Tilburg University

Health-related quality of life predicts long-term survival in patients with peripheral artery disease

Issa, S.M.; Hoeks, S.E.; Scholte Op Reimer, W.J.M.; van Gestel, Y.R.B.M.; Lenzen, M.J.; Verhagen, H.J.M.; Pedersen, S.S.; Poldermans, D.

Published in:
Vascular Medicine

Publication date:
2010

Document Version
Publisher's PDF, also known as Version of record

[Link to publication in Tilburg University Research Portal](#)

Citation for published version (APA):
Issa, S. M., Hoeks, S. E., Scholte Op Reimer, W. J. M., van Gestel, Y. R. B. M., Lenzen, M. J., Verhagen, H. J. M., Pedersen, S. S., & Poldermans, D. (2010). Health-related quality of life predicts long-term survival in patients with peripheral artery disease. *Vascular Medicine*, 15(3), 163-169.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Vascular Medicine

<http://vmj.sagepub.com>

Health-related quality of life predicts long-term survival in patients with peripheral artery disease

Samson M Issa, Sanne E Hoeks, Wilma JM Scholte op Reimer, Yvette RBM Van Gestel, Mattie J Lenzen, Hence JM Verhagen, Susanne S Pedersen and Don Poldermans

Vasc Med 2010; 15; 163

DOI: 10.1177/1358863X10364208

The online version of this article can be found at:

<http://vmj.sagepub.com/cgi/content/abstract/15/3/163>

Published by:

<http://www.sagepublications.com>

Additional services and information for *Vascular Medicine* can be found at:

Email Alerts: <http://vmj.sagepub.com/cgi/alerts>

Subscriptions: <http://vmj.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.co.uk/journalsPermissions.nav>

Citations <http://vmj.sagepub.com/cgi/content/refs/15/3/163>

Health-related quality of life predicts long-term survival in patients with peripheral artery disease

Samson M Issa^{1,2}, Sanne E Hoeks³, Wilma JM Scholte op Reimer⁴, Yvette RBM Van Gestel³, Mattie J Lenzen², Henc JM Verhagen⁵, Susanne S Pedersen^{1,2} and Don Poldermans⁵

Abstract

We examined whether health-related quality of life (HRQoL) predicts long-term survival in patients with peripheral artery disease (PAD) independent of established prognostic risk factors. In 2004, data on 711 consecutive patients with PAD undergoing vascular surgery were collected from 11 hospitals in The Netherlands. After 1 year, patients were contacted to complete the EuroQol Questionnaire (EQ-5D), of which 503 complied. HRQoL assessed by the EQ-5D was divided into tertiles (i.e. poor, intermediate and good HRQoL). Mortality was subsequently assessed 3 years after surgery. Of the 503 patients, 55 (11%) patients died during follow-up. Mortality was 21% in patients with poor HRQoL, 8% in patients with intermediate HRQoL, and 5% in patients with good HRQoL. Patients with poor HRQoL (HR = 5.4; 95% CI 2.3–12.5) had a worse survival compared to patients with a good HRQoL, after adjusting for established prognostic factors. In conclusion, the study indicates that poor HRQoL predicts long-term survival in patients with PAD, and provides prognostic value above established risk factors.

Keywords

disease management; health-related quality of life; peripheral artery disease; prognosis; vascular surgery

Introduction

Peripheral artery disease (PAD) is a marker of generalized atherosclerosis affecting multiple vascular beds simultaneously.¹ This polyvascular disease phenomenon frequently leads to conditions such as intermittent claudication, myocardial infarction (MI), dementia, and stroke.^{1,2}

PAD is associated with increased cardiovascular morbidity, poor physical functioning, and adverse health outcomes.^{3,4} Long-term survival after vascular surgery in patients with PAD is predominantly determined by the associated risk of coronary artery disease (CAD).⁵ Despite the known risk, patients with PAD do not achieve comparable risk control as patients with other cardiovascular diseases.^{6,7} Patients with PAD have poor long-term survival – even more so than patients with CAD only.⁸ Taken together, patients with PAD constitute a high-risk group that needs stringent risk management and monitoring.²

