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Assessment of Functional Status and Quality of Life in Claudication

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Abstract

Background—Treadmill walking is commonly used to evaluate walking impairment and efficacy of treatment for intermittent claudication (IC) in clinical and research settings. Although this is an important measure, it does not provide information about how patients perceive the effects of their treatments on more global measures of health-related quality of life (HRQOL).

Methods—PubMed/Medline was searched to find publications about the most commonly used questionnaires to assess functional status and/or general and disease-specific HRQOL in patients with PAD who experience IC. Inclusion criteria for questionnaires were based on existence of a body of literature in symptomatic PAD.

Results—Six general questionnaires and 7 disease-specific questionnaires are included with details about the number of domains covered and how each tool is scored. The Medical Outcomes Study Short Form 36 item questionnaire and Walking Impairment Questionnaire are currently the most used general and disease-specific questionnaires at baseline and following treatment for IC, respectively.

Conclusions—The use of tools which assess functional status and HRQOL has importance in both the clinical and research areas to assess treatment efficacy from the patient perspective. Therefore, assessing HRQOL in addition to treadmill-measured walking ability provides insight as to effects of treatments on patient outcomes and may help guide therapy.

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BACKGROUND

Peripheral artery disease (PAD) results from atherosclerotic plaque in the major arteries of the lower extremities, causing decreased blood flow in the legs during exertion. Symptomatic PAD patients experience intermittent claudication (IC), which is characterized by cramping, fatigue and/or aching in the calves, thighs or buttocks typically brought on by walking and relieved by rest and which also causes impairments in quality of life.[1] Because of claudication pain, individuals with PAD often avoid physical activity, especially ambulation, thus leading to additional declines in functional status and health-related quality of life (HRQOL) (defined as the patient's perceived physical, emotional and social well-being and function).[2–4] PAD patients with IC may be limited in performing certain activities of daily living and may also feel that they are a burden to themselves as well as their family.[5] It is important to assess how an individual perceives their own health as this information may be useful for determining appropriate treatment strategy and subsequently providing positive outcomes.[6] This review describes the impairments of functional status and HRQOL experienced by symptomatic PAD patients, as assessed by both general and PAD-specific questionnaires. The effects of PAD treatment (e.g., supervised and unsupervised exercise, endovascular therapy, open-surgery procedures, medications) on functional status and HRQOL for patients with IC and the potential usage and relevance of these instruments in clinical and/or research settings is also discussed.

EPIDEMIOLOGY OF SYMPTOMATIC PAD

It has been estimated that 8 to 12 million adults have PAD in the U.S. and that approximately one-third experience IC.[7–8] According to the Trans-Atlantic Societal Consensus II international guidelines, the prevalence of symptomatic PAD is approximately 2–7% in patients aged 50 to 70 years.[1] In addition to the high prevalence of IC, all persons with PAD have a significantly increased risk of cardiovascular morbidity and mortality.[9–10]

OBJECTIVE MEASURES OF FUNCTIONAL STATUS IN CLAUDICATION

Treadmill testing is an established means to objectively determine walking ability in PAD patients and is highly predictive of long-term morbidity and mortality outcomes.[11–12] Typically, time and/or distance to onset of claudication and maximal time and/or distance walked until test termination due to leg pain are considered gold standard endpoints by which to assess walking ability for patients with IC. Other validated, objective physical measurements of functional status include the 6-minute walk test and the Short Physical Performance Battery.[13–14] These functional performance measures are more strongly associated with physical activity levels during daily life than treadmill walking and both are valid and reliable in objectively assessing physical function for patients with IC.[15–17] However, none of these tests address a patient's perception of their walking ability or HRQOL. In addition, other important elements of health status such as mental health, emotional well-being and social functioning can be assessed only by questionnaires.

FUNCTIONAL STATUS/HRQOL QUESTIONNAIRES FOR SYMPTOMATIC PAD

Functional status can be defined "…as the level of activities performed by an individual to realize needs of daily living in many aspects of life including physical, psychological, social, spiritual, intellectual, and roles."[18] HRQOL can be defined as an individual's multi-faceted perception of their overall health and well-being, including the impact of illness, treatment and other aspects of their daily life.[19–20] Questionnaire utilization has been a part of research studies seeking to evaluate functional status and HRQOL in cross-sectional evaluation or at

