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Romanian Translation and Validation of Vascular Quality of Life Questionnaire "VascuQOL-6" in Patients with Lower Extremity Arterial Disease

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ABSTRACT

Background: Patient reported outcomes are valuable components in the assessment of results of treatment for peripheral arterial disease (PAD). The aim of the study was to translate the six item Vascular Quality of Life Questionnaire (VascuQoL-6) survey into Romanian, and to validate the psychometric performance of the questionnaire in a representative cohort of patients with lower extremity arterial disease.
Material and Methods: Translation of the VascuQoL-6 questionnaire was performed following accepted methodology. The overall validation cohort included 100 patients with PAD (86% with chronic limb-threatening ischemia) undergoing lower limb revascularization. In 20 patients with stable PAD two questionnaires were offered preoperatively with a median interval of 15 days. Another 22 patients were re-tested after revascularization at a median interval of 30 days.
Results: The median time required for completion of the VascuQoL-6 survey was 2 (IQR 2-3) minutes. The translated version demonstrated high internal consistency (Cronbach's alpha – 0.81) and there was no difference in the preoperative median VascuQoL-6 scoring during the test re-test assessment. Area under the ROC curve for ability to discriminate intermittent claudication from chronic limb-threatening ischemia was 0.897. The median VascuQoL-6 score increased from 10 (IQR 8-12) points preoperatively to 18.5 (IQR 14.7-20) points post-operatively ($p < 0.0001$) with a standardized response mean of 2.94.
Conclusion: The Romanian version of the VascuQoL-6 survey demonstrated good reliability, validity and responsiveness and can thus be recommended for use in patients with lower limb PAD.
Key words: patient reported outcomes, health-related quality of life, peripheral arterial disease, chronic limb-threatening ischemia, lower limb revascularization

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INTRODUCTION

Patient reported outcomes are increasingly recognized as a valuable compo-

nent in comprehensive assessment of the results of medical and interventional treatment for peripheral arterial disease (PAD). Current clinical practice guidelines on the management of chronic limb ischemia recommend reporting of treatment outcomes based on a combination of objective clinical, anatomical, hemodynamic criteria and evaluation of health-related quality of life (HRQoL) (1). In contrast to a large variety of generic HRQoL questionnaires usually available in multiple linguistic versions, the number of disease-specific tools designed for the cohort of patients with PAD is still limited. The Vascular Quality of Life questionnaire (VascuQoL) questionnaire was developed in 2001 and initially comprised 25 items (2). Nearly a decade later, the short version – the six item VascuQoL questionnaire (VascuQoL-6) was developed and included the six most informative items selected from the original questionnaire based on both classical psychometric methods and item response theory. The VascuQoL-6 demonstrated high validity, reliability and high correlation with the original extended version (3). Since then, VascuQoL-6 has been translated into many languages, and the favorable psychomteric properties have been confirmed by additional validation studies in other countries (Norwegian, Portuguese, Dutch) and there are several ongoing clinical trials registered for validation in other languages (German, Spanish) (4,5). The VascuQoL questionnaire is currently used in the most important randomized clinical trials in patients with chronic limb threatening ischemia: BASIL-2, BASIL-3 and BEST-CLI (1) and the VascuQoL-6 is being used both in the large registry-based RCT SWEDEPAD that investigate drug-coated devices in PAD (6) and in the phase 3 trial STRIDE on the effect of semaglutide on walking ability in PAD patients (https://clinicaltrials.gov/ct2/show/NCT04560998). To the best of our knowledge no PAD-specific validated HRQoL questionnaires are available in Romanian, hindering the reporting of outcomes and scientific research in the field of vascular surgery at the national level.

The aim of present study was to translate and linguistically validate the VascuQoL-6 questionnaire in Romanian, and to prospectively validate the translated version in a representative cohort of patients with chronic lower limb ischemia.