Health-related quality of life (HRQoL) reflects a patient's physical, mental and social beliefs and perceptions in relation to health. HRQoL has been shown to have prognostic value in predicting adverse clinical events independent of conventional risk factors in CAD.^{9–12} Prognostic information is pertinent for providing tailored patient management. Importantly, information about HRQoL and health status, as perceived by the patient, can help optimize

patient-centred care in clinical practice.¹³ In addition, poor HRQoL has been shown to predict poor prognosis independent of indicators of disease severity in patients with CAD and heart failure.¹⁴ Although HRQoL and the risk of mortality in patients with PAD are generally comparable to that of patients with CAD,¹⁵ the impact of HRQoL on mortality in PAD has not yet been investigated. HRQoL might help to

¹CoRPS-Center of Research on Psychology in Somatic Diseases, Tilburg University, Tilburg, The Netherlands

²Department of Cardiology, Thoraxcenter, Erasmus Medical Centre, Rotterdam, The Netherlands

³Department of Anaesthesiology, Erasmus Medical Centre, Rotterdam, The Netherlands

⁴Amsterdam University of Applied Sciences, School of Nursing, Amsterdam, The Netherlands

⁵Department of Vascular Surgery, Erasmus Medical Centre, Rotterdam, The Netherlands

Corresponding author:

Don Poldermans

Erasmus Medical Center

Room H805

's-Gravendijkwal 230

3015 GD Rotterdam, The Netherlands

Email: d.poldermans@erasmusmc.nl

identify patients with PAD at high risk for adverse health outcomes and may provide independent prognostic information, other than established biomedical risk factors, as shown in a recent systematic review of the impact of HRQoL on survival in CAD and congestive heart failure.¹⁴

Hence, the objective of the present study was to examine if HRQoL predicts long-term survival in patients with PAD beyond established biomedical risk factors.

Methods

Study population

The study population was derived from The Netherlands Heart Foundation Health Care Programme, entitled Peripheral Arterial Disease Survey. Details are only reported here as relevant to the current analyses. More details on the study population and methods of data collection can be found in an earlier publication on this survey.¹⁶ Between May and December 2004, data on 711 patients with PAD undergoing non-cardiac vascular surgery were collected from 11 hospitals in The Netherlands. The consecutively enrolled patients were seen at the participating vascular surgery departments when undergoing endovascular or open procedures. Endovascular surgery procedures included aortic endografts or peripheral angioplasties with and without stenting. The open procedures comprised abdominal aortic surgery, carotid endarterectomy, or infrainguinal arterial reconstruction. All patients were asked for informed consent before participation. The 11 participating hospitals met the requirements for ethical approval based on local standards.

One year after surgery, 634 of 711 (89%) patients were still alive. Survivors were sent the EuroQol Questionnaire and questions concerning their cardiovascular events by mail, which they were asked to complete.

Data collection

Baseline measurements, patient characteristics and risk factors were collected before surgery by trained research assistants. The hospital charts were searched for information on relevant clinical characteristics, such as history of chronic obstructive pulmonary disease (COPD), diabetes mellitus, and renal insufficiency as cardiovascular morbidity. Data with respect to the incidence of angina pectoris (AP), myocardial infarction (MI), history of revascularization, prior arrhythmias, history of congestive heart failure, and history of cerebrovascular disease were once again updated 1 year after surgery. All data were entered into the electronic Case Record Form and transferred regularly via the Internet to the central database at the Erasmus Medical Centre, Rotterdam, The Netherlands. Three years after surgery, survival status (all-cause mortality) was obtained through the civil registries.

