

File ID 166844
Filename Chapter 8: Determinants of disability and quality of life in critical limb
ischemia

SOURCE (OR PART OF THE FOLLOWING SOURCE):

Type Dissertation
Title Diagnosis and treatment of critical limb ischemia
Author R. Met
Faculty Faculty of Medicine
Year 2010
Pages 163
ISBN 978-90-9025149-3

FULL BIBLIOGRAPHIC DETAILS:

<http://dare.uva.nl/record/333529>

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Chapter 8

Determinants of Functional Disability and Quality of Life in Patients with Critical Limb Ischemia

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ABSTRACT

Objective: To describe the level of disability and quality of life (QoI) of patients with critical limb ischemia (CLI) and to explore the relative contributions of factors explaining these functional health indices.

Methods: All consecutive patients with chronic CLI (Fontaine stage III and IV) presenting in our hospital were eligible. Risk factors for atherosclerosis, ankle pressure at rest and toe pressure were recorded. Disability was measured with the AMC Linear Disability Score (ALDS) and QoI was measured using the Vascular Quality of Life Questionnaire (VascuQoI). Univariate relations between patient characteristics and functional outcomes were analyzed. Additionally, all significant determinants (univariate *P* value set at .30) were entered into multiple linear regression models.

Results: In a 20-months period, 92 patients (mean age 68 years, \pm SD 13), were included. Twenty-nine (32%) patients had ischemic rest pain and 63 (69%) patients had ischemic tissue loss. The ALDS was significant lower in females, patients with a history of stroke, and older patients. The combination of these 3 characteristics accounted for 24% of the variance of the scores on the ALDS. However, in both the univariate and multivariate analysis, we could not demonstrate significant factors explaining patients' QoI.

Conclusion: Baseline level of functional ability, measured by the ALDS, was lower in specific subgroups of patients with critical limb ischemia, whereas QoI was equal for all groups.

INTRODUCTION

Patients with critical limb ischemia (CLI) experience a low quality of life (QoL).¹⁻³ Several factors are associated with impaired QoL, such as female sex, disease severity, carotid artery disease (both symptomatic as well as asymptomatic), and diabetes mellitus.⁴⁻⁷

QoL encompasses different health domains, like social health, mental health and physical health. As some domains of QoL expresses subjective health perception, it is not surprising that a patient's personal traits also determine QoL.⁸ Disability in activities of daily life (ADL) is one of the domains of QoL. Compared to QoL, disability is more closely related to the disease process itself and as such a more objective clinical outcome indicator.⁹ It has been shown that activities of daily life (ADL) are significantly impaired in patients with critical limb ischemia.¹⁰ Little is known about the impact of patient and clinical characteristics on patient's functional ability.

The main objectives of this study were to describe the disability level, using the ALDS, and QoL, using the VascuQoL, of patients with CLI and to explore the relative contributions of multiple demographic factors and clinical parameters explaining these functional health indices. In addition, we explored the correlation between level of functional disability and QoL.

METHODS

Patients

The study population comprised patients with CLI who participated in the baseline assessment of an ongoing prospective longitudinal project investigating the course of CLI. All consecutive patients with chronic CLI presenting in at our hospital were eligible. They were included between May 2007 and December 2008. Inclusion criteria were chronic CLI (Fontaine stage III and IV) with duration of complaints of > 2 weeks. Exclusion criteria were a life expectancy < 6 months and inability to give informed consent. The study was approved by the local Institutional Review Board and all patients gave informed consent.

Assessments

History and physical examination. We recorded risk factors for atherosclerosis (diabetes mellitus, smoking, hypertension, renal failure, hypercholesterolemia, history of coronary artery disease, history of stroke, and family history), and history of vascular interventions (endovascular and surgical). A specific anamnesis was directed to the presence of rest pain or ischemic skin lesions and self reported walking distance. Physical examination included inspection of the ulcer. Additional examinations included ankle/brachial index (ABI) at rest, toe pressure (TP),

transcutaneous oxygen pressure, and duplex ultrasonography of the lower extremity. Patients received treatment as agreed with their physician independent of the study. This could be either conservative, a percutaneous or surgical revascularization, or an amputation.

