Clinical Indicators and Psychosocial Aspects in Peripheral Arterial Disease

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Hypothesis: Patients with peripheral arterial disease (PAD) often experience substantial impairment in health status and quality of life (QOL), but factors associated with these outcomes are unknown. We hypothesized that subjective pain symptoms in the legs and social support and stress (the degree to which situations are appraised as stressful) are associated with impaired health status and QOL.

Design: Cross-sectional observational study.

Setting: Vascular outpatient clinic of a teaching hospital.

Patients: The study included consecutive patients seeking treatment for the first time because of walking pain. Diagnosis and severity of PAD were based on history, physical examination, treadmill-walking distance, and ankle-brachial pressure indexes (ABPIs). Patients with PAD (n=188) and patients with atypical leg symptoms (n=57) completed the 10-item version of the Perceived Stress Scale (perceived stress), the 12-item version of the Perceived Social Support Scale–Revised (social support), the RAND 36-Item Health Survey (health status), and the World Health Organization Quality of Life Assessment Instrument-100.

Main Outcome Measures: Health status and QOL.

Results: Both groups had equally poor health status and QOL, with patients with atypical leg symptoms reporting more bodily pain \( (P = .004) \). In patients with PAD, the ABPI \( (P = .008) \) and perceived stress \( (P = .001) \) were associated with maximum walking distance. Furthermore, the health status domain of physical functioning was affected by the ABPI \( (P = .002) \), cardiac disease \( (P = .005) \), body mass index \( (P = .007) \), and perceived stress \( (P < .001) \). Overall QOL in patients with PAD was independently influenced by sex \( (P = .04) \), carotid disease \( (P = .03) \), and perceived stress \( (P < .001) \).

Conclusions: Subjective pain in the legs is associated with impaired health status and QOL. Stress adversely influences the health status and QOL of patients with PAD above and beyond the influence of clinical indicators. These findings indicate the importance of accounting for perceived stress in patients with PAD.

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See Invited Critique at end of article

Peripheral arterial disease (PAD) is a marker of systemic atherosclerotic disease, which leads to an increased risk of stroke, myocardial infarction, and cardiovascular death.\(^5,6\) One of the most frequent symptoms of PAD is intermittent claudication (IC), walking-induced pain that is relieved by rest.\(^7,8\) Intermittent claudication can cause severe limitations in patients’ walking ability,\(^7,9\) leading to impaired physical functioning\(^2,3\) and a poor quality of life (QOL).\(^8\)

Because of the increased interest in health status and QOL in cardiovascular research,\(^9,10\) identifying determinants of these patient-based measures has become increasingly important.\(^9\) Previous studies\(^11-13\) have shown that disease severity indexes such as the ankle-brachial pressure index (ABPI) only partially determine patient-based measures. However, the influence of other factors on health status and QOL in PAD is not fully understood. Previously, stress has been related to cardiovascular reactivity\(^14\) and an increased risk of cardiovascular events,\(^15,16\) indicating that stress may contribute to the atherosclerotic process.\(^14\) Stress has also been associated with poor mental health status in young adults\(^17\) and impaired QOL in middle-aged women.\(^18\) Another factor that has been shown to influence QOL is social support.\(^17,18\) Lack of social support has been associated with poor QOL in patients with coronary artery disease\(^19\) and a lower ABPI score in patients with PAD, indicating more severe PAD.\(^20\)
However, in other patients (n=57), the pain symptoms in the legs were caused by obstruction of the arteries in the lower limbs. A total of 188 patients were diagnosed as having IC, a common symptom of PAD. Their limitations in walking capacity were caused by obstruction of the arteries in the lower limbs. As a consequence, they were referred back to their general physician. These patients were included as a control group in the present study.

The study population consisted of patients who visited the vascular outpatient clinic of St Elisabeth Hospital in Tilburg, the Netherlands, for the first time between September 2001 and March 2004. All patients were referred by their general physicians because of walking pain. In total, 284 patients were invited to participate in the study, and 251 patients (88%) agreed. Six patients were excluded because of cognitive impairment (2 patients), recent myocardial infarction, visual problems, illness (influenza), and participation in another study, leaving 245 patients in the study. After their first visit to the vascular surgeon, all patients completed questionnaires concerning perceived stress, social support, health status, and QOL. Subsequently, patients were scheduled for a treadmill performance test. Patients were unaware of their diagnosis when they completed the questionnaires. The local ethics committee approved the study, and each patient gave written informed consent.