Health-related quality of life

HRQoL was measured 1 year after surgery with the Dutch version of the EuroQol Questionnaire.^{17,18} This instrument

consists of two facets, the EQ-5D and the EQ visual analogue scale. To intensively investigate the clinical application of HRQoL assessment, the focus of this cohort was on the EQ-5D. The validated EQ-5D is a standardized, generic measure of self-reported HRQoL that has been used in patients with PAD¹⁶ and other cardiovascular diseases.⁹ The EQ-5D descriptive system assesses the following five clinically relevant dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of these dimensions has three levels of severity, corresponding to 'no problems', 'moderate problems' and 'severe problems'. Patients were asked which statement best described their health. More details on and instructions for the EQ-5D can be found on <http://www.euroqol.org/>.

Statistical analyses

Descriptive statistics included count plus percentages for nominal variables, and mean values with corresponding standard deviations for continuous variables. Responders were compared with non-responders by use of Pearson chi-square tests. Differences between survivors and deceased patients on demographic and clinical characteristics in relation to survival were compared by use of univariable Cox regression analysis. The five dimensions of the EQ-5D were computed to form a utility score using a standard set of general population weights. These scores can range from -0.594 to 1, with a score < 0 regarded as a HRQoL that is worse than death and 1 representing full health, from the perspective of the general population. The general population weights were obtained on value sets derived from the Dutch population by the time trade-off valuation technique.¹⁷ To examine the effect of a high score on the EQ-5D versus one that is lower in rank, the utility scores were divided into tertiles for parsimony (i.e. poor HRQoL, intermediate HRQoL, and good HRQoL). The Kaplan-Meier curves were computed for each tertile with all-cause mortality as the endpoint. To investigate the prognostic ability of the individual dimensions of the EQ-5D, the dimensions were dichotomized into: 'no problems' versus a cluster of 'moderate problems' and 'severe problems', prior to statistical analyses. Univariable Cox regression analyses were conducted to determine the prognostic ability of the HRQoL utility score, tertiles, and individual dimensions on mortality. Multivariable Cox regression analyses were performed to adjust for potential confounders including age, sex, AP, MI, history of revascularization, prior arrhythmias, history of congestive heart failure, cerebrovascular disease, COPD, renal insufficiency, and diabetes mellitus. Sensitivity analyses were performed to adjust for (1) medication use (statins, aspirins, beta-blockers) and (2) the entity of PAD (i.e. peripheral occlusive disease of the lower limbs, abdominal aortic aneurysms and carotid stenosis). Results from the Cox regression analyses are presented as hazard ratios (HR) with 95% confidence intervals (CI). For all tests, a probability value < 0.05 (two-sided) was considered significant. All statistical analyses were performed with SPSS statistical software, version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics of survey responders versus non-responders

Of 634 patients, 503 (79%) completed the questionnaire, comprising the sample available for statistical analyses in this study (Figure 1, Table 1). The characteristics of the patients who did not complete the EuroQol Questionnaire (21%) were compared with the sample included in the analyses. Comparison of the responders ($n = 503$) versus the non-responders ($n = 131$) showed great similarities, with the exception of non-responders being less likely to be males (73.2% vs 57.3%; $p < 0.001$) but more likely to have congestive heart failure (3.4% vs 7.6%; $p = 0.021$). During the follow-up period, 17 (13%) patients died from the non-responders.

Baseline characteristics for the total sample and stratified by survival status

The mean age 1 year after surgery of the 503 included patients was 67 ± 10 years and 73% were male. During the follow-up period, 55 (11%) patients died. Patients who died during follow-up had in general more risk factors compared to survivors (Table 2). Univariable Cox regression analysis revealed significant increased risk of mortality for age ≥ 70 years (HR = 3.6; 95% CI 2.0–6.5), COPD (HR = 2.8; 95% CI 1.5–5.1), renal insufficiency (HR = 3.2; 95% CI 1.5–6.8), prior arrhythmias (HR = 2.3; 95% CI 1.1–4.5), and history of congestive heart failure (HR = 2.6; 95% CI 1.1–6.1).