Disability. Functional health was measured by using the 29 item version of the AMC Linear Disability Score (ALDS). The ALDS is a generic instrument measuring the ability of a patient to perform ADL, ranging from very easy activities, like 'go to the toilet', to complex activities, like 'travel by local bus or tram'. The score range is 0 to 100, with higher scores indicating better functional ability. The ALDS has already been validated in patients with different chronic diseases.¹¹⁻¹⁴ In patients with peripheral arterial disease, the instrument has shown excellent reliability, and good clinical validity and construct validity.¹⁰ The ALDS was administered by one of the investigators (RM).

Quality of life. Quality of life was measured using the VascuQoL. The VascuQoL questionnaire consists of 25 questions on five domains, i.e. Pain (4 items), Activity (8), Emotional (7), Symptoms (4) and Social (2). Each question is rated as a seven point response scale, with a score of one being the worst and a score of seven the best possible. The total average score is the sum of all 25 items scores divided by 25. For each separate domain an average score can be calculated (sum of all items of one domain divided by the number of items of that domain). So, both the overall score as well as the scores per domain range from one to seven.¹⁵ The VascuQoL has shown to be a reliable and valid instrument for assessment of QoL in patients with PAD.^{2,16} The VascuQoL was filled in by the patient at home.

Possible determinants of functional health

Based on previous QoL studies,⁴⁻⁷ we hypothesized that QoL and ADL ability would be lower in patients with comorbidity (diabetes mellitus, coronary artery disease, stroke, renal failure), in women, in patients of older age, and in patients with a higher BMI and in patients with an advanced stage of disease (Fontaine IV).

Statistical analysis

Patient characteristics and functional health status were summarized using descriptive statistics. Differences in patient characteristics between those who did and did not participate in the study, were analyzed using the chi-square test, Fisher's exact test, or Mann-Whitney U test, when appropriate. We performed a univariate analysis to explore the relation between patient and clinical characteristics on the one hand, and functional health status on the other. For this purpose, subgroups based on age and BMI were made according to the mean or median, dependent on the distribution of the data. Additionally, all significant determinants (univariate *P* value

set at .30) were entered into multiple linear regression models (backward elimination).

The association between the ALDS and the VascuQol was investigated with a Pearson or Spearman's rank correlation coefficient, when appropriate. Finally, the associations between the ALDS and the VascuQol and toe and ankle pressures were expressed as Pearson or Spearman's rank correlation coefficients, when appropriate. Statistical analyses were performed using SPSS 15.0 software (SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at $P=.05$. In view of the explorative nature of this study, we did not correct for multiple comparisons.¹⁷ All analyses with the ALDS were performed using the theta.¹⁰

RESULTS

In a nineteen months period, 119 patients were potentially eligible. Fifteen patients declined to participate, 12 patients were excluded because of inability to give informed consent, leaving 92 patients included in the study. There were no significant differences in clinical characteristics, disease severity or comorbidity between patients who participated in the study and those who declined to participate.

Demographic characteristics and comorbidity are shown in Table 1. Mean age of the population was 68 years (± 13). Sixty-three (69%) patients had ischemic tissue loss and 29 (32%) only ischemic restpain. Renal failure was present in more than one-third of the population and 40% of the patients had a history of coronary artery disease. Before intervention, thirteen patients did not use anticoagulant therapy and twenty-five patients did not use a statin. After the intervention, all patients, except two in whom it was contraindicated, were prescribed anticoagulant therapy, statin therapy was yet prescribed in 9 patients. Forty-nine patients had a history of invasive vascular treatment.

Table 2 shows additional patient characteristics in terms of functional ability, quality of life, and type of treatment. Approximately half of the patients was not able to walk outside, however, most of the patients (88%) were still able to live independently. 59% of the patients were not able to walk any meters without pain.

Table 1. Demographic patient characteristics and comorbidity at assessment (n=92).

Characteristics	Mean (\pm SD) or median (range) or n (%)
Gender, male	55 (60%)
Age (years)	68 (\pm 13)
Body Mass Index (BMI) in kg/m ²	25.9 (\pm 4.7)
<i>Diabetes mellitus</i>	
No	55 (60%)
Non-insulin dependent	22 (24%)
Insulin dependent	15 (16%)
<i>Smoking</i>	
Never	20 (22%)
Former smoker	41 (45%)
Current smoker	31 (34%) ^a
<i>Hypertension</i>	
No	19 (21%)
Controlled by 1 or 2 drugs	34 (37%)
Uncontrolled or > 2 drugs	39 (42%)
<i>Renal failure</i>	
Unknown	7 (8%)
No	52 (57%)
Mild (creatinine 110-220 μ mol/l)	14 (15%)
Ntx, dialysis or severe failure	19 (21%) ^a
<i>Hypercholesterolemia</i>	
Unknown	36 (39%)
No	41 (45%)
Yes	15 (16%)
History of coronary artery disease	37 (40%)
History of stroke	19 (21%)
Positive family history of cardiovascular disease	44 (48%)
Previous intervention ^b	49 (53%)
<i>Fontaine stage</i>	
Fontaine III	29 (32%)
Fontaine IV	63 (69%) ^a
Use statin	67 (73%)
Use anticoagulant therapy ^c	79 (86%)

^a Sum of percentages is more than 100% due to round off.

