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# Gender Disparities in Disease-specific Health Status in Postoperative Patients with Peripheral Arterial Disease

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## WHAT THIS PAPER ADDS

- Gender differences in perceived health status do exist in postoperative PAD patients. Men and women experienced a disparate change in overall health status from 3- to 5-year follow-up. Attention should be paid to gender disparities in postoperative PAD patients, since men and women seem to experience different levels of HS over time.

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ABSTRACT

*Objectives:* To investigate gender disparities in disease-specific health status (HS), 3- and 5-year post-intervention in peripheral arterial disease (PAD) patients.
*Design:* Cohort study.
*Methods:* Data of 711 consecutively enrolled vascular surgery patients were collected in 11 hospitals in The Netherlands in 2004. HS was assessed with the Peripheral Artery Questionnaire (PAQ). Our sample included patients for whom it was possible to calculate a PAQ summary score at 3- and 5-year follow-up ($n = 351$).
*Results:* Women experienced worse physical health (52.1 vs. 62.0, $P = 0.012$), greater disability (64.5 vs. 71.1, $P = 0.026$), and worse overall HS (58.1 vs. 66.7, $P = 0.007$) at 3-year follow-up than men. At 5-year follow-up, however, male and female patients reported similar levels of HS. Mean changes in overall HS from 3- to 5-year follow-up were significantly different for men and women (−4.12 vs. 1.69, $P = 0.014$). In male patients, overall HS was significantly lower at 5-year follow-up compared to the 3-year follow-up (66.7 vs. 62.6, $P = 0.001$). In female patients, there was no significant difference (58.1 vs. 59.8, $P = 0.393$).
*Conclusions:* Men and women experience different levels of HS over time. Attention should be paid to gender disparities in postoperative PAD patients.


Peripheral arterial disease (PAD) is a progressive athero-thrombotic disease that has serious systemic consequences.[1] As a result, PAD is associated with increased all-cause and cardiovascular mortality.[2] This progressive atherosclerotic disease currently affects approximately 16% of the general population aged 55 years and older.[1]

Patients with PAD are faced not only with an increased risk of mortality, but also with disability and reduced health status (HS). Patient-reported outcomes, such as HS, are gaining increasing recognition as indicators of the quality of care.[3] Although both generic and disease-specific measures are being used for this purpose, disease-specific measures are more sensitive to detect small but clinically meaningful differences in outcome as they tap into patient limitations specific to the disease.[4] In patients with PAD, poor health-related quality of life (HRQoL) has been shown to

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predict mortality independent of indicators of disease severity.[5] An increasing number of studies in PAD patients are also focussing on patient-reported outcomes. Particularly, patients who are older – have more severe disease, experience more pain and have more co-morbidities – are at risk for poor health status and HRQoL.[6–12] However, patients undergoing vascular interventions seem to experience improvements in HS and HRQoL.[13–20]

Given that arterial disease in terms of anatomy, physiology and clinical manifestations has shown to differ according to gender,[21] one might also expect that male and female PAD patients experience different levels of HS and HRQoL. A paucity of studies has examined gender disparities in patient-centred outcomes in PAD. Some studies reported worse HS and HRQoL in women as compared to men,[22–24] while others found the opposite result.[25] However, none of these studies examined potential gender differences in HS or HRQoL after vascular repair. Given findings from other vascular patient populations showing more postoperative impairment in HS and HRQoL after surgical intervention in women,[26–29] it might be expected that female PAD patients experience worse HS and HRQoL after vascular repair.

The majority of studies examining differences in HS and HRQoL in cardiovascular disease populations tend to have focussed on differences in mean scores between groups rather than intra-individual changes, which masks changes within individuals.[30] A distinct advantage of studying intra-individual changes over time is that it provides information about patients who experience a clinically meaningful decline in HS or HRQoL over time, which might indicate that their treatment regimen needs to be adjusted in order to prevent a further decline in HS and in order to enhance secondary prevention.

In the current study, we investigated gender disparities in disease-specific HS, measured with the Peripheral Artery Questionnaire (PAQ), 3- and 5-years post-intervention in a consecutive cohort of PAD patients undergoing vascular surgery, using both a between-group and an intra-individual approach.