Impact of HRQoL

There was a clear relationship between HRQoL and mortality. Mean utility scores were 0.79 ± 0.22 in survivors versus 0.64 ± 0.27 in those who died ($p < 0.001$). The mean utility score and range of the individual tertiles were 0.48 ± 0.24 (–0.26–0.77) for poor HRQoL, 0.80 ± 0.03 (0.78–0.86) for

Figure 1. Flow chart of patient selection. (FU, follow-up.)

intermediate HRQoL, and 0.97 ± 0.05 (0.90–1.00) indicating good HRQoL. Mortality was 21% in patients with poor HRQoL, 8% in patients with intermediate HRQoL, and 5% in patients with good HRQoL. Kaplan-Meier curves revealed similar results (i.e. patients with poor HRQoL had the poorest prognosis, followed by intermediate HRQoL) (Figure 2). To examine if HRQoL predicts mortality beyond conventional clinical risk factors, analyses were adjusted for potential confounders including age, sex, AP, MI, history of revascularization, prior arrhythmias, history of congestive heart failure, cerebrovascular disease, COPD, renal insufficiency, and diabetes mellitus. The adjusted analyses showed impaired HRQoL as a predictor of mortality: poor versus

Table 1. Baseline clinical characteristics of all patients ($N = 711$), survivors at 1 year post surgery ($N = 634$) and responders on the EuroQol Questionnaire ($N = 503$)

Characteristics	All patients	N (%)	Survivors	N (%)	Responders	N (%)
N	711		634		503	
Age (years)						
mean $\pm$ SD	67 ± 10		66 ± 10		66 ± 10	
≥ 70 years	299	(42%)	244	(39%)	192	(38%)
Sex, male	496	(70%)	443	(70%)	368	(73%)
COPD	101	(14%)	82	(13%)	65	(13%)
Diabetes mellitus	149	(21%)	126	(20%)	93	(19%)
Renal insufficiency	51	(7%)	37	(6%)	28	(6%)
Stroke or TIA	123	(17%)	98	(16%)	76	(15%)
Arrhythmias	77	(11%)	59	(9%)	47	(9%)
Heart failure	38	(5%)	27	(4%)	17	(3%)
Angina pectoris	99	(14%)	89	(14%)	70	(14%)
Myocardial infarction	106	(15%)	92	(15%)	74	(15%)
Previous coronary revascularization	129	(18%)	113	(18%)	87	(17%)

N, number; SD, standard deviation; COPD, chronic obstructive pulmonary disease; TIA, transient ischaemic attack.

Table 2. Clinical characteristics 1 year after surgery of the total sample; stratified by survival status 3 years post surgery

Characteristics	Total	N (%)	Alive	N (%)	Dead	N (%)	HR (95% CI) for mortality
N	503	(100%)	440	(88%)	55	(11%)	
Age (years)							
mean $\pm$ SD	67 $\pm$ 10		66 $\pm$ 10		74 $\pm$ 10		1.1 (1.0–1.1)
$\geq$ 70 years	208	(41%)	167	(38%)	39	(71%)	3.6 (2.0–6.5)
Sex, male	368	(73%)	320	(73%)	43	(78%)	1.2 (0.7–2.4)
COPD	65	(13%)	49	(11%)	15	(27%)	2.8 (1.5–5.1)
Diabetes mellitus	93	(19%)	79	(18%)	13	(24%)	1.4 (0.8–2.7)
Renal insufficiency	28	(6%)	20	(5%)	8	(15%)	3.2 (1.5–6.8)
Stroke or TIA	83	(17%)	72	(16%)	9	(16%)	1.0 (0.5–2.1)
Arrhythmias	51	(10%)	39	(9%)	11	(20%)	2.3 (1.1–4.5)
Heart failure	26	(5%)	19	(4%)	7	(13%)	2.6 (1.1–6.1)
Angina pectoris	75	(15%)	68	(16%)	7	(13%)	0.7 (0.3–1.6)
Myocardial infarction	80	(16%)	69	(16%)	11	(20%)	1.2 (0.6–2.4)
Previous coronary revascularization	90	(18%)	76	(17%)	13	(24%)	1.5 (0.8–2.8)

N, number; HR, hazard ratio; CI, confidence interval; SD, standard deviation; COPD, chronic obstructive pulmonary disease; TIA, transient ischaemic attack.