baseline and after treatment for claudication. However, assessment of functional status and HRQOL in clinical settings using valid and reliable questionnaires is important in that appropriate questionnaires can assist healthcare providers in determining the level of impairment and selecting appropriate care for patients with IC. Questionnaires are often compared to objective measures such as treadmill walking in order to establish validity. There is also practical value for using questionnaires from a clinical standpoint, in that treadmill tests are more expensive than questionnaires. Typically, two types of questionnaires are employed in patients with IC. Functional status questionnaires focus primarily on the ability to carry out physical activities and self-reported walking ability.[21] Domains such as life satisfaction, morale and happiness are assessed by broader quality of life questionnaires that address overall well-being and function stemming from emotional and social aspects of life.[22] These types of questionnaires can be further divided into two main categories: general and disease-specific. General assessment tools are applicable to a wide range of patient populations, in contrast to disease-specific questionnaires. Tables 1 and 2 summarize the originating and/or validation studies for general and disease-specific questionnaires for PAD used in assessing functional status and HRQOL in symptomatic PAD patients.

General questionnaires

An important aspect of general health questionnaires is that comparative analyses can be performed in patient populations across disease states, thus providing the ability to describe the relative severity and impact of the disease in question. A number of general health questionnaires have been used to assess functional status and HRQOL for PAD patients with IC. Table 3 describes functional status and/or HRQOL following exercise training for patients with IC. Table 4 summarizes the HRQOL outcomes following vascular procedures for the other tools described in this review. Table 5 describes the impact of pharmacological therapies on quality of life assessed by questionnaires for patients with IC.

Short Form 36-item questionnaire (SF-36)—The Medical Outcomes Study (MOS) Short Form questionnaires were constructed in part to provide practical tools for routine monitoring of patient outcomes in medical practice as well as for research.[23] The SF-36 provides a brief yet comprehensive assessment of HRQOL.[6] Eight domains (physical, role and social functioning, mental health, patient health perceptions, vitality, bodily pain, change in health) are measured. The SF-36, for which each individual domain is transformed to a score of 0 to 100 with 100 being the best possible score (results can also be separated into physical and mental component summary scores), has been extensively validated for assessing HRQOL in symptomatic PAD patients. It is one of the most commonly used general health questionnaires for this purpose in addition to its broad use across many disease states.[24] PAD patients with IC report lower scores in physical functioning, physical limitations and bodily pain when compared to healthy controls and the general population.[25–26] The MOS questionnaires have been used extensively to assess the results of bypass surgery, endovascular procedures, supervised exercise rehabilitation and pharmacologic treatment. Recently, Mazari et al[27] examined the HRQOL of symptomatic PAD patients using the SF-36 before and 12 weeks after endovascular therapy, supervised exercise and a combination of the two groups. Endovascular therapy and exercise training each independently resulted in improvements in the domains of physical functioning and physical role limitations. However, the combined interventions demonstrated the greatest impact on perceived quality of life, as 6 of the 8 total domains of the SF-36 significantly improved. There have been a number of studies comparing HRQOL across the different treatment options. Table 6 depicts a summary of the functional status and/or HRQOL questionnaires nested within individual studies following multiple interventions. Briefly, the

most effective interventions for improving patient's quality of life included combinations of treatments.

Short Form 12-item questionnaire (SF-12)—The SF-12 extracts select items from all 8 domains of the SF-36 and includes the same physical and mental component summary scores.[28] It was designed to be a simpler version of the SF-36, scored in the same way as the SF-36. Using the SF-12, Smolderen et al[29] assessed baseline HRQOL of symptomatic PAD patients compared to chronic heart failure patients. Results indicated that the physical domains were affected to a greater extent in PAD patients, whereas the mental domains were significantly worse in chronic heart failure patients. Safley et al[30] established that the physical component summary scores improved following endovascular therapy in a cohort of mostly PAD patients with claudication and a small number of patients with critical limb ischemia (CLI), similar to studies using other versions of the MOS Short Form. More research is needed to determine the impact of other treatment methods on SF-12 scores for symptomatic PAD patients. However, because it is a relatively short questionnaire compared to other general health questionnaires, it may be practical for use in clinical settings.

European Quality of Life questionnaire (EuroQOL)—The EuroQOL is a combined functional status and HRQOL instrument that assesses 5 domains including mobility, self-care, usual activities, pain/discomfort and anxiety/depression.[31–32] The questionnaire administrator scores the EuroQOL by applying a single summary index from 0 to 1, with 0 representing the worst health state and 1 representing perfect health. A second, separate part of the EuroQOL is the visual analogue scale (VAS), which asks patients to draw a line on a 0 to 100 "thermometer" scale, rating their health from worst imaginable health to best imaginable health (transformed to the summary index of 0 to 1 as well). The EuroQOL has been used to examine the effects of endovascular therapy for PAD patients. Generally, endovascular therapy improved many of the domains included in the questionnaire.[30,33–38] Several studies have also compared treatments, including supervised exercise, endovascular therapy and optimal medical therapy.[39–41] Spronk et al[41] found that endovascular therapy and supervised exercise training both resulted in improved EuroQOL scores 6 and 12 months after treatment. There were no differences between the treatment groups, suggesting that supervised exercise and endovascular therapy have similar value for improving HRQOL for up to 1 year. The EuroQOL is a brief, easy to use questionnaire which may have practical value for use in clinical settings.