^b Either endovascular, surgical or amputation.

^c Either aspirin, clopidogrel, coumadin, or dipyridamole.

Table 2. Patient characteristics in terms of functional ability, quality of life and type of treatment received.

Characteristics	Mean (\pm SD) or median (range) or n (%)
<i>Level of walking at admission</i>	
Inside and outside	50 (54%)
Only inside	32 (35%)
Wheel chair bonded or bedridden	10 (11%)
<i>Living situation</i>	
Independent	81 (88%)
Dependent	11 (12%)
Pain-free walking distance 0 meters	54 (59%)
Maximum walking distance < 10 meters	30 (33%)
ALDS	65 (\pm 19)
VascuQol Total	3.0 (\pm 0.9)
VascuQol Activity	2.4 (\pm 1.1)
VascuQol Symptoms	3.4 (\pm 1.2)
VascuQol Pain	2.4 (\pm 1.1)
VascuQol Emotional	3.8 (\pm 1.4)
VascuQol Social	3.2 (\pm 1.8)
Absolute ankle pressure (mmHg) affected extremity	68 (\pm 30)
Absolute toe pressure (mmHg) affected extremity	20 (0-107)
Length of admission (days)	5 (1-100)
Complications	19 (21%)
Re-interventions	14 (15%)

The associations between (potential) determinants of Qol and disability are shown in Table 3. Both in the univariate and multivariate analysis we could not identify significant determinants of patients' Qol. There was a trend towards a higher quality of life in patients with renal failure. Conversely, in the univariate and multivariate analysis we could demonstrate significant factors explaining patients' level of disability. The ALDS was lower in females (ALDS 59 versus 70), patients with a history of stroke (ALDS 58 versus 68) and patients of older age (ALDS 59 versus 72). The combination of female sex, a history of stroke and older age accounted for 24% of the variance of the ALDS. The VascuQol and ALDS did not differ between patients with rest pain or ischemic tissue loss.

The correlation between the ALDS and VascuQol was very weak (Pearson correlation coefficient 0.33). There were low, non-significant correlations between Qol and disability on the one side and toe and ankle pressures on the other (Table 4).

Table 3. Determinants of quality of life (VascuQol) and disability (ALDS).

		VascuQol Total ^a	<i>P</i> univariate	<i>P</i> multivariate ^b	ALDS ^a	<i>P</i> univariate	<i>P</i> multivariate ^b
Sex	Male	3.13 (0.87)	0.18*	0.14	69.8 (18.5)	0.01*	0.02
	Female	2.86 (1.01)			59.0 (18.5)		
Diabetes mellitus	No	3.10 (1.01)	0.29*	0.12	67.2 (19.6)	0.28*	0.15
	Yes	2.89 (0.81)			62.8 (18.4)		
Coronary artery disease	No	2.98 (1.06)	0.66	-	65.5 (20.0)	0.65*	-
	Yes	3.07 (0.71)			65.3 (18.1)		
Stroke	No	2.95 (0.87)	0.13*	0.19	67.5 (18.5)	0.02*	0.02
	Yes	3.31 (1.12)			57.5 (20.2)		
Fontaine	III	3.04 (0.90)	0.88	-	68.0 (17.3)	0.29*	0.74
	IV	3.01 (0.95)			64.2 (20.0)		
Renal failure	No	2.88 (0.98)	0.06*	0.09	66.1 (18.3)	0.77	-
	Yes	3.27 (0.79)			64.2 (20.8)		
Age	High (≥ 68 y)	3.17 (1.01)	0.13*	0.24	58.7 (20.7)	0.00*	0.01
	Low (< 68 y)	2.88 (0.84)			71.6 (15.4)		
Body mass index	High (≥ 26)	2.98 (0.91)	0.64	-	63.7 (17.2)	0.18*	0.35
	Low (< 26)	3.07 (0.97)			67.2 (21.0)		

^a data represent mean (SD)

^b *P*-values based on multiple linear regression

* indicates that the concerning variable was entered into the linear regression model (univariate *P*-value > 0.30)

Multivariate analysis was performed using the enter method; R^2 of the model with the ALDS was 24%.