Figure 2. Survival stratified by differences in HRQoL.

good HRQoL (HR = 5.4; 95% CI 2.3–12.5) and intermediate versus good HRQoL (HR = 2.0; 95% CI 0.8–4.8). Age $\geq$ 70 years (HR = 2.6; 95% CI 1.4–4.8), COPD (HR = 3.2; 95% CI 1.7–6.2), renal insufficiency (HR = 3.2; 95% CI 1.4–7.2) and AP (HR = 0.4; 95% CI 0.1–0.9) were also significant predictors of mortality in the adjusted analyses. Sensitivity analysis adjusting for medication use (statins, aspirins, beta-blockers) revealed comparable results: poor versus good HRQoL (HR = 5.4; 95% CI 2.3–12.6) and intermediate versus good HRQoL (HR = 2.0; 95% CI 0.8–4.9). Additionally, sensitivity analysis adjusting for the entity of PAD also showed similar results: poor versus good HRQoL (HR = 5.3; 95% CI 2.3–12.4) and intermediate versus good HRQoL (HR = 1.9; 95% CI 0.8–4.7).

There was also a clear relationship between the severity of impairment on the individual dimensions of the EQ-5D and long-term mortality. The more severely impaired the HRQoL dimension, the lower the survival rate (Figure 3). Multivariable analyses revealed significant associations between reporting problems and long-term mortality for the dichotomized dimensions of the EQ-5D. Patient-rated problems reached statistical significance for mortality in all of the dimensions of the EQ-5D. The results of the adjusted analyses were significant for mobility (HR = 2.7; 95% CI 1.3–5.6), self-care (HR = 4.5; 95% CI 2.5–8.2), usual activities (HR = 2.2; 95% CI 1.2–4.0), pain/discomfort (HR = 1.8; 95% CI 1.0–3.4), and for anxiety/depression (HR = 1.9; 95% CI 1.0–3.6) (Table 3).

Figure 3. Long-term mortality, according to severity of reported problems on the EuroQol dimensions. (ns, not significant.)

Discussion

To our knowledge, this is the first study to investigate the relationship between HRQoL and mortality in PAD. This

study demonstrates HRQoL, as measured by the EQ-5D, to be strongly associated with long-term survival in patients with PAD. After adjusting for other established risk factors, poor HRQoL remained an independent predictor of mortality, with the risk being fivefold compared to patients with a good HRQoL. The risk factors that were adjusted for in multivariable analyses are known for being the most important predictors of mortality in patients with PAD.⁷ In addition, impaired health status assessed by the EQ-5D has previously been shown to independently predict mortality in CAD patients as well.⁹

HRQoL assessments provide unique information about the impact of the disease as perceived by the patient, which was confirmed in the current study, as poor HRQoL had predictive value in addition to established biomedical risk factors. Quality of life assessed by questionnaires such as the Short Form Health Survey 36 (SF-36) Physical Component, the 46-item Patient Concerns Checklist, and the quality-of-life Index-Cardiac Version have also shown to be independent predictors of mortality in patients with CAD and congestive heart failure.^{10,14}

The primary goal of therapy in patients with PAD is to improve HRQoL. In previous research, surrogates of objective measures of disease, including the ankle-brachial

Table 3. Comparison of symptom reports on the EuroQol Questionnaire; stratified by survival status 3 years post surgery