The vascular surgeon based the diagnosis on history, physical examination, and the results of the treadmill test (pain-free and maximum treadmill-walking distance and ABPI score). A total of 188 patients were diagnosed as having IC, a common symptom of PAD. Their limitations in walking capacity were caused by obstruction of the arteries in the lower limbs. However, in other patients (n=57), the pain symptoms in the legs were not associated with PAD or any other form of disease at that time. They were diagnosed as having atypical pain symptoms in the legs. As a consequence, they were referred back to their general physician. These patients were included as a control group in the present study.

MEASURES

Disease Severity

In all patients, ABPI was measured as an index of PAD severity. The ABPI is defined as the ratio of the ankle systolic blood pressure to the brachial artery systolic blood pressure and has a normal resting value of approximately 1.0. An ABPI value of less than 0.90 is 95% sensitive to detect PAD in the lower extremities and was shown to be a strong predictor of cardiovascular disease and mortality. All patients with PAD had an ABPI value less than 0.90, whereas patients with atypical leg symptoms had an ABPI value between 0.90 and 1.29, indicating no PAD (Table 1). This is in accordance with the cutoff value of 0.90 used in previous studies.

Walking Impairment

To determine walking impairment, the pain-free and maximum walking distance were assessed in all patients using a standardized treadmill-walking test. Patients had to walk on a treadmill on a 5% incline, for a maximum of 1000 m, at a speed of 3.5 km/h.

Cardiovascular Risk Factors and Comorbidity

Diabetes mellitus, smoking, hypertension, hyperlipidemia, and cardiac, carotid, renal, and pulmonary status were registered in all patients according to the recommended standards of the Society for Vascular Surgery/North American Chapter of the International Society for Cardiovascular Surgery. The presence of back, knee, and hip symptoms unrelated to PAD was also recorded because this may influence patients’ walking ability. In addition, body mass index (calculated as weight in kilograms divided by the square of height in meters) was determined in all patients.

Table 1. Characteristics of 188 Patients With Intermittent Claudication and 57 Patients With Atypical Leg Symptoms

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intermittent Claudication</th>
<th>Atypical Leg Symptoms</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, M/F, %</td>
<td>63.3/36.7</td>
<td>61.4/38.6</td>
<td>.80</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>64.7 (9.9)</td>
<td>62.1 (10.9)</td>
<td>.09</td>
</tr>
<tr>
<td>Education, mean (SD), y</td>
<td>9.8 (3.1)</td>
<td>9.6 (3.0)</td>
<td>.61</td>
</tr>
<tr>
<td>Partner, %</td>
<td>64.4</td>
<td>80.7</td>
<td>.02</td>
</tr>
<tr>
<td>Body mass index, mean (SD)*</td>
<td>25.8 (5.6)</td>
<td>27.9 (6.7)</td>
<td>.02</td>
</tr>
<tr>
<td>Ankle-brachial pressure index, mean (SD)</td>
<td>0.61 (0.23-0.89)</td>
<td>1.94 (0.90-1.29)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pain-free treadmill walking distance, mean (SD)</td>
<td>111.8 (141.6)</td>
<td>211.3 (295.1)</td>
<td>.02</td>
</tr>
<tr>
<td>Maximum treadmill walking distance, mean (SD)</td>
<td>363.4 (320.8)</td>
<td>526.4 (385.9)</td>
<td>.006</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>19.1</td>
<td>21.1</td>
<td>.76</td>
</tr>
<tr>
<td>Tobacco use, %</td>
<td>54.3</td>
<td>36.8</td>
<td>.03</td>
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<tr>
<td>Hypertension, %</td>
<td>44.1</td>
<td>42.1</td>
<td>.82</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>49.5</td>
<td>49.1</td>
<td>.92</td>
</tr>
<tr>
<td>Cardiac status, %</td>
<td>27.7</td>
<td>38.6</td>
<td>.09</td>
</tr>
<tr>
<td>Carotid status, %</td>
<td>10.1</td>
<td>14.0</td>
<td>.36</td>
</tr>
<tr>
<td>Renal status, %</td>
<td>4.3</td>
<td>NA</td>
<td>.12</td>
</tr>
<tr>
<td>Pulmonary status, %</td>
<td>8.5</td>
<td>8.8</td>
<td>.89</td>
</tr>
<tr>
<td>Back symptoms, %</td>
<td>11.7</td>
<td>26.3</td>
<td>.007</td>
</tr>
<tr>
<td>Hip or knee symptoms, %</td>
<td>9.6</td>
<td>8.8</td>
<td>.86</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.
*Calculated as weight in kilograms divided by the square of height in meters.
Perceived Stress

