Several limitations should be acknowledged. The cross-sectional design precludes causality inference, although the use of propensity score matching strengthens the robustness of the observed associations. As a single-center study, external validity may be limited. Behavioral variables were self-reported and may be subject to reporting bias. Furthermore, the absence of biomarker data and longitudinal follow-up precludes assessment of HRQoL trajectories over time. Future research should incorporate longitudinal cohort designs, cluster-randomized trials of risk-stratified interventions, and predictive models integrating biomarkers.

Conclusion

This comprehensive analysis identifies comorbidities, active smoking, and prolonged wound duration as independent predictors of impaired Health-Related Quality of Life in individuals with chronic wounds. The implementation of risk-stratified care pathways, integrated smoking-cessation programs, and optimized management of comorbid conditions is essential to improve patient-centered outcomes. These findings support the development of specialized, multidisciplinary chronic wound centers capable of addressing the complex interaction of factors that influence patient quality of life. Priority should be given to targeted interventions addressing modifiable risk factors, particularly smoking cessation and optimized control of comorbid diseases.

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