EQ-5D	Total	N (%)	Alive	N (%)	Dead	N (%)	Univariate HR (95% CI) for mortality	Multivariate HR (95% CI) for mortality
N	503	(100%)	440	(88%)	55	(11%)		
Mean ± SD	0.77 ± 0.23		0.79 ± 0.22		0.64 ± 0.27		1.2 (1.1–1.3) ^a	1.2 (1.1–1.4) ^a
Tertiles								
Good	178	(35%)	166	(38%)	9	(16%)	1	1
Intermediate	187	(37%)	168	(38%)	17	(31%)	2.3 (1.0–5.6) ^b	2.0 (0.8–4.8) ^b
Poor	138	(27%)	106	(24%)	29	(53%)	5.8 (2.5–13.2) ^b	5.4 (2.3–12.5) ^b
Dimensions								
Mobility							3.3 (1.6–6.8) ^c	2.7 (1.3–5.6) ^c
no problems	196	(39%)	185	(42%)	10	(18%)		
moderate problems	303	(60%)	254	(58%)	42	(76%)		
severe problems	4	(1%)	1	(0%)	3	(6%)		
Self-care							5.7 (3.3–9.8) ^c	4.5 (2.5–8.2) ^c
no problems	439	(87%)	399	(91%)	33	(60%)		
moderate problems	55	(11%)	37	(8%)	17	(31%)		
severe problems	9	(2%)	4	(1%)	5	(9%)		
Usual activities							2.5 (1.4–4.5) ^c	2.2 (1.2–4.0) ^c
no problems	272	(54%)	247	(56%)	19	(35%)		
moderate problems	205	(41%)	177	(40%)	27	(49%)		
severe problems	26	(5%)	16	(4%)	9	(16%)		
Pain/discomfort							2.0 (1.1–3.7) ^c	1.8 (1.0–3.4) ^c
no problems	219	(44%)	199	(45%)	17	(31%)		
moderate problems	249	(50%)	214	(49%)	32	(58%)		
severe problems	35	(7%)	27	(6%)	6	(11%)		
Anxiety/depression							1.7 (0.9–3.0) ^c	1.9 (1.0–3.6) ^c
no problems	405	(81%)	359	(82%)	40	(73%)		
moderate problems	86	(17%)	70	(16%)	14	(26%)		
severe problems	12	(2%)	11	(3%)	1	(2%)		

N, number; HR, hazard ratio; CI, confidence interval; SD, standard deviation.

^aHazard per 0.1 decline in EQ-5D utility score.

^bReference group for analyses is the tertile that represents a good HRQoL.

^cTo examine the relationship between reporting problems on the EQ-5D dimensions and survival by use of Cox regression, the three levels of severity were dichotomized in: 'no problems' versus reporting problems (a cluster of 'moderate problems' and 'severe problems').

index, has been shown to correlate weakly with HRQoL.¹⁹ In addition, physician evaluated health status of cardiac patients are known to have limited reproducibility and sensitivity with regard to clinical changes.^{13,20} Routine clinical practice often does not assess directly unobservable components such as self-care, social functioning, general health perception and coping with illness that are imbedded in self-rated health. Therefore, it is important to assess HRQoL as rated by the patient.

Taken together, owing to the unique prognostic value of patient-rated HRQoL, it may be timely to adopt HRQoL assessments in clinical practice in order to guide treatment and enhance secondary prevention in patients with cardiovascular disease.^{9,10,14,21} The prognostic ability of HRQoL may complement traditional clinical practice, by identifying patients at high risk for mortality independent of biomedical factors. Further research is warranted to investigate the mechanisms that may be responsible for the relationship between HRQoL and mortality. Thus far, depression and the distressed (Type D) personality have been shown to predict impaired HRQoL and poor survival independent of disease status.^{22,23} In addition, depression is associated with poor medication adherence independent of somatic sensations due to disease as experienced by the patient.²⁴ Nevertheless, even if there is still no clear evidence concerning the mechanisms, patients with impaired HRQoL may benefit from more aggressive medical treatment. These high-risk patients should be monitored more carefully and be invited to clinical follow-ups more frequently, and may also profit from more aggressive disease management. Such disease management should probably be multifactorial, consisting of adjustment in medication, exercise training, behavioural intervention, and the adoption of a confronting coping strategy, which have been shown to improve HRQoL.²⁵⁻²⁷ Smoking cessation and following a careful diet may also be beneficial.