## Methods

### *Design and study population*

This study was based on data from 711 PAD patients enrolled at 11 hospitals across The Netherlands between May and December 2004, who were followed up for 5 years after vascular surgery. The study was part of the Dutch Euro Heart Survey Programme. All patients were seen at the participating vascular surgery departments and were undergoing non-cardiac vascular surgery (endovascular or open procedures). Endovascular procedures included aortic endograft procedures and peripheral angioplasties with or without stenting. Open procedures included elective abdominal aortic surgery, carotid endarterectomy or infrainguinal arterial reconstruction. Local ethics committees of the involved centres all approved the study, and all patients provided informed consent for follow-up contact. After 3 and 5 years, information on the patient's vital status was obtained from the civil registries. All survivors were contacted to fill in the PAQ. Our sample only included PAD patients for whom it was possible to calculate a PAQ summary score at 3- and 5-year follow-up.

### *Measures*

#### *Demographic and clinical variables*

Information on demographics and the medical history was abstracted from patients' medical records and questionnaires at the time of procedure. Information included age, ischaemic heart disease (IHD), angina pectoris, myocardial infarction, previous revascularisation, heart failure, stroke or trans-ischaemic attack (TIA), obesity, hypertension, diabetes mellitus, renal insufficiency, chronic obstructive pulmonary disease (COPD), endovascular procedure, open procedure, aspirin, beta-blockers and statins.

#### *Disease-specific HS*

To measure disease-specific HS, the Dutch translation of the disease-specific PAQ was used.[31] The PAQ quantifies physical limitations, symptoms (frequency, severity and recent change over time), quality of life, social function and treatment satisfaction.[32] The PAQ has shown to be a reliable, valid and responsive measure with good clinical validity.[31,32] The instrument consists of 20 items, with one item identifying the most symptomatic leg and the other items rated on variable Likert scales with equidistant response gradations. The Dutch version of the PAQ is composed of three overarching domains: physical limitation, perceived disability and treatment satisfaction.[31] In this study, treatment satisfaction was left out, because it is not included in the summary score. Since the response categories are different across items, standardised scoring algorithms are applied to obtain domain scores ranging from 0 to 100, with higher scores indicating better HS. A summary score is calculated as the average of the physical limitation and perceived disability domain scores.

Change scores on the PAQ domains and the PAQ summary score are defined as the difference between the 3- and 5-year follow-up scores. A change of 8 points on the 100-point PAQ domain scales and summary scale was used to define a clinically meaningful change. This 8% change was considered to represent a clinically meaningful difference according to Sloan et al.,[33] who concluded that a medium effect size corresponded to a change of 8% of the range of the instrument used to assess HS. In addition, Cohen defined a medium effect size as 50% of the standard deviation (SD) of an instrument, which is 16.7% of any scale on the basis of the fact that 99% of observations fall within 3 SDs of the mean. Change scores of $\geq -8$ points were defined as a clinically meaningful decline, and all other change scores as 'not declined'.

### *Statistical analysis*

Baseline demographic and clinical characteristics for male and female patients were compared using Pearson's chi-square and Student's *t*-tests. Absolute scores for Physical Limitation, Perceived Disability and PAQ summary at 3- and 5-year follow-up and change scores from 3- to 5-year follow-up are listed as means with 95% confidence intervals (CI)s for male and female patients separately. Comparisons of the mean scores between male and female patients at 3- and 5-year follow-up and the mean change scores from 3- to 5-year follow-up were performed using Student's *t*-tests for independent samples. To compare mean Physical Limitation, Perceived Disability and PAQ summary scores from 3- to 5-year follow-up within both sexes, Student's *t*-tests for paired samples were used. Furthermore, the proportion (%) of patients that reported clinically meaningful declines ('declined') and the proportion that did not make clinically meaningful declines ('not declined') on Physical Limitation, Perceived Disability and PAQ summary are shown for both sexes separately. Comparisons of the proportion of male and female patients that were classified as 'declined' and 'not declined' on Physical Limitation, Perceived Disability and PAQ summary were made using Pearson's chi-square tests. General linear mixed model (GLMM) analyses were used to analyse changes in overall HS over time, with gender as a factor and all other baseline characteristics as covariates. This type of statistical analysis was chosen because it models group means as fixed effects while simultaneously modelling individual subject variables as random effects.[34] The

fixed effects were follow-up, gender, age, all cardiovascular and clinical risk factors, type of procedure and the interaction between follow-up and gender. An autoregressive structure was used. Sensitivity analyses were performed to adjust for the entity of PAD (i.e., peripheral arterial occlusive disease of the lower limbs, abdominal aortic aneurysms and carotid stenosis). For all tests, a *P*-value $<0.05$ was considered significant. All statistical analyses were performed using SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA).