DISCUSSION

In this study, we demonstrated that the ADL disability was significantly associated with advanced age, female sex and a history of stroke. Quality of life, using the VascuQol, did not differ significantly between various subgroups. The level of functional ability and Qol did not show any correlation with ABI and toe pressures.

Table 4. Associations, expressed as correlation coefficient, between the ALDS and VascuQol and clinical indicators (n = 92).

	ALDS	VascuQol Total
Toepressure	0.036*	0.0188*
Ankle pressure	-0.144*	-0.105#

*, Spearman's correlation coefficient; #, Pearson's correlation coefficient.

We found no significant differences in Qol between subgroups. However, there was an unexpected tendency towards higher VascuQol scores in patients with renal failure. Also patients with a stroke tended to have higher Qol scores. This is in contrast with previous studies.^{4,6,7,18} We cannot explain this finding. The trend towards a higher perceived Qol in the presence of severe comorbidity can simply be the result of chance. However, it can also be of true meaning and the consequence of an

overreacted 'response shift'. This means that internal standards and values of chronically diseased patients change over time and subsequently, a patient's self-evaluation of quality of life changes. This psychological phenomenon could also play a role in our sample of patients with critical limb ischemia.¹⁹ We also found that QoL was slightly, yet non-significantly, lower in women. This is in agreement with previous studies, which demonstrated that men generally experience a higher QoL compared to women with a similar severity of PAD.^{6,7,18}

Since there are no such specific instruments like the ALDS measuring impairment in ADL, less is known about disability in patients with critical limb ischemia. Indeed there is the Walking Impairment Questionnaire (WIQ), but this instrument only focuses on walking, and does not cover a broader spectrum of functional ability. In addition, the WIQ has been developed specifically for patients with intermittent claudication, and is not useful for patients with critical limb ischemia.^{20,21} The ALDS was able to detect differences between various subgroups with critical limb ischemia. The ALDS is a fairly objective measure, and, in comparison with quality of life, less influenced by patient's personal traits. It simply measures whether a patient is able to perform a daily activity or not. As expected, the ALDS was lower in patients who had had a stroke. One can also imagine that older patients are more limited in ADL. In line with quality of life, the ability to perform ADL was impaired in women. Previous studies suggested the lower muscle volume and strength in women, results in a greater functional impairment, which consequently accounts for a lower QoL.⁶ This is not supported by our data that showed a very weak correlation between the VascuQoL and ALDS ($r = 0.33$).

Some limitations of this study should be recognized. The study was performed in one academic hospital. This hospital serves as a regional hospital but is also a referral center for surrounding regional hospitals. This can result in inclusion of more severe diseased patients, which can limit the generalization of the results. Thirdly, the cross-sectional design of this study with all assessments conducted at one point in time precludes inferences about causality or predicting ability of the explanatory factors studies. In this study, patients were asked to complete the VascuQoL questionnaire by themselves. Patients received the questionnaire at home, so it can not be ruled out that other persons than the patient completed the questionnaire.

At this moment, the ALDS is ready to use in research to determine the effect of an intervention for PAD. After all, one of the aims of treatment is to improve patient's level of functional ability, for example by decreasing pain. In the future, the ALDS could be used for treatment allocation. It is known, for example, that patients with

poor pre-operative status do not benefit from revascularization.²² The ALDS can be used as objective measure to determine preoperative status.

In conclusion, baseline level of functional ability, measured by the ALDS, was lower in specific subgroups of patients with critical limb ischemia, whereas quality of life was equal for all groups.

ACKNOWLEDGEMENT

The authors thank the patients for their willingness to participate in this research.