MATERIAL AND METHODS

This study was conducted in the Vascular Surgery Clinic at the Department of General surgery, „Nicolae Testemitanu" State University of Medicine and Pharmacy from Republic of Moldova. The translation process was performed during January-February 2021 and collection of the data for validation of the translated version was done between June 2021 and February 2022. The authors of VascuQoL-6 (JN, MM) granted permission for translation of the questionnaire. The study was conducted according to the principles outlined in the Declaration of Helsinki and approved by the university's ethical committee as a component part of the doctoral research project of the second author (PA).

Translation process

According to current recommendations translation of the VascuQoL-6 questionnaire was done in several consecutive steps (7). Initially, three attending vascular surgeons (native speakers in Romanian and B2 or higher level in English language) independently translated the original version of VascuQoL-6 to Romanian. Next, the same researchers performed the backward translation from Romanian to English exchanging the translated versions between the experts. All translated versions were analyzed by authors of the VascuQoL-6 questionnaire (JN, MM), then discussed as a group until a consensus was reached. At the following stage, three other vascular specialists (not involved in translation process) and five patients with PAD, all – native speakers in Romanian, performed an evaluation of each translated item, answering the following questions: "Is the question formulated clear and easy to understand?"; "Is the question relevant to lower limb ischemia?"; "Should this question be modified?". Thereafter, the adjustment of the final version of the questionnaire was done and approved by the developers. The original and Romanian versions of "VascuQoL-6" questionnaire are presented in *table 1*.

Validation cohort

According to the recommendation provided by Hatcher et al (2014) a minimal sample size of 100 participants was chosen for the validation process (8). During the study period all consecutive patients managed at the institution for objectively confirmed PAD and chronic limb ischemia were invited to participate. Twenty-three participants were excluded due to the following reasons: refusal to participate – 5; not a native Romanian speaker – 9; severe comorbidities and/or dependent status – 6; altered mental status or cognitive impairment – 3 patients.

The Romanian version of "VascuQoL-6" was provided to study participants on the day of admission to the Department or during the primary consultation

Table 1 - The original (3) and Romanian versions of VascuQoL-6 quality of life questionnaire.

Items (questions)	Answers	Itemi (întrebări)	Răspunsuri
(1) Because of the poor circulation in my legs, the range of activities that I would have liked to do in the past two weeks has been:	• Severely limited – most activities not done (1 p) • Very limited (2 p) • Very slightly limited (3 p) • Not limited at all – have done all the activities that I wanted to (4 p)	(1) Din cauza circulației slabe de sânge în picioare, varietatea de activități pe care mi-aș fi dorit să le fac în ultimele două săptămâni a fost:	• Sever limitată – majoritatea activităților nu au fost făcute (1 p) • Moderat limitată (2 p) • Foarte puțin limitată (3 p) • Deloc limitată – am efectuat toate activitățile pe care le-am dorit (4 p)
(2) During the past two weeks, my legs felt tired or weak:	• All of the time (1 p) • Some of the time (2 p) • A little of the time (3 p) • None of the time (4 p)	(2) În ultimele două săptămâni am simțit că picioarele mele sunt obosite sau slabe:	• Tot timpul (1 p) • O oarecare parte din timp (2 p) • O mică parte din timp (3 p) • Niciodată (4 p)
(3) During the past two weeks, because of the poor circulation in my legs, my ability to walk has been:	• Totally limited, couldn't walk at all (1 p) • Very limited (2 p) • A little limited (3 p) • Not at all limited (4 p)	(3) În ultimele două săptămâni din cauza circulației slabe de sânge în picioare capacitatea mea de a merge a fost:	• Complet limitată, nu puteam merge deloc (1 p) • Foarte limitată (2 p) • Puțin limitată (3 p) • Deloc limitată (4 p)
(4) During the past two weeks, I have been concerned about having poor circulation in my legs:	• All of the time (1 p) • Some of the time (2 p) • A little of the time (3 p) • None of the time (4 p)	(4) În ultimele două săptămâni am fost îngrijorat de circulația slabă de sânge în picioarele mele:	• Tot timpul (1 p) • O oarecare parte din timp (2 p) • O mică parte din timp (3 p) • Niciodată (4 p)
(5) During the past two weeks, because of the poor circulation in my legs, my ability to participate in social activities has been:	• Totally limited, couldn't socialize at all (1 p) • Very limited (2 p) • A little limited (3 p) • Not at all limited (4 p)	(5) În ultimele două săptămâni, din cauza circulației slabe de sânge în picioare, capacitatea mea de a participa la activitățile sociale a fost:	• Complet limitată, nu am putut participa la nici o activitate socială (1 p) • Foarte limitată (2 p) • Puțin limitată (3 p) • Deloc limitată (4 p)
(6) During the past two weeks, when I have had pain in the leg (or foot) it has given me:	• A great deal of discomfort or distress (1 p) • A moderate amount of discomfort or distress (2 p) • Very little discomfort or distress (3 p) • No discomfort or distress (4 p)	(6) În ultimele două săptămâni, când am avut durere în gambă (sau picior) aceasta mi-a provocat:	• Un disconfort sau suferință mare (1 p) • Un disconfort sau suferință moderată (2 p) • Un disconfort sau suferință foarte mică (3 p) • Nici un disconfort sau suferință (4 p)
Individual answers to each of the six items are scored from 1 to 4 points and the total score ranges from 6 to 24 points (higher score indicates better health status)		Răspunsurile individuale la fiecare dintre cele șase itemi sunt cuantificate cu 1 și până la 4 puncte, iar scorul total variază de la 6 până la 24 de puncte (scorul mai mare indică o stare de sănătate mai bună)	