## Results

### *Responders versus non-responders*

The original sample consisted of 711 PAD patients undergoing vascular surgery at baseline (Fig. 1). This sample consisted of 496 men (69.8%) and 215 women (30.2%). After 5 years of follow-up, 200 patients had died, of whom 144 (72.0%) were male and 56 (28%) were female. Twenty-five patients (13 men, 12 women) were lost to follow-up. All 486 surviving patients were sent questionnaires, of which 390 responded (80.2% response rate). The final sample included 351 patients (72.2%), for whom both PAQ summary scores (at 3- and 5-year follow-up) could be computed. This sample consisted of 251 men (71.5%) and 100 women (28.5%). To investigate response bias, responders were compared with non-responders. No systematic differences were found on baseline characteristics.

### *Baseline characteristics*

Baseline characteristics of the total sample and stratified by gender are listed in Table 1. The mean age of patients was $64.8 \pm 9.6$ years. Men had a significantly higher prevalence of IHD (31.9% vs. 16.0%, $P = 0.003$), myocardial infarction (17.5% vs. 8.0%, $P = 0.023$) and previous revascularisation (18.7% vs. 7.0%, $P = 0.006$) compared to women. In addition, men more often underwent an open vascular procedure (53.8% vs. 30.0%, $P < 0.001$) compared to women.

### *HS 3- and 5-years post-intervention*

The mean Physical Limitation, Perceived Disability and PAQ summary score at 3- and 5-years post-intervention are shown in Table 2 and Fig. 2A and B. Women experienced poorer physical health (52.1 vs. 62.0, $P = 0.012$), greater perceived disability (64.5 vs. 71.1, $P = 0.026$) and worse overall HS (58.1 vs. 66.7, $P = 0.007$) at 3-year follow-up as compared with men. At 5-year follow-up, however, there were no statistically significant differences between men and women on HS. Generally, the total cohort of PAD patients experienced poorer physical health (55.7 vs. 59.1, $P = 0.005$) and overall HS (61.8 vs. 64.3, $P = 0.022$) at 5-year follow-up compared to 3-year follow-up. Male patients reported not only poorer physical health (56.9 vs. 62.0, $P = 0.002$) and overall HS (62.6 vs. 66.7, $P = 0.001$), but also greater perceived disability (68.4 vs. 71.1, $P = 0.032$) at 5-year follow-up compared to 3-year follow-up.