REFERENCES

1. Chetter IC, Scott DJ, Kester RC. An introduction to quality of life analysis: the new outcome measure in vascular surgery. *Eur J Vasc Endovasc Surg.* 1998;15(1):4-6.
2. Nguyen LL, Moneta GL, Conte MS, Bandyk DF, Clowes AW, Seely BL; PREVENT III Investigators. Prospective multicenter study of quality of life before and after lower extremity vein bypass in 1404 patients with critical limb ischemia. *J Vasc Surg.* 2006;44(5):977-983.
3. Kleivsgård R, Risberg BO, Thomsen MB, Hallberg IR. A 1-year follow-up quality of life study after hemodynamically successful or unsuccessful surgical revascularization of lower limb ischemia. *J Vasc Surg.* 2001;33(1):114-122.
4. Aquarius AE, de Vries J, van Berge Henegouwen DP, Hamming JF. Clinical indicators and psychosocial aspects in peripheral arterial disease. *Arch Surg* 2006;141(2):161-166.
5. Aquarius AE, Denollet J, de Vries J, Hamming JF. Poor health-related quality of life in patients with peripheral arterial disease: type D personality and severity of peripheral arterial disease as independent predictors. *J Vasc Surg.* 2007;46(3):507-512.
6. Collins TC, Suarez-Almazor M, Bush RL, Petersen NJ. Gender and peripheral arterial disease. *J Am Board Fam Med.* 2006;19(2):132-140.
7. Oka RK, Sanders MG. The impact of type 2 diabetes and peripheral arterial disease on quality of life. *J Vasc Nurs.* 2005;23(2):61-66.
8. Barsky AJ, Cleary PD, Klerman GL. Determinants of perceived health status of medical outpatients. *Soc Sci Med.* 1992;34(10):1147-1154.
9. Weisscher N, de Haan RJ, Vermeulen M. The impact of disease-related impairments on disability and health-related quality of life: a systematic review. *BMC Med Res Methodol.* 2007;7:24.
10. Met R, Reekers JA, Koelemay MJ, Legemate DA, de Haan RJ. The AMC Linear Disability Score (ALDS): a cross-sectional study with a new generic instrument to measure disability applied to patients with peripheral arterial disease. *Health Qual Life Outcomes.* 2009;7:88.
11. Holman R, Weisscher N, Glas CA, et al. The Academic Medical Center Linear Disability Score (ALDS) item bank: item response theory analysis in a mixed patient population. *Health Qual Life Outcomes.* 2005;3:83.
12. Weisscher N, Wijbrandts CA, de Haan R, Glas CA, Vermeulen M, Tak PP. The Academic Medical Center Linear Disability Score item bank: psychometric properties of a new generic disability measure in rheumatoid arthritis. *J Rheumatol.* 2007;34(6):1222-1228.
13. Weisscher N, Post B, de Haan RJ, Glas CA, Speelman JD, Vermeulen M. The AMC linear disability score in patients with newly diagnosed Parkinson disease. *Neurology.* 2007;69(23):2155-2161.
14. Weisscher N, Vermeulen M, Glas CA, Roos YB, de Haan RJ. The AMC Linear Disability Score itembank: a new generic disability measure in stroke. In: Weisscher N, Thesis: The AMC Linear Disability Score (ALDS): Measuring disability in clinical studies. Amsterdam 2008; 81-92. [<http://dare.uva.nl/record/270674>]
15. Morgan MB, Crayford T, Murrin B, Fraser SC. Developing the Vascular Quality of Life Questionnaire: a new disease-specific quality of life measure for use in lower limb ischemia. *J Vasc Surg.* 2001;33(4):679-687.
16. de Vries M, Ouwendijk R, Kessels AG, et al. Comparison of generic and disease-specific questionnaires for the assessment of quality of life in patients with peripheral arterial disease. *J Vasc Surg.* 2005;41(2):261-268.
17. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology.* 1990;1(1):43-46.
18. Sprangers MA, de Regt EB, Andries F, et al. Which chronic conditions are associated with better or poorer quality of life? *J Clin Epidemiol.* 2000;53(9):895-907.
19. Sprangers MA, Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. *Soc Sci Med.* 1999;48(11):1507-1515.

20. Regensteiner JG, Steiner JF, Panzer RJ, Hiatt WR. Evaluation of walking impairment by questionnaire in patients with peripheral arterial disease. *J Vasc Med Biol.* 1990;2(3):142-152.
21. McDermott MM, Liu K, Guralnik JM, Martin GJ, Criqui MH, Greenland P. Measurement of walking endurance and walking velocity with questionnaire: validation of the walking impairment questionnaire in men and women with peripheral arterial disease. *J Vasc Surg.* 1998;28(6):1072-1081.
22. Taylor SM, Kalbaugh CA, Blackhurst DW, et al. Preoperative clinical factors predict postoperative functional outcomes after major lower limb amputation: an analysis of 553 consecutive patients. *J Vasc Surg.* 2005;42(2):227-235.