at the outpatient facility. In 20 (20%) patients with stable PAD two questionnaires were offered with an interval between "test" and "re-test" raging from 14 to 30 days (median – 15 days). Another 22 (22%) patients were re-tested following open or endovascular revascularization of the affected lower limb at a median interval of 30 days (range 30 – 90 days). The study flowchart is presented in *fig. 1*.

Clinical workup, definitions and classifications

Study participants were required to complete a clinical examination, measurement of the ankle-brachial index (ABI) and vascular imaging (duplex ultrasound, computed tomography angiography and/or digital sub-traction angiography). In patients with intermittent claudication, the self-reported pain-free walking distance was recorded. Symptomatic lower extremity PAD was defined as presence of typical symptoms of chronic (more than 2 weeks) limb ischemia, abnormal ABI and ≥50% stenosis or occlusion of aorto-iliac, femoro-popliteal or infragenicular arteries. If these criteria were associated with rest pain, presence of plantar ulcer or gangrene, chronic limb threatening ischemia (CLTI) was diagnosed (1). The severity of ischemia was classified by Fontaine stages and the risk of major limb amputation was stratified according to the WIfI (Wound, Ischemia, foot Infection) classification. The mean WIfI score were calculated as proposed by Darling (9). In the 22 patients who completed

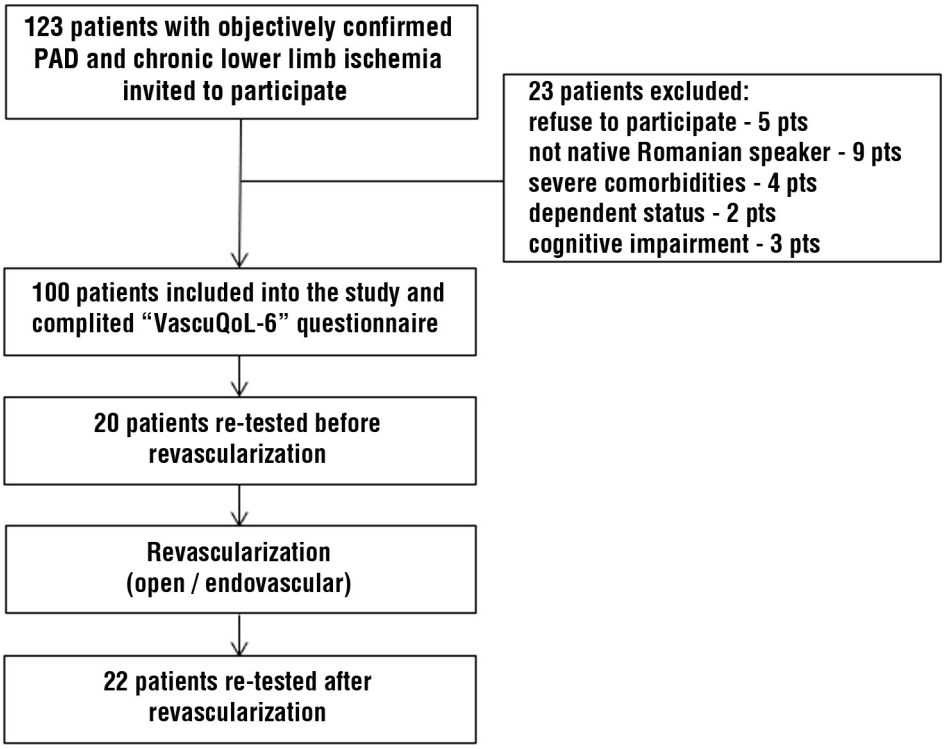

Figure 1 - Study flow-chart demonstrating the inclusion of patients for validation of translated version of VascuQoL-6 questionnaire.

the VascuQoL-6 questionnaire after revascularization, the corresponding changes in ABI and WIfI stage were registered during the same follow-up visit.

Statistical analysis

The Shapiro-Wilk test was used to test normality of data distribution. Continuous variables are presented as means ± standard deviation or as medians with 25-75% interquartile range (IQR). Categorical variables are presented as number with percentage. Difference of medians was assessed by Mann-Whitney test, and difference between proportions – by Fisher exact test. Correlation coefficient was calculated to measure relationship between variables. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using „GraphPad Prism" (v. 8.0.1, GraphPad Software, San Diego, California, USA) and SPSS 16.0 (SPSS Inc., Chicago, IL, USA) software.