Nottingham Health Profile (NHP)—The NHP evaluates both functional status and HRQOL and has been used for patients with IC, primarily in European studies.[22,42–43] The NHP contains two sections: Section I is composed of 38 yes/no response items and 6 domains that include: sleep, energy, emotional reactions, social isolation, physical mobility and pain. Section II examines patient difficulties with daily activities via 7 general yes/no questions. These include the areas of employment, housework, family relationships, social and sex life and hobbies and holidays. Higher scores indicate greater health problems, on a scale of 0 to 100. Studies have examined HRQOL using the NHP for claudicants compared to controls or CLI patients.[44–46] Khaira et al[46] demonstrated that symptomatic PAD patients have greater impairments in the NHP domains of energy, pain, emotional reactions, sleep and physical mobility compared with age and sex-matched controls. Klevsgard et al[44] determined that the areas of pain, sleep and physical mobility are significantly better for PAD patients with IC when compared to CLI patients, with no differences in energy, emotional reaction or social isolation. Other studies have yielded mixed results when examining the change in HRQOL following vascular intervention for IC.[47–55] Koivunen and Lukkarinen[47] determined that revascularization improved the domains of emotional reactions, energy and social isolation. Additionally, lower extremity bypass surgery also

improved pain, physical mobility and sleep 1 year after the intervention.[47] However, recently it was found that quality of life returned to pre-surgery levels in the domains of pain and physical mobility at 1 year follow-up.[48] These findings suggest that, although endovascular therapy improves HRQOL acutely, long-term outcomes may not be as durable. The NHP is comprehensive and has been examined extensively in research settings. This questionnaire may be practical for use in clinical settings because it takes only 5–10 minutes to complete.[53,55]

World Health Organization Quality of Life (WHOQOL) assessment instrument 100—The WHOQOL-100 was designed for cross-cultural applicability and thus was developed in several different languages.[56–60] The instrument is composed of 6 domains including physical health, psychological, level of independence, social relations, environment and spirituality/religion/personal beliefs, incorporating 24 quality of life "facets" and 100 total items. Responses are determined from 5-point Likert scales (e.g., very dissatisfied = 1; very satisfied = 5). Using a reduced version of the WHOQOL-100 (17 facets), Breek and colleagues[60] established that patients with IC had lower scores in the domains of physical health and level of independence as well as many facets compared to healthy controls. In one of the few studies to use the WHOQOL-100 to evaluate an intervention (i.e., angioplasty, bypass surgery, endarterectomy, amputation) for patients with IC, there were improvements in physical health and level of independence.[61] While the WHOQOL-100 is well established in other disease states, more studies are warranted to determine the impact of treatment on HRQOL for IC. The original questionnaire is probably too long to be practical for clinical use but the reduced version may have value for use in the clinical setting.[57]

McMaster Health Index Questionnaire (MHIQ)—The MHIQ is composed of 59 health-related items covering physical, social and emotional dimensions. The physical function domain consists of 24-items including physical activities, mobility and self-care activities. There are a total of 25 social function items that assess general welfare, family and friend's support/participation and global social function. The 25 emotional function items include self-esteem, feelings about personal relationships, thoughts about the future, critical life events and global emotional function. Because some of the items address both social and emotional function within the same question, the consolidated number of items is 59. For each of the 3 dimensions, scores are based on index values of 0 to 1 with lower scores indicating worse function. Compared to other general questionnaires, few studies have used the MHIQ to assess HRQOL in patients with IC.[62–63] However, findings indicate impairments in general health and physical, social and emotional function when compared to age-matched controls.[63] Following 24 weeks of pharmacologic therapy, Brevetti et al[64] found that patients randomized to receive propionyl-L-carnitine improved physical and emotional function and the global scores compared with the group receiving a placebo. There may be use for this questionnaire in clinical settings.