The short 10-item version of the Perceived Stress Scale was used.25,26 This questionnaire assesses the degree to which situations within a person’s life are appraised as stressful. Responses were given on a 4-point scale, ranging from never (1) to always (4). The 10-item Perceived Stress Scale measures perceived stress without any loss of psychometric quality compared with the 14-item version of the Perceived Stress Scale23 and has good reliability and validity.27

Social Support

The total score of the 12-item version of the Perceived Social Support Scale–Revised27 was used to examine perceived social support from family, friends, and significant others. The item’s rating scale varied from 1 (very strongly disagree) to 7 (very strongly agree). In cardiac patients, reliability and validity were good.28

Health Status

The RAND 36-Item Health Survey (RAND-36)28,29 is a generic measure that assesses 8 health concepts: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, vitality, bodily pain, and general health perception. Scores on each dimension of RAND-36 range from 0 to 100, in which 100 represents best functioning or well-being. The RAND-36 and the Medical Outcomes Study 36-Item Short-Form Health Survey30 are similar health status measures; however, concerning the dimensions of bodily pain and general health perception, the scoring is somewhat different.28 The RAND-36 has good reliability and validity.31

Quality of Life

The World Health Organization Quality of Life Assessment Instrument-100 (WHOQOL-100)32,33 is a generic QOL measure that consists of 100 questions that assess QOL with 24 facets within 6 domains. In the present study, an abbreviated version of the WHOQOL-100 was used, which had previously been reduced for patients with IC.34 This version included 10 QOL facets: the QOL domain of physical health consists of 3 facets, and the QOL domain of level of independence includes 4 facets. In addition, 3 separate facets were included: overall QOL and general health, negative feelings, and participation in and opportunities for recreation and leisure. The WHOQOL-100 has good reliability and validity.33

Statistical Analyses

Frequencies and descriptive were used to determine the patient characteristics. We used $t$ tests for independent samples (continuous variables) and chi-square tests (nominal variables) to examine differences between patients with IC and those with atypical leg symptoms in demographic and medical characteristics, health status, and QOL. Before we performed multiple regression analyses, we decided to reduce the number of predictors to prevent loss of statistical power. Therefore, univariate regression analyses were performed to examine the association among cardiovascular risk factors, comorbidity (including back, hip, and knee symptoms), and body mass index on the one hand and maximum walking distance, health status, and QOL on the other. Based on the relatively large number of subscales in both the RAND-36 and WHOQOL-100, we decided to use only 1 subscale for each of these questionnaires. Previous research1 found that the RAND physical functioning subscale was an independent predictor of hospitalization for PAD at 1-year of follow-up. Therefore, we used this subscale to represent health status. The WHOQOL-100 facet of overall QOL and general health was used to represent QOL because it gives an overall impression of patients’ QOL and their general health perceptions.

Finally, multiple regression analyses (enter method) were performed for patients with PAD to examine the influence of social support and perceived stress in addition to demographics (age and sex) and clinical indicators (ABI and, when significant in univariate analyses, cardiovascular risk factors, comorbidity, or body mass index) on the maximum walking distance, RAND-36 subscale of physical functioning, and the WHOQOL-100 facet of overall QOL. All statistical analyses were performed with SPSS statistical software, version 11.5 (SPSS Inc, Chicago, Ill).