RESULTS

Patient characteristics and intervention

Mean age of the participants was 67±8 years (range 48-89 years) and 69% were male. Intermittent claudication that restricted daily life activities that was resistant to medical treatment and exercise was diagnosed in 14 (14%) patients, and CLTI in 86: Fontaine stage III – 23 (23%), Fontaine stage IV – 63 (63%) patients. The WIfI stage 1 (very low risk of amputation) was diagnosed in 9 patients, stage 2 (low risk) – in 44, stage 3 (moderate risk) – in 28, and stage 4 (high risk) – in 15 cases (in 4 patients the WIfI stage was not possible to determine due to unreliable ABI values). Open surgical bypass was performed in 54 (54%) patients (11 for aorto-iliac disease and 43 - for infrainguinal disease). Endovascular revascularization (plain balloon angioplasty ± stenting) was used in 46 (46%) cases: aorto-iliac segment – 5, femoro-popliteal and/or infrapopliteal segment – 41.

Psychometric evaluation of the translated VascuQoL-6 questionnaire

All study participants completed the provided questionnaires without asking for assistance or additional explanations. Median time required for completion of the VascuQoL-6 was 2 (IQR 2-3) minutes. Analysis of returned questionaries did not detect any missed items or voluntarily left out responses.

In the entire study cohort, the median value of VascuQoL-6 scored 10 (IQR 8-12) points preoperatively,

ranging from 6 to 19 points. The percentage of persons reporting scores below 8 points (< 10% percentile) and above 15 points (> 90% percentile) was 7% and 8%, respectively, demonstrating lack of relevant floor or ceiling effects in the target population. The translated version demonstrated a high reliability with a Cronbach's alpha coefficient for internal consistency of 0.81. The results of the inter-item correlation matrix assessment varied from 0.24 (Q4 with Q5) to 0.64 (Q1 with Q3).