PAD-specific Questionnaires

Disease-specific HRQOL questionnaires for PAD were developed to examine how IC impacts the well-being and ability of patients to function. Although less generalizable than HRQOL questionnaires developed for use across disease states, these tools allow for a more in-depth assessment of specific health issues related to PAD. This is particularly important because of the debilitating effects of IC on HRQOL, particularly in the physical domains as opposed to the psychosocial domains.[65]

Walking Impairment Questionnaire (WIQ)—The WIQ was one of the first disease-specific questionnaires for assessing functional status in PAD patients and remains widely

used.[66] The WIQ was validated in several large studies and is available in many different languages.[67–72] In the initial validation as well as in subsequent studies, the questionnaire results were correlated to treadmill measures of performance (i.e., peak walking distance, peak oxygen consumption, and onset of claudication pain) in PAD patients.[66] The WIQ assesses how limited patients are in walking defined distances and speeds and the degree of difficulty climbing flights of stairs. Symptoms that limit walking are also assessed. Scoring is on a 0–100% scale. Using the WIQ, it has been established that limitations in walking speeds and distances as well as stair climbing are present in patients with IC compared to controls.[4,73] The WIQ has also been shown to detect impairment in PAD patients who have mild symptoms or are asymptomatic.[74]

The WIQ has been used extensively to evaluate the efficacy of several types of therapy for IC including exercise training,[66,75–79] peripheral bypass surgery,[66,80] endovascular therapy[81–82] and many types of medications.[83–86] In the initial development and validation, Regensteiner et al[66] compared WIQ scores of claudication patients before and after 12 weeks of supervised treadmill walking and 6 weeks following bypass surgery. Both treatments significantly improved the distance and speed domains as well as treadmill walking, demonstrating the positive impact of both treatments. Additionally, Matsuo and Shigematsu[85] examined changes in functional status assessed by the Japanese version of the WIQ for IC patients. Patients were stratified by ankle-brachial index values and treated for 8 weeks with prostaglandin E_1 in lipid microspheres (lipo-PGE_1). The WIQ subscales improved for all groups, demonstrating sensitivity to lipo-PGE_1 treatment. Thus, the WIQ is a valid, reliable and sensitive tool for assessing functional status of PAD patients for available treatment options. This questionnaire is brief and can be used in the clinical or research settings to provide information about walking impairment.

Claudication Scale (CLAU-S)—The CLAU-S was originally developed in Germany and has been translated into a number of different languages including French, English, Flemish and Swiss.[38,87–88] The different versions of this scale are composed of Likert scale items, each with a number of domains. The 6 domain version includes daily living, pain, complaints, social life, disease-specific fears and mood. Scoring is on a 0 to 100 scale (i.e., 0 worst score, 100 best score). The majority of studies using the CLAU-S in European settings have examined the effects of naftidrofuryl ($5HT_2$ receptor antagonist), a peripheral vasodilator, on IC and have demonstrated mixed results for specific domains, although walking improvement has been observed. Daily living, pain, disease-specific fears and mood improved significantly when compared to patients who received a placebo.[89] However, D'Hooge et al[90] found no changes in disease-specific fears and mood and an improvement in social life scores following naftidrofuryl treatment. Several vascular intervention studies have evaluated changes in HRQOL demonstrating both short and long term improvements in most of the domains of the CLAU-S.[38,91] To the best of our knowledge, the CLAU-S has only been used in the research setting to date.

Peripheral Artery Occlusive Disease 86 questionnaire (PAVK-86)—The PAVK-86 consists of 86 items and 7 HRQOL domains which include functional status, pain, general complaints, mood, anxiety, social life and evaluation of treatment. Scoring is from 1–4, with 1 indicating no impairment and 4 indicating high impairment. Holler and colleagues[92] examined PAVK-86 scores spanning PAD severity according to the Fontaine Classification system (stages II to IV). Patients experienced greater impairments in pain and functional status between Fontaine Classification Stage IIb (moderate to severe claudication) compared to IIa (mild claudication), indicating that the more advanced disease and subsequent shorter distance to onset of leg pain leads to a greater impairment of the PAVK-86 physical domains. The PAVK-86 has been used to evaluate changes in HRQOL following pharmacological treatment, supervised and unsupervised exercise training and

combined pharmacological and supervised exercise training.[93–95] Briefly, all domains except general complaints improved in patients with IC following 12 weeks of supervised treadmill walking.[94] The largest improvement was demonstrated in the pain and functional status domains, indicating that physical domains for IC patients are generally the most improved by exercise training. One drawback is that the questionnaire has proven difficult and lengthy for patients to complete.[92]