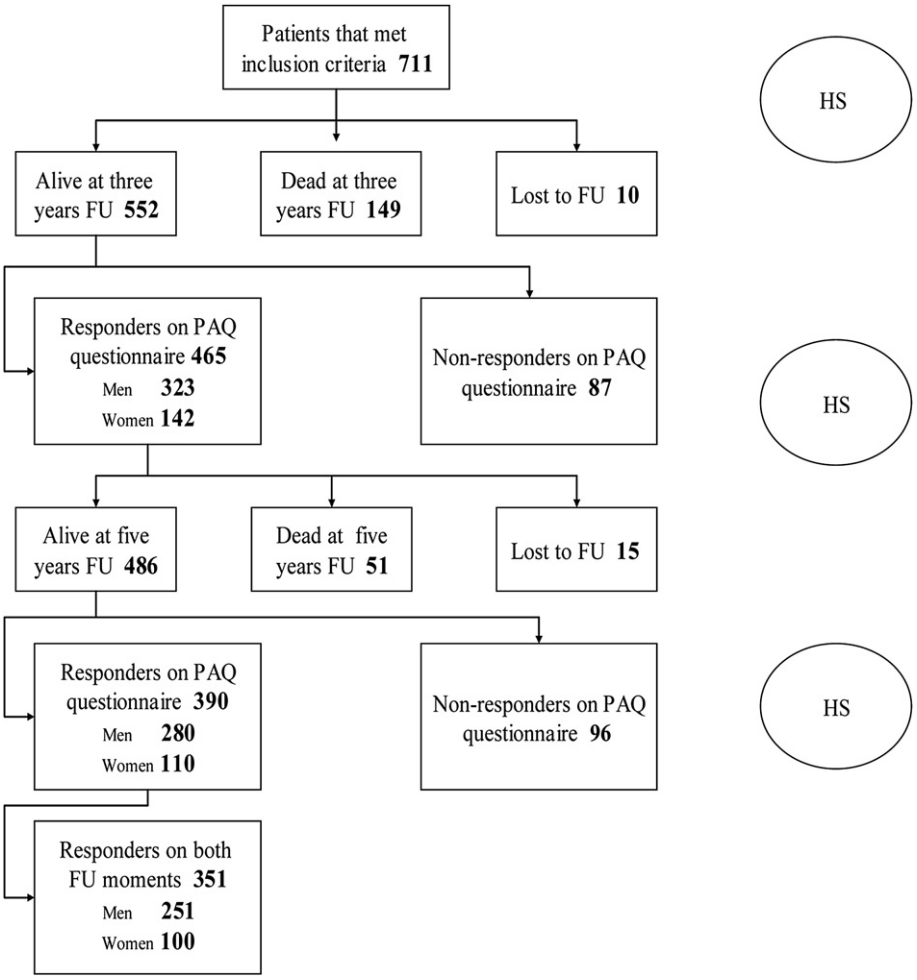


**Figure 1.** Flowchart *FU*, follow-up.

**Table 1**
Baseline characteristics for the total population and stratified by gender.[a]

| | Total | Men | Women | *P*-value |
|---|---|---|---|---|
| *n* | 351 (100) | 251 (71.5) | 100 (28.5) | |
| Demographics | | | | |
| Mean age (±SD) | 64.8 (9.6) | 65.1 (9.0) | 63.9 (11.0) | 0.331 |
| Cardiovascular history | | | | |
| IHD | 96 (27.4) | 80 (31.9) | 16 (16.0) | 0.003 |
| Angina pectoris | 52 (14.8) | 41 (16.3) | 11 (11.0) | 0.204 |
| Myocardial infarction | 52 (14.8) | 44 (17.5) | 8 (8.0) | 0.023 |
| Previous revascularization | 54 (15.4) | 47 (18.7) | 7 (7.0) | 0.006 |
| Heart failure | 8 (2.3) | 4 (1.6) | 4 (4.0) | 0.173 |
| Stroke or TIA | 46 (13.1) | 36 (14.3) | 10 (10.0) | 0.277 |
| Clinical risk factors | | | | |
| Obesity | 39 (11.1) | 26 (10.4) | 13 (13.0) | 0.477 |
| Hypertension | 135 (38.5) | 101 (40.2) | 34 (34.0) | 0.278 |
| Diabetes mellitus | 62 (17.7) | 47 (18.7) | 15 (15.0) | 0.409 |
| Renal insufficiency | 18 (5.1) | 15 (6.0) | 3 (3.0) | 0.254 |
| COPD | 34 (9.7) | 27 (10.8) | 7 (7.0) | 0.283 |
| Surgical procedure | | | | |
| Endovascular | 200 (57.0) | 125 (49.8) | 75 (75.0) | <0.001 |
| Open | 165 (47.0) | 135 (53.8) | 30 (30.0) | <0.001 |
| Medication use | | | | |
| Aspirin | 263 (74.9) | 187 (74.5) | 76 (76.0) | 0.770 |
| Beta-blockers | 175 (49.9) | 131 (52.2) | 44 (44.0) | 0.166 |
| Statins | 218 (62.1) | 159 (63.3) | 59 (59.0) | 0.449 |

*n*, number; SD, standard deviation; IHD, ischaemic heart disease; TIA, transient ischaemic attack; COPD, chronic obstructive pulmonary disease.
[a] Presented as *n* (%), unless otherwise indicated.

On the contrary, female patients experienced similar levels of HS at both follow-up moments.

*Changes in HS*

The mean change scores on Physical Limitation, Perceived Disability and PAQ summary from 3- to 5-years post-intervention are shown in Table 3 and Fig. 3. Mean changes in overall HS from 3- to 5-year follow-up were significantly different for men and women (−4.12 vs. 1.69, $P = 0.014$).