The analysis of test-retest reliability showed favorable results. Thus, there was no statistical difference between the median VascuQoL-6 score as obtained during the first and second preoperative visit – 13.5 (IQR 9-17) and 13.0 (IQR 8.25-16.75) points, respectively ($p > 0.05$). The interclass correlation coefficient for the entire questionnaire was 0.86 (95% CI 0.67-0.93), indicating excellent reliability.

The median value of the VascuQoL-6 in patients with intermittent claudication was significantly higher – 15 (IQR 13-18) points, comparing to the patients with CLTI: 10 (IQR 8-12) points in Fontaine stage III and 10 (IQR 8-11) points in Fontaine stage IV, respectively ($p < 0.0001$). The area under ROC (Receiver Operating Characteristic) curve for the ability of the VascuQoL-6 to discriminate intermittent claudication from CLTI was 0.897, confirming acceptable diagnostic performance of the translated questionnaire (*fig. 2*). The cut-off value of less than or equal to 12 points offered a sensitivity of 86% and a specificity of 85% in the detection of chronic limb-threatening ischemia.

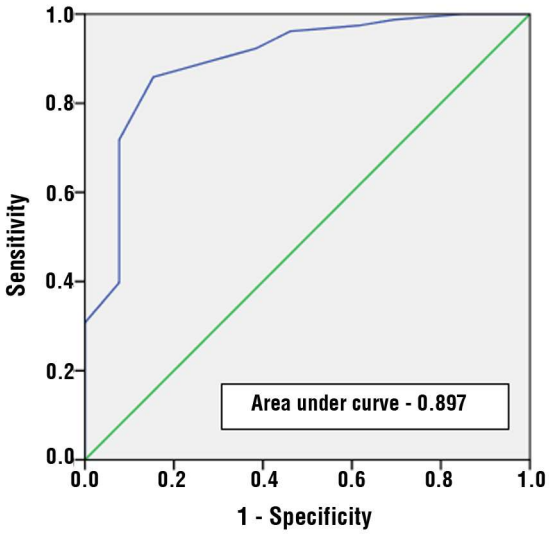

Figure 2 - The ROC curve for ability of VascuQoL-6 questionnaire to discriminate between patients with intermittent claudication and with limb threatening ischemia.

The Romanian version of VascuQoL-6 demonstrated modest but statistically significant correlation with preoperative clinical criteria used for routine stratification of the patients by severity of ischemia. Thus, the correlation coefficient for HRQoL scores was: $r = 0.44$ (95% CI 0.26-0.59) with the ABI values; $r = 0.37$ (95% CI 0.18-0.53) with pain free walking distance; and $r = -0.36$ (95% CI (-0.51) – (-0.17)) with the mean WIfI score.

Technical success of revascularization was accomplished in all CLTI patients that were re-evaluated regarding HRQoL postprocedurally. The mean increase in the ABI value postoperatively was 0.45 ± 0.16, $p < 0.0001$. At a median follow-up interval of 30 (IQR 30-60) days the downgrading of WIfI with at least one stage was registered in all patients. The WIfI stage 0 was diagnosed in 6 (27.2%) case, stage 1 – in 15 (68.1%) cases and stage 2 – in one case. The median VascuQoL-6 score increased from 10 (IQR 8-12) points preoperatively to 18.5 (IQR 14.7-20) points postoperatively ($p < 0.0001$) with higher score in patients categorized postoperatively as WIfI stage 0 vs WIfI stage 1 – 20 (IQR 18.5-22) vs 17 (IQR 13.7-19.2) points, the difference being of borderline statistical significance ($p = 0.05$). The standardized response mean (mean score difference divided by the standard deviation of the mean score difference) for the VascuQoL-6 questionnaire was 2.94 (Q1 – 1.36, Q2 – 1.46, Q3 – 1.63, Q4 – 1.61, Q5 – 1.09, Q6 – 2.12) indicating a large observable effect size of the invasive intervention by the VascuQoL-6. There was also a moderate positive correlation between the observed ABI increase after intervention and the corresponding change in HRQoL scores: $r = 0.45$ (95% CI 0.01-0.74).