The major advantage of the EQ-5D is its brevity, making the transition to implement, understand, and use HRQoL as an additional tool in clinical practice less taxing both for health care professionals and patients. The EQ-5D consists of five questions, whereas most other HRQoL measures predicting mortality are much more lengthy.¹⁰⁻¹² Despite its brevity, the EQ-5D clearly differentiated between PAD patients with a poor versus good survival in the current study. Furthermore, the EQ-5D has shown to have a comparable sensitivity and specificity to more lengthy questionnaires, such as the generic questionnaire SF-36 and the disease-specific questionnaire the Vascular Quality of Life in preoperative patients with PAD.²⁸

The results of the current study should be interpreted with some caution. First, the study may be subject to selection bias, which is an inherent limitation of cohort studies due to non-response. Nevertheless, responder versus non-responder baseline characteristics analyses showed almost no differences. Second, we had no information on socioeconomic status that may serve as a confounder on the relationship between HRQoL and mortality. Third, the use of tertiles and dichotomization of HRQoL is arbitrary, even though dichotomization enhances the clinical applicability

of the results.²⁹ Fourth, despite the link between HRQoL and long-term mortality in patients with PAD, we do not know whether HRQoL is a risk marker for a third variable on the causal pathway between HRQoL and mortality, nor which mechanisms (e.g. behavioural or biological) may explain the link with mortality. As there were no specific interventions or assessments that had been registered after the HRQoL assessment in this study, it is undecided whether aggressive treatment and/or improvement in HRQoL would have had an impact on survival in the study population. Finally, although this cohort demonstrates HRQoL as a predictor of long-term survival in patients with PAD, there was no data available on HRQoL prior to surgery, so we still need to know the effect of HRQoL on different time points. As only survivors at 1 year were included in our analyses (deceased patients, $n = 77$), selection bias cannot be excluded.

In conclusion, patients with PAD constitute a high-risk group that needs stringent risk management and monitoring. Patient-rated HRQoL, as measured by the EQ-5D, identifies patients with PAD at high risk for mortality independent of established biomedical risk factors. The EQ-5D could be used in clinical practice to identify patients at high risk, who may benefit from more aggressive treatment, behavioural intervention and support but also as a performance measure to enhance the quality of care in clinical practice, as advocated by others.¹³

Acknowledgements

Sources of funding

This work was funded by The Netherlands Heart Foundation, The Hague, The Netherlands (2000T101). SEH and YRBMvG are supported by an unrestricted research grant from Lijf & Leven Foundation, Rotterdam, The Netherlands.

The authors report there are no other disclosures.

References

1. Mohler ER III. Peripheral arterial disease: identification and implications. *Arch Intern Med* 2003; 163: 2306-2314.
2. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg* 2007; 45(suppl S): S5-67.
3. Nehler MR, McDermott MM, Treat-Jacobson D, Chetter I, Regensteiner JG. Functional outcomes and quality of life in peripheral arterial disease: current status. *Vasc Med* 2003; 8: 115-126.
4. Stewart KJ, Hiatt WR, Regensteiner JG, Hirsch AT. Exercise training for claudication. *N Engl J Med* 2002; 347: 1941-1951.
5. Back MR, Leo F, Cuthbertson D, Johnson BL, Shamesmd ML, Bandyk DF. Long-term survival after vascular surgery: specific influence of cardiac factors and implications for preoperative evaluation. *J Vasc Surg* 2004; 40: 752-760.
6. Cacoub PP, Abola MT, Baumgartner I, et al. Cardiovascular risk factor control and outcomes in peripheral artery disease patients in the Reduction of Atherothrombosis for Continued Health (REACH) Registry. *Atherosclerosis* 2009; 204: e86-92.