Vascular Quality of Life questionnaire (VascuQOL)—The VascuQOL was originally developed for use in patients with Fontaine classification II-IV (i.e., ranging from mild IC to ulceration/gangrene) and has been translated into multiple languages.[96] The questionnaire contains 25-items subdivided into the domains of pain, symptoms, activities and social and emotional well-being. Scores are based on responses from a 7 point scale for each item (1 being lowest score, 7 being highest). Several studies have used it to evaluate the impact of IC on quality of life.[39,97] de Vries et al[39] established that the instrument discriminated disease severity among PAD patients. Additionally, the tool has been demonstrated to be sensitive to change in HRQOL following various treatments for IC.[27,39–40,98] For instance, Roberts et al[98] found that an unsupervised, home-based exercise program improved all domains of the VascuQOL, except for the social domain. The original study indicated that the questionnaire was easy for patients to understand and took an average of 9.6 minutes to complete, indicating it may have value in clinical settings.[96]

Peripheral Artery Questionnaire (PAQ)—The PAQ is a disease-specific health status questionnaire for patients with PAD.[82,99–100] There are 20-items (scored from worst to best, 0–100) relating to domains specific to PAD including the following: 1) identification of the most symptomatic leg, 2) degree to which PAD limits normal activities, 3) questions regarding recent improvement or deterioration in symptoms, 4) the frequency and intensity of claudication, 5) questions regarding patient satisfaction with current treatment, 6) standard quality of life and current symptoms and limitations as compared with their desired level of functioning and 7) social function.[82] In the initial validation study using revascularization, scores improved significantly in all PAQ domains. Currently, there are several studies examining the validity of the PAQ, including several using a Dutch version of the scale.[30,101–102] The questionnaire is relatively brief and may be useful in the clinical setting.

Sickness Impact Profile – Intermittent Claudication (SIP_{IC})—Developed from the generic HRQOL 136-item SIP, the SIP_{IC} is a condensed version of the original, containing 12 items from 6 domains.[103–105] The domains that comprise the SIP_{IC} are sleep and rest, home management, ambulation, mobility, social interaction and alertness and behavior. Scoring is completed by a positive response to a specific question (e.g., 1 point for acknowledgment of walking shorter distances or stopping to rest often). While many studies use the original SIP across various disease states, relatively few have used the SIP_{IC} version for symptomatic PAD patients following treatment.[40,106] Taft et al[106] examined differences in HRQOL assessed by the SIP_{IC} in stable IC following several different interventions. Patients who received endovascular therapy/bypass surgery significantly improved SIP_{IC} scores and also demonstrated larger improvements from baseline than both the supervised exercise training and control groups. There may be utility in the clinical setting for this questionnaire because of its brevity.

Intermittent Claudication Questionnaire (ICQ)—The ICQ consists of an index of 16 items that focuses on limitations imposed by claudication while performing various tasks, such as walking specific distances or performing errands.[107] This questionnaire is a relatively new tool for assessing HRQOL in PAD patients following treatment. Cheetham et

al[108] demonstrated that a supervised exercise program improved ICQ scores by 43% from baseline scores, whereas an advice-only group had a non-significant improvement of 16% (also used SF-36). Additionally, Kakkos and colleagues[109] examined quality of life at baseline and following supervised and unsupervised exercise and intermittent pneumatic compression for patients with stable IC. Both supervised exercise and intermittent pneumatic compression improved ICQ scores at 6 weeks and 6 months post baseline. The questionnaire has also been validated in Turkish.[110] Overall, testing for use in symptomatic PAD patients has been limited. However, the ICQ may be a practical tool for use in clinical settings, as the average time for completing the questionnaire is 3.7 minutes.[107]

CLINICAL RELEVANCE OF HRQOL AND FUNCTIONAL STATUS ASSESSMENT

The questionnaires discussed above have been more commonly used in the research setting than the clinical setting. Finding reports about results of questionnaire use in the clinical setting is difficult because often clinicians may not publish results of a questionnaire used only in this way. Although many study results are adopted into clinical practice, there are not direct examples in the literature of a claudication research trial substantially altering clinical management as a result of questionnaire use. However, the role for questionnaires in the clinical setting should be further explored since patient outcomes provide important information as to treatment efficacy. For instance, understanding patient goals may help in making treatment decisions. The treatment options presented to the patient may not meet their expectations, which may affect adherence to the treatment and could adversely affect the patient's physical, mental and emotional satisfaction with care.[111] Assessing HRQOL and functional status may assist in circumventing future problems with treatment choice and ultimately improve the health of PAD patients with claudication.

CONCLUSIONS

HRQOL is defined as a patient's perceived physical, emotional and social well-being and function. It has been estimated that over 2 million individuals with IC have a reduced quality of life, particularly relating to limitations in ambulation.[10,112] It is important for healthcare providers to evaluate the burden of the disease which ultimately will guide selection of appropriate treatments for improving the HRQOL of PAD patients. Thus, questionnaires that are simple, accurate and effective for determining perceived quality of life and functional status in patients with IC have utility in clinical as well as research settings. Future research should move toward a consensus on the best questionnaires available for symptomatic PAD patients and standardize the implementation and interpretation of these tools in clinical settings.