DISCUSSION

There are several generic and disease-specific QoL questionnaires used for evaluation of patient reported outcomes in peripheral vascular interventions (10). The main advantage of disease-specific tools is their ability to focus on details directly related to the pathological condition and, as a result, an increased sensitivity to modifications in disease severity due to natural progression or after different treatments provided. Comparing to other HRQoL questionaries designed for patients with PAD ("PAQ", "CLAU-S", "PAVK-86") that include from 20 to 86 items, the VascuQoL-6 survey is substantially more practical to use for both patients and practitioners (11-13). Although the median time required for completion of the VascuQoL-6 questionnaire was somewhat longer than that reported by the

authors of the original version (1.4 minutes) in the current study (3), it still was highly acceptable for reasonably convenient routine use in clinical practice.

Results of the psychometric evaluation of the Romanian version of VascuQoL-6 were similar to the data reported by other researchers who have translated and validated the questionnaire into other languages. Thus, internal consistency measured by Cronbach's alpha coefficient was 0.82 for the Norwegian version (4) and 0.84 for the Brazilian-Portuguese version (5). The interclass correlation coefficient of 0.84, determined by de Almeida Correia for test-retest reliability of VascuQoL-6, was almost identical to that presented in current study (5). In contrast to above mentioned studies that included exclusively (4) or predominantly (5) patients with intermittent claudication, CLTI cases represented nearly 90% in our cohort. Despite this fact, the coefficient of correlation between the total VascuQoL-6 score and pain free walking distance determined in current study (r = 0.37) was similar to that reported for another version – 0.39 (5), emphasizing the usefulness of VascuQoL-6 also in CLTI.

The ability of disease-specific QoL questionnaires to correlate with the results of applied treatments is important. Results in the current study demonstrated appropriate responsiveness of translated version of VascuQoL-6 to invasive revascularization procedures. Successful revascularization thus resulted in significant increase in total VascuQoL-6 score with a mean increase value of 7.4±2.3 points. This observed HRQoL change should also be considered clinically important based on the principle of "more than half of standard deviation" as proposed by Norman (> 1.4 points in our cohort) (14). It should be mentioned however, that the effect size assessed by standardized response mean in current study was even higher than in original version of VascuQoL-6 – 1.15 and in Norwegian version – 1.13 (3,4). We suppose that this difference could be explained by a more pronounced clinical benefit of revascularization in case of CLTI as compared with intermittent claudication.

There are several limitations of our study. The small number of patients treated for intermittent claudication limited the possibilities to analyze the responsiveness of the translated VascuQoL-6 version in this particular subgroup. The results of conservative treatments and impact of failed revascularization attempts upon HRQoL were also not evaluated in the present study which might be considered a limitation and may warrant future study.

CONCLUSION

The translated version of the VascuQoL-6 questionnaire into Romanian was subjected to a comprehensive psychometric evaluation in a representative cohort of patients with lower limb PAD where the majority of patients had CLTI. The characteristics of the Romanian VascuQoL-6: reliability, validity and responsiveness have matched the original version and previous translations of the questionnaire into other languages. Based on this validation study, the VascuQoL-6 questionnaire can thus be recommended for both routine clinical use in patients with PAD as well as for research purposes within the field of vascular surgery.

Authors' Contributions

Study design (DC, AP, VC); translation of questionnaire and linguistic validation (all authors); data collection and analysis (DC, AP); writing (DC, AP), manuscript revision and final approval (all authors).

Conflicts of interests

MM has copyright to the VascuQoL-25, and MM and JN has copyright to the VascuQoL-6, and must be contacted prior to use. Neither MM or JN received any reimbursement in relation to this study. No other potential conflict of interests is stated by the authors.

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