Furthermore, a higher but non-significant percentage of men compared to women experienced a clinically meaningful increase in perceived disability (31.5% vs. 23.0%, $P = 0.115$) and a decline in overall HS (35.5% vs. 26.0%, $P = 0.088$) over time, as indicated by a change of ≥−8 points on Perceived Disability and PAQ summary from 3- to 5-year follow-up. A similar percentage of men and women experienced a clinically meaningful decline in physical health from 3- to 5-year follow-up ($P = 0.906$).

GLMM analysis showed a significant interaction effect of follow-up moment × gender for overall HS ($\beta = -5.81$, $P = 0.014$), which signifies that male and female patients experienced disparate changes in overall HS from 3- to 5-years post-intervention. Separate analyses for male and female patients were therefore conducted (Table 4). In male patients, analysis showed that overall HS was significantly lower at 5-year follow-up compared to the 3-year follow-up ($\beta = -4.12$, $P = 0.001$). Moreover, older men reported lower levels of HS than younger men ($\beta = -0.43$, $P = 0.017$). Likewise, male patients with concomitant diabetes experienced worse HS than male patients without diabetes ($\beta = -8.30$, $P = 0.038$). In female patients, the effect of follow-up moment was non-significant, which indicates that women reported similar levels of HS at 3- and 5-year follow-up. However, overall HS was lower for older women than for younger women ($\beta = -0.53$, $P = 0.018$). Sensitivity analyses adjusting for the entity of PAD showed similar results. In male patients with peripheral arterial occlusive disease of the lower limbs, overall HS was predicted by follow-up moment ($\beta = -4.22$, $P = 0.010$), age ($\beta = -0.64$, $P = 0.004$) and IHD ($\beta = -8.38$, $P = 0.049$). The effect of diabetes was non-significant. In female patients with peripheral arterial occlusive disease of the lower limbs, overall HS was predicted by age ($\beta = -0.60$, $P = 0.013$) and diabetes ($\beta = -16.25$, $P = 0.033$).

**Table 2**
PAQ domain and summary scores 3- and 5-years post-intervention for male and female PAD patients.

| | Total *n* = 351 | Men *n* = 251 | Women *n* = 100 | *P*-value |
|---|---|---|---|---|
| | Mean (95% CI) | Mean (95% CI) | Mean (95% CI) | |
| *3-years follow-up*[a] | | | | |
| Physical Limitation | | | | |
| Score | 59.12 (53.61–64.63) | 61.98 (55.44–68.52) | 52.13 (42.19–62.07) | 0.012 |
| Perceived Disability | | | | |
| Score | 69.24 (65.04–73.44) | 71.09 (66.21–75.97) | 64.46 (56.40–72.52) | 0.026 |
| Summary Score | | | | |
| Score | 64.28 (59.72–68.84) | 66.74 (61.38–72.10) | 58.12 (49.72–66.52) | 0.007 |
| *5-years follow-up*[b] | | | | |
| Physical Limitation | | | | |
| Score | 55.68 (50.40–60.96)[c] | 56.85 (50.55–63.15)[c] | 52.57 (42.91–62.23) | 0.273 |
| Perceived Disability | | | | |
| Score | 67.20 (63.08–71.32) | 68.41 (63.54–73.28)[c] | 64.15 (56.50–71.80) | 0.143 |
| Summary Score | | | | |
| Score | 61.82 (57.37–66.27)[c] | 62.62 (57.30–67.94)[c] | 59.81 (51.67–67.95) | 0.369 |

*n*, number; 95% CI, 95% confidence interval; PAQ, peripheral arterial questionnaire.
[a] Missing scores on PAQ ranging from 0 to 7%.
[b] Missing scores on PAQ ranging from 0 to 11%.
[c] Significant decrease in PAQ domain or summary score from 3- to 5-years post-intervention.

## Discussion

To our knowledge, this is the first prospective study that focussed on gender disparities in disease-specific HS in a consecutive cohort of postoperative PAD patients. Generally, women experienced poorer HS as compared to men at 3-year follow-up, while at 5-year follow-up male and female patients reported similar levels of HS. Moreover, a higher but non-significant percentage of men compared to women experienced a clinically meaningful increase in perceived disability and a decline in overall HS from 3- to 5-years post-intervention. Furthermore, men and women experienced a disparate change in overall HS from 3- to 5-year follow-up.