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Table 1

Original development and validation studies for general questionnaires used in assessing functional status and/or HRQOL in symptomatic PAD patients.

Questionnaires	Authors & Year	Domains/Subscales	Items	† Scoring Range
[1] SF-36	Ware & Sherbourne 1992[6] McHorney et al 1993[113]	8	36	0 to 100
[2] SF-12	Ware et al 1996[28]	8	12	0 to100
[3] EuroQOL	EuroQOL-Group 1990[31] †† Brooks 1996[32]	5	5	0 to 1
[4] NHP	Hunt et al 1980[43] Hunt & McEwen 1980[42]	7	45	100 to 0
[5] WHOQOL-100	WHOQOL-Group 1994[114] WHOQOL-Group 1994[115]	*6	100	**4 to 20
[6] MHIQ	Chambers et al 1976[116] Sackett et al 1977[117] Chambers 1984[118]	3	59	0 to 1

† Indicates worst to best.

†† Description for 5 dimension version.

* Composed of 24 “facets” within the 6 quality of life domains.

** Scoring for each “facet” or domain.

[1] SF-36 = Short Form 36-item questionnaire;

[2] SF-12 = Short Form 12-item questionnaire;

[3] EuroQOL = European Quality of Life questionnaire;

[4] NHP = Nottingham Health Profile;

[5] WHOQOL-100 = World Health Organization Quality of Life assessment instrument 100;

[6] MHIQ = McMasters Health Index Questionnaire

Table 2

Original development and validation studies for disease-specific questionnaires used in assessing functional status and/or HRQOL in symptomatic PAD patients.

Questionnaires	Authors & Year	Domains/Subscales	Items	† Scoring Range
[a] WIQ	Regensteiner et al 1990[66]	4	22	0–100
[b] CLAU-S	Finger et al 1995[87]	5	47	0–100
[c] PAVK-86	Heidrich et al 1995[119]	7	86	4-1
[d] VascuQOL	Morgan et al 2001[96]	5	25	1–7
[e] PAQ	Spertus et al 2004[82]	7	20	0–100
[f] SIP_{IC}	Gilson et al 1975[103] Bergner et al 1976[104] * Arfvidsson et al 1993[105]	*6	*12	*12-0
[g] ICQ	Chong et al 2002[107]	1	16	0–100

† Indicates worst to best

* Describes the SIP_{IC} version of the questionnaire

[a] WIQ = Walking Impairment Questionnaire;

[b] CLAU-S = Claudication Scale;

[c] PAVK-86 = Peripheral Artery Occlusive Disease 86-item questionnaire;

[d] VascuQOL = Vascular Quality of Life questionnaire;

[e] PAQ = Peripheral Artery Questionnaire;

[f] SIP_{IC} = Sickness Impact Profile – Intermittent Claudication;

[g] ICQ = Intermittent Claudication Questionnaire

Table 3

Functional status and/or HRQOL following exercise training for patients with IC.

Authors & Year (* sample size; interval)	Questionnaires	Type of training	Outcome
** Regensteiner et al 1996[76] (n = 21; 24 wks)	[a] WIQ	supervised exercise strength training non-exercise	supervised group improved WIQ & SF-20 scores, specifically the physical domains
Patterson et al 1997[120] (n = 38; 24 wks)	[1] SF-36	supervised exercise home-based exercise	improvement in physical function, pain & physical component scores for both groups
** Regensteiner et al 1997[79] (n = 20; 12 wks)	WIQ	supervised exercise unsupervised exercise	supervised group improved WIQ walking distance & speed scores & SF-20 physical functioning scores
Wullink et al 2001[77] (n = 24; 24 wks)	WIQ	† unsupervised exercise	pain, distance, speed & stair climbing domains improved but not significant
Nicolai et al 2009[78] (n = 91; 12 wks)	SF-36 [2] EuroQOL WIQ	supervised exercise	all WIQ domains improved; largest effect for SF-36 was pain & physical functioning; EuroQOL index improved
Nicolai et al 2010[75] (n = 252; 1 year)	SF-36 WIQ	supervised exercise †† supervised exercise unsupervised	physical summary score of SF-36 improved, no improvement in mental summary score; total WIQ scores improved

* Indicates final sample size for claudicants & final outcome assessment time point.

** Also employed SF-20 which was not discussed in this review.

† Employed additional coaching in the home-based setting but did not directly supervise exercise.

†† Provided an accelerometer to patients for additional feedback.