RESULTS

Baseline characteristics and distribution of risk factors of the participating patients with IC and those with atypical pain symptoms in the legs are given in Table 1. Patients with IC were more likely to smoke ($P = .03$). Patients with atypical leg pain symptoms had higher body mass indexes ($P = .02$) and more often had a partner ($P = .02$). Despite this, no significant differences were found with regard to social support between both groups ($P = .29$). Since it was part of the diagnosis for PAD, both groups differed significantly with regard to ABI ($P < .001$), pain-free walking distance ($P = .02$), and maximum walking distance ($P = .006$). Furthermore, patients with atypical leg symptoms were more likely to report back symptoms ($P = .007$). No other differences were found regarding cardiovascular risk factors and other comorbidity, age, sex, education years, or perceived stress ($P = .57$).

DISEASE STATUS, HEALTH STATUS, AND QOL

Regarding health status, no significant differences were found between patients with IC and patients with atypical pain symptoms in the legs, except for bodily pain. Patients with atypical leg pain symptoms in the legs reported more pain than patients with IC, indicated by the lower scores on the RAND-36 scale of bodily pain ($P = .004$) (Table 2). With regard to QOL, no significant differences between patient groups were found (Table 2). Both groups were equally impaired in their QOL.

PSYCHOSOCIAL DETERMINANTS OF WALKING IMPAIRMENT IN PAD

Univariately, cardiovascular risk factors, comorbidity, and body mass index were not significantly related to maximum walking distance in patients with IC (data not shown). However, cardiac status was nearly statistically significant ($P = .07$) and was therefore included in the multivariate regression analysis. Results from the multivariate analyses showed that ABI ($P = .008$) and perceived stress ($P = .001$) were independently associated with maximum walking distance in patients with IC (Table 3). A higher ABI score was associated with a better max-
maximum walking distance. Furthermore, patients with less perceived stress had a better maximum walking distance. Social support did not influence maximum walking distance.

PSYCHOSOCIAL DETERMINANTS OF HEALTH STATUS IN PAD

With regard to the risk factors, univariate analyses showed that cardiac (P = .004), renal (P = .04), pulmonary (P = .01), and carotid status (P = .06) and hypertension (P = .08) were (almost) significantly related to physical functioning. Therefore, these risk factors were included in the multivariate regression model. Results from the multiple regression analysis showed that a higher ABPI score (P = .002), the absence of cardiac disease (P = .005), lower body mass index (P = .007), and less perceived stress (P < .001) were all independently associated with better physical functioning in patients with PAD (Table 3). Social support was not related to physical functioning in patients with PAD.

### PSYCHOSOCIAL DETERMINANTS OF QOL IN PAD

Univariate analyses showed that of the risk factors, renal (P = .003) and carotid status (P = .001) were related to overall QOL in PAD. In addition, diabetes (P = .09) and pulmonary status (P = .05) were almost statistically significant. Therefore, these variables were included in the multivariate analyses. Results from the multiple regression analysis showed that overall QOL in patients with PAD was independently influenced by sex (P = .04), the absence of carotid disease (P = .03), and less perceived stress (P < .001) (Table 3). Disease severity (ABPI) was not associated with overall QOL in patients with PAD. In addition, social support did not influence patients’ QOL.

### COMMENT

To understand the overall effects of having PAD on patients’ lives, PAD should be evaluated not only in terms of...
of objective clinical outcomes but also in terms of patient-based measures, such as health status and QOL. Getting more insight into the factors associated with these patient-based measures is therefore important. In the present study, we examined the effect of disease status (having PAD or not) with regard to health status and QOL and the effect of social support and perceived stress on walking impairment, health status, and QOL in PAD. Results showed that poor health status and impaired QOL are related to pain symptoms in the legs. Furthermore, perceived stress was adversely associated with the walking ability, health status, and QOL of patients with PAD above and beyond the influence of clinical indicators.

Health status and QOL were equally poor in patients with PAD and patients with atypical leg symptoms. When comparing the RAND-36 and WHOQOL-100 scores of both groups with the average scores of a sample of healthy elderly people,15,29 both patient groups were found to be severely impaired in their health status and QOL. At the time they completed the questionnaires, patients were unaware of their disease status. Thus, this cannot have influenced the results. These findings may suggest that poor health status and impaired QOL are not just the consequence of disease status (the presence of PAD). Rather, poor health status and impaired QOL are related to pain symptoms in the legs.