7. Welten GM, Schouthern O, Chonchol M, et al. Prognosis of patients with peripheral arterial disease. *J Cardiovasc Surg (Torino)* 2009; 50: 109–121.
8. Welten GM, Schouten O, Hoeks SE, et al. Long-term prognosis of patients with peripheral arterial disease: a comparison in patients with coronary artery disease. *J Am Coll Cardiol* 2008; 51: 1588–1596.
9. Lenzen MJ, Scholte op Reimer WJ, Pedersen SS, et al. The additional value of patient-reported health status in predicting 1-year mortality after invasive coronary procedures: a report from the Euro Heart Survey on Coronary Revascularisation. *Heart* 2007; 93: 339–344.
10. Rumsfeld JS, MaWhinney S, McCarthy M Jr, et al. Health-related quality of life as a predictor of mortality following coronary artery bypass graft surgery. Participants of the Department of Veterans Affairs Cooperative Study Group on Processes, Structures, and Outcomes of Care in Cardiac Surgery. *JAMA* 1999; 281: 1298–1303.
11. Soto GE, Jones P, Weintraub WS, Krumholz HM, Spertus JA. Prognostic value of health status in patients with heart failure after acute myocardial infarction. *Circulation* 2004; 110: 546–551.
12. Spertus JA, Jones P, McDonnell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. *Circulation* 2002; 106(1): 43–49.
13. Spertus JA. Evolving applications for patient-centered health status measures. *Circulation* 2008; 118: 2103–2110.
14. Mommersteeg PM, Denollet J, Spertus JA, Pedersen SS. Health status as a risk factor in cardiovascular disease: a systematic review of current evidence. *Am Heart J* 2009; 157: 208–218.
15. Regensteiner JG, Hiatt WR, Coll JR, et al. The impact of peripheral arterial disease on health-related quality of life in the Peripheral Arterial Disease Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) Program. *Vasc Med* 2008; 13: 15–24.
16. Hoeks SE, Smolderen KG, Scholte Op Reimer WJ, Verhagen HJ, Spertus JA, Poldermans D. Clinical validity of a disease-specific health status questionnaire: The Peripheral Artery Questionnaire. *J Vasc Surg* 2009; 49: 371–377.
17. Lamers LM, McDonnell J, Stalmeier PF, Krabbe PF, Busschbach JJ. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. *Health Econ* 2006; 15: 1121–1132.
18. EuroQol – a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy* 1990; 16: 199–208.
19. Long J, Modrall JG, Parker BJ, Swann A, Welborn MB 3rd, Anthony T. Correlation between ankle-brachial index, symptoms, and health-related quality of life in patients with peripheral vascular disease. *J Vasc Surg* 2004; 39: 723–727.
20. Raphael C, Briscoe C, Davies J, et al. Limitations of the New York Heart Association functional classification system and self-reported walking distances in chronic heart failure. *Heart* 2007; 93: 476–482.
21. Krumholz HM. The year in epidemiology, health services, and outcomes research. *J Am Coll Cardiol* 2005; 46: 1362–1370.
22. Aquarius AE, Denollet J, Hamming JF, Breek JC, De Vries J. Impaired health status and invasive treatment in peripheral arterial disease: a prospective 1-year follow-up study. *J Vasc Surg* 2005; 41: 436–442.
23. Barth J, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. *Psychosom Med* 2004; 66: 802–813.
24. Carney RM, Freedland KE, Eisen SA, Rich MW, Skala JA, Jaffe AS. Adherence to a prophylactic medication regimen in patients with symptomatic versus asymptomatic ischemic heart disease. *Behavioral Medicine (Washington, DC)* 1998; 24: 35–39.
25. Gartenmann C, Kirchberger I, Herzig M, et al. Effects of exercise training program on functional capacity and quality of life in patients with peripheral arterial occlusive disease. Evaluation of a pilot project. *Vasa* 2002; 31: 29–34.
26. Stanton AL, Revenson TA, Tennen H. Health psychology: psychological adjustment to chronic disease. *Annu Rev Psychol* 2007; 58: 565–592.
27. Tsai JC, Chan P, Wang CH, et al. The effects of exercise training on walking function and perception of health status in elderly patients with peripheral arterial occlusive disease. *J Intern Med* 2002; 252: 448–455.
28. 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: 261–268.
29. Rumsfeld JS, Magid DJ, Plomondon ME, et al. History of depression, angina, and quality of life after acute coronary syndromes. *Am Heart J* 2003; 145: 493–499.