[1] SF-36 = Short Form 36-item questionnaire;

[2] EuroQOL = European Quality of Life questionnaire

[a] WIQ = Walking Impairment Questionnaire

Table 4

Functional status and/or HRQOL in symptomatic PAD patients following endovascular therapy and/or bypass surgery.

Authors & Year (* sample size; interval)	Questionnaires	Vascular Procedure	Outcomes
Regensteiner et al 1993[80] (n = 14; 12 wks)	[a] WIQ	bypass surgery	all domains improved
Cook et al 1996[33] (n = 29; 6 wks)	[1] EuroQOL	endovascular therapy	both EuroQOL total & [**] VAS scores improved
Cook & Galland 1997[34] (n = 24; 1 year)	EuroQOL	endovascular therapy	EuroQOL total & VAS scores improved, except VAS perceived health state score
Chetter et al 1998[35] (n = 117; 1 year)	[2] SF-36 EuroQOL	endovascular therapy	improved most domains, depending on site/severity of disease; no effect on psychological domains
[†] Bosch et al 1999[36] (n = 101; 2 years)	SF-36 EuroQOL	endovascular therapy	greatest effect in SF-36 physical functioning, physical role limitations & bodily pain; EuroQOL improved
[†] Bosch & Hunink 2000[37] (n = 72; 1 year)	SF-36 EuroQOL	endovascular therapy	improvement in all SF-36 domains; increase in EuroQOL mobility, usual activities, pain/discomfort domains
Klevsgard et al 2000[54] (n = 67; 24 wks)	[3] NHP	endovascular therapy bypass surgery	improved all domains except sex life
Klevsgard et al 2001[52] (n = 84; 1 year)	NHP	endovascular therapy bypass surgery	improvements in Part I scores except social isolation for successful endovascular therapy; improved Part II scores of pain, emotional reactions
Klevsgard et al 2002[53] (n = 40; 4 wks)	SF-36 NHP	endovascular therapy bypass surgery	[††] no improvement for SF-36 mental health or social functioning; no improvement for NHP social isolation, which was a zero value pre & post
Wann-Hansson et al 2004[55] (n = 38; 1 year)	SF-36 NHP	endovascular therapy bypass surgery	significant improvements in SF-36 bodily pain & physical functioning; no improvements in NHP scores
Spertus et al 2004[82] (n = 35; 6 wks)	SF-36 WIQ [b] PAQ	endovascular therapy	improvements in SF-36 physical, social domains & all WIQ & PAQ domains
Wann-Hansson et al 2005[49] (n = 51; 4 years)	NHP	endovascular therapy bypass surgery	total NHP score improved compared to baseline
Murphy et al 2005[81] (n = 35; 1 year)	SF-36 WIQ	endovascular therapy	SF-36 physical functioning, role physical, bodily pain, & vitality improved; all WIQ domains improved
Safley et al 2007[30] (n = 258; 1 year)	[4] SF-12 EuroQOL PAQ	endovascular therapy	improvements in SF-12 & EuroQOL physical scores; all PAQ scores improved except treatment satisfaction
Egberg et al 2010[38] (n = 41; 1 year)	EuroQOL [c] CLAU-S	endovascular therapy	EuroQOL total index score & all 5 dimensions of CLAU-S improved

[*] Indicates final sample size for claudicants & final outcome assessment time point.

[**] VAS = visual analogue scale

[†] Also used health utilities index, time tradeoff, standard gamble & rating scale instruments.

[††] Following successful revascularization.

[1] EuroQOL = European Quality of Life questionnaire;

[2] SF-36 = Short Form 36-item questionnaire;

[3] NHP = Nottingham Health Profile;

[4] SF-12 = Short Form 12-item questionnaire

[a] WIQ = Walking Impairment Questionnaire;

[b] PAQ = Peripheral Artery Questionnaire;

[c] CLAU-S = Claudication Scale

Table 5

Effects of pharmacological therapy on functional status and/or HRQOL in symptomatic PAD patients.