At 3-years post-intervention, women reported poorer HS as compared to men, with differences in physical health, perceived disability and overall HS being statistically significant and clinically relevant. This result is consistent with an earlier finding, demonstrating that female PAD patients are more likely to report poor HRQoL in the long term.[24] A number of studies including other vascular patient populations also found female sex to be associated with inferior postoperative HS.[35–38] In our study, however, at 5-years post-intervention male and female patients experienced similar levels of HS. While women reported comparable HS at both follow-up moments, men rated their HS lower at 5-years post-intervention. The reason for this result is not well understood, but it may be attributed to the similar age of patients at time of treatment and the different life expectancies for men and women at the age of about 65.

Investigating group changes showed that women barely perceived a change in overall HS from 3- to 5-year follow-up, while in the same period of time men experienced a decline. However, clinically meaningful individual changes cannot be extracted from group changes, since one cannot assume that each individual experienced the group mean differential.[30] Therefore, we also defined intra-individual HS changes in male and female patients from 3- to 5-year follow-up. Our results showed that a higher but

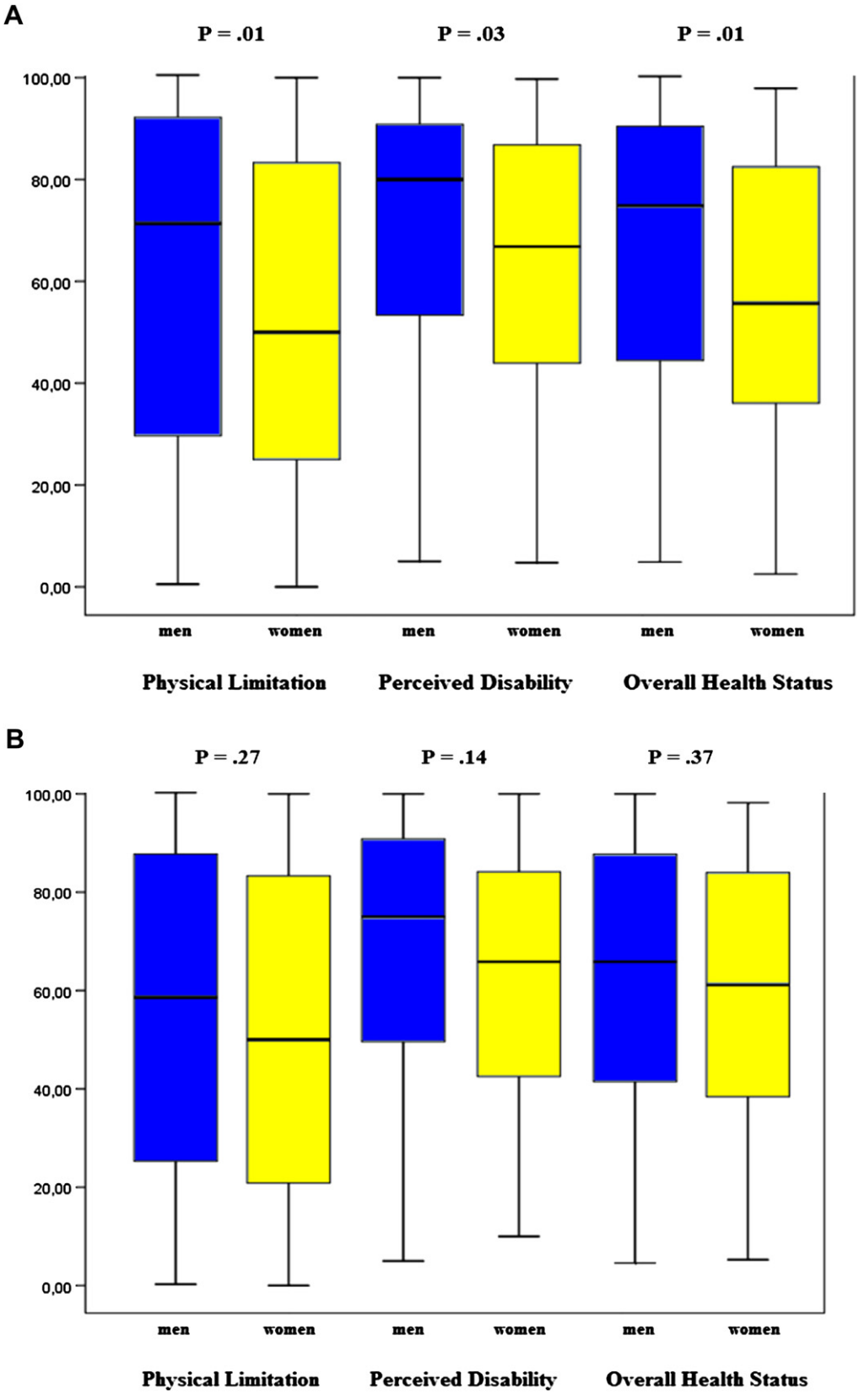


**Figure 2.** (A) Mean scores on the PAQ domains and summary for male and female PAD patients at 3-years follow-up. (B) Mean scores on the PAQ domains and summary for male and female PAD patients at 5-years follow-up.