Results from the present study showed that ABPI was associated with walking distance and health status, but ABPI could not predict QOL in patients with PAD. This finding is in line with previous studies. Although indexes of PAD severity may predict functional impairment,34 they only partially determine patient-based outcomes such as QOL.11-13

Although it has been suggested that lack of social support is related to poor QOL in patients with coronary artery disease,19 results from the present study could not confirm this notion. In line with studies in other cardiovascular patient groups, we found that the level of perceived stress was independently associated with walking ability and patient-based measures. Patients who experience high levels of stress are impaired in their walking ability, physical functioning, and overall QOL. It has been argued that highly stressed patients with cardiovascular disease are at increased risk of poor QOL.35,36 It has also been found that patients with cardiovascular disease who experience high levels of stress are at increased risk of more adverse health outcomes,14 such as stroke or coronary heart disease.13 These findings may suggest the predisposition of some patients to experience higher levels of perceived stress than others, irrespective of disease severity. Identifying highly stressed patients enables us to provide more accurate treatment for these high-risk individuals. For example, psychosocial interventions aimed at reducing stress could be implemented in these patients. Previous studies have already shown the beneficial effects of stress management programs on patients’ QOL37 and cardiac prognosis.38 Relaxation training and stress management are effective in reducing stress in patients with cardiac disease.39 Stress-reducing interventions may lead to improvements in walking ability, health status, and QOL in patients with PAD as well.

The present study has some limitations. Because of the cross-sectional design of the study, we cannot infer any causal relationship between perceived stress and patient-based measures. High levels of perceived stress may cause a more negative perception of health status and QOL, but poor health status and impaired QOL could also lead to more perceived stress. Despite this cross-sectional design, most of our findings are in line with previous studies in other cardiovascular patient groups. Furthermore, although the atypical patients were PAD-free at the time of the study, their poor health status and impaired QOL could be an indication of underlying morbidity. Previous studies5,11 have shown that health status and QOL are both severely impaired in patients with PAD. However, in the present study, the atypical patients had equally poor health status and QOL. This could indicate the presence of some form of disease. Finally, in the present study, we did not account for the effect of taking mood-altering medications such as analgesics, which could have influenced the results.

In conclusion, the present study showed that poor health status and impaired QOL are related to pain symptoms in the legs. Furthermore, high levels of perceived stress adversely influence the walking ability, health status, and QOL of patients with PAD above and beyond the influence of clinical indicators. These findings indicate the importance of accounting for perceived stress in patients with PAD.

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REFERENCES

The increasing prevalence of PAD of the lower extremities, the wide range of therapies available to treat PAD, and the renewed emphasis on evidence-based outcomes to justify and guide treatment practices make it imperative that the therapeutic strategies used should improve functional status and QOL and preserve limb viability. The authors of an article in the current issue of the ARCHIVES assessed the contribution of psychosocial factors to the QOL of patients with PAD using several well-established assessment instruments. They found that in addition to the well-recognized objective clinical indicators, walking distance, physical function, and overall QOL were adversely affected by perceived stress. Quantifying the impact of health status from the patient’s perspective is especially pertinent to individuals with intermittent claudication because therapy in most cases is directed primarily toward improving health status rather than preserving life or limb.

Limitations of this study are that it was performed at a single institution and that the participants were evaluated on only one occasion. In addition, the cross-sectional nature of the study makes it difficult to establish a direct casual relationship between perceived stress and the patients’ perceptions of their disease. Another modifying factor not fully addressed is the influence of medications on perceived stress in patients with intermittent claudication. Because many of these patients use medications that alter the perception of their symptoms, this study raises the intriguing prospect of the benefits of anxiolytic agents or relaxation techniques in conjunction with conventional treatment for PAD. This article emphasizes the need for evaluating the impact of PAD and its management on QOL and health status in addition to objective measures of functional improvement if patients with PAD are to be restored to their previous state of health.

Glenn C. Hunter, MD