Authors & Year (* sample size; intervals)	Questionnaires	Medication	Outcomes
Creutzig et al 1997[93] (n = 93; 12 wks)	[1] SF-36 [a] PAVK-86	** PGE_1 – 50 μg	greatest enhancements for SF-36 domains physical function, pain & physical role limitations; pain & functional status most improved PAVK-86 domains
Money et al 1998[121] (n = 212; 16 wks)	SF-36 [b] WIQ	cilostazol – 100 mg placebo	improvement in SF-36 physical domains & WIQ walking speed & measures of walking difficulty compared to placebo
Beebe et al 1999[122] (n = 413; 24 wks)	SF-36 WIQ	cilostazol – 100 mg cilostazol – 50 mg placebo	physical health domains of SF-36 improved for both cilostazol groups compared to placebo; WIQ walking speed & distance better in both cilostazol groups
Hiatt et al 2001[123] (n = 155; 24 wks)	SF-36 WIQ	propionyl-L-carnitine – 6 mg placebo	propionyl-L-carnitine improved SF-36 domains of physical role functioning, bodily pain & health transition scores; also improved WIQ distance & speed scores
Strandness et al 2002[86] (n = 286; 24 wks)	SF-36 WIQ	cilostazol – 100 mg cilostazol – 50 mg placebo	time point analysis indicated improvements in all physical domains for cilostazol vs. placebo groups
Hiatt et al 2004[83] (n = 300; 24 wks)	SF-36 WIQ	† AT-1015 – 10 mg AT-1015 – 20 mg AT-1015 – 40 mg placebo	no differences among SF-36 & WIQ scores between groups
Hiatt et al 2004[84] (n = 328; 1 year)	WIQ	avasimibe – 50 mg avasimibe – 250 mg avasimibe – 750 mg placebo	greatest enhancement in WIQ distance score seen in group receiving 50 mg dosage
Creager et al 2008[124] (n = 214; 24 wks)	SF-36 WIQ	iloprost – 50 μg iloprost – 100 μg iloprost – 150 μg pentoxifylline – 400 mg placebo	no differences between groups for SF-36; stair-climbing only WIQ domain to improve

* Indicates final sample size of claudicants & final outcome assessment time point.

** PGE_1 = prostaglandin E_1.

† 5-HT2A serotonin receptor antagonist.

[1] SF-36 = Short Form 36-item questionnaire

[a] PAVK-86 = Peripheral Artery Occlusive Disease 86-item questionnaire;

[b] WIQ = Walking Impairment Questionnaire

Table 6

Studies employing general and disease-specific questionnaires to assess functional status and/or HRQOL in symptomatic PAD patients within multiple interventions.

Authors & Year (* sample size; interval)	Questionnaires	Interventions	Most effective intervention
Currie et al 1995[125] (n = 186; 12 wks)	[1] SF-36	endovascular therapy bypass surgery unsupervised exercise	endovascular therapy & bypass surgery
Whyman et al 1996[51] (n = 62; 24 wks)	[2] NHP	endovascular & medical therapy medical therapy	endovascular & medical therapy
Whyman et al 1997[50] (n = 62; 2 years)	NHP	endovascular & medical therapy medical therapy	no differences between groups
de Vries et al 2005[39] (n = 348; 24 wks)	SF-36 [3] EuroQOL [a] VascuQOL	endovascular therapy bypass surgery medical therapy	did not distinguish HRQOL between groups
** Kakkos et al 2005[109] (n = 26; 1 year)	SF-36 [b] WIQ [c] ICQ	supervised exercise unsupervised exercise † IPC	IPC & supervised exercise
Imfeld et al 2006[95] (n = 55; 24 wks)	SF-36 WIQ [d] PAVK-86	supervised exercise supervised exercise & †† medication home-based exercise	inconclusive
Mehta et al 2006[40] (n = 70; 24 wks)	SF-36 EuroQOL VascuQOL [e] SIP_{IC} [f] CLAU-S	endovascular therapy medical therapy	endovascular therapy
Nylaende et al 2007[91] (n = 48; 2 years)	SF-36 ††† EuroQOL CLAU-S	endovascular & medical therapy medical therapy	endovascular & medical therapy
Spronk et al 2008[41] (n = 150; 1 year)	SF-36 EuroQOL	endovascular therapy supervised exercise	supervised exercise
Mazari et al 2010[27] (n = 157; 12 wks)	SF-36 VascuQOL	endovascular therapy χ supervised exercise combined group	combined group

* Indicates final sample size for claudicants & final outcome assessment time point.

** Six month active treatment time point described; outcomes at 1 year time point also examined but unclear how many patients analyzed.

† IPC = intermittent pneumatic compression.

†† 75 mg of clopidogrel once daily.

††† Used the visual analogue scale (VAS).

χ Patients' completed a circuit exercise program.

[1] SF-36 = Short Form 36-item questionnaire;

[2] NHP = Nottingham Health Profile;

[3] EuroQOL = European Quality of Life questionnaire

[a] VascuQOL = Vascular Quality of Life questionnaire;

[b] WIQ = Walking Impairment Questionnaire;

[c] ICQ = Intermittent Claudication Questionnaire;

[d] PAVK-86 = Peripheral Artery Occlusive Disease 86-item questionnaire;

[e] SIP_{IC} = Sickness Impact Profile – Intermittent Claudication;

[f] CLAU-S = Claudication Scale