**Table 3**
Mean change scores on PAQ domains and summary for male and female PAD patients and proportions stratified by gender and 'declined' vs 'not declined'.[a]

| PAQ | Change in PAQ scores[b,c] | | | |
|---|---|---|---|---|
| | Total $n = 351$ | Men $n = 251$ | Women $n = 100$ | *P*-value |
| | Mean (95% CI) | Mean (95% CI) | Mean (95% CI) | |
| Physical Limitation | | | | |
| Score | −3.47 (−7.11 to −0.17) | −4.40 (−8.59 to −0.21) | −1.15 (−8.38 to 6.08) | 0.235 |
| *Declined* | 34.5 (29.7–39.6) | 34.7 (29.0–40.7) | 34.0 (25.4–43.7) | 0.906[d] |
| *Not declined* | 65.5 (60.4–71.0) | 65.3 (59.3–71.1) | 66.0 (56.3–74.6) | |
| Perceived Disability | | | | |
| Score | −1.81 (−4.95 to 1.33) | −2.59 (−6.35 to 1.17) | 0.21 (−5.46 to 5.88) | 0.215 |
| *Declined* | 29.1 (24.6–34.0) | 31.5 (26.0–37.5) | 23.0 (15.8–32.2) | 0.115 |
| *Not declined* | 70.9 (66.0–75.5) | 68.5 (62.5–74.0) | 77.0 (67.8–84.2) | |
| Summary Score | | | | |
| Score | −2.46 (−5.84 to 0.92) | −4.12 (−8.10 to −0.14) | 1.69 (−4.55 to 7.93) | 0.014 |
| *Declined* | 32.8 (28.1–37.8) | 35.5 (29.8–41.6) | 26.0 (18.4–35.4) | 0.088 |
| *Not declined* | 67.2 (62.2–71.9) | 64.5 (58.4–70.2) | 74.0 (64.6–81.6) | |

*n*, number; 95% CI, 95% confidence interval; PAQ, peripheral arterial questionnaire.
[a] Presented as % (95% CI), unless otherwise indicated.
[b] The change in PAQ domain and summary scores from 3- to 5-year follow-up (5-years post-intervention minus 3-years post-intervention scores). *SD,* standard deviation; *Declined,* number and percentage of patients with a change score of $\leq -8$; *Not declined,* number and percentage of patients with a change score of $> -8$.
[c] Missing change scores on PAQ ranging from 0 to 13%.
[d] To test whether male and female patients have different outcomes (declined vs not declined) on PAQ domains and summary.

non-significant percentage of men compared to women experienced a clinically meaningful increase in perceived disability and a decline in overall HS from 3- to 5-year follow-up. Additional analyses demonstrated that male and female patients did perceive a disparate change in overall HS from 3- to 5-years post-intervention. Whereas postoperative HS in men was predicted by follow-up moment (worse HS at 5-years post-intervention), this was not the case for women. Older age was predictive of worse HS in both sexes and concomitant diabetes predicted lower levels of HS in male PAD patients and female patients with peripheral arterial occlusive disease of the lower limbs. Furthermore, IHD was predictive of worse HS in male patients with peripheral arterial occlusive disease of the lower limbs. These results are consistent with previous findings, demonstrating that PAD patients who are older and those with co-morbid diabetes and IHD are at greater risk of experiencing lower levels of HS and HRQoL.[10,12,39–41] The aforementioned results demonstrate that it is necessary to investigate intra-individual changes in HS in addition to group mean changes, since it yields valuable information for clinical practice that cannot be extracted from between-group comparisons.

The findings of the current study should be interpreted with some caution. First, we had no information on HS at baseline. Consequently, we do not know whether male and female patients already displayed differences in HS prior to vascular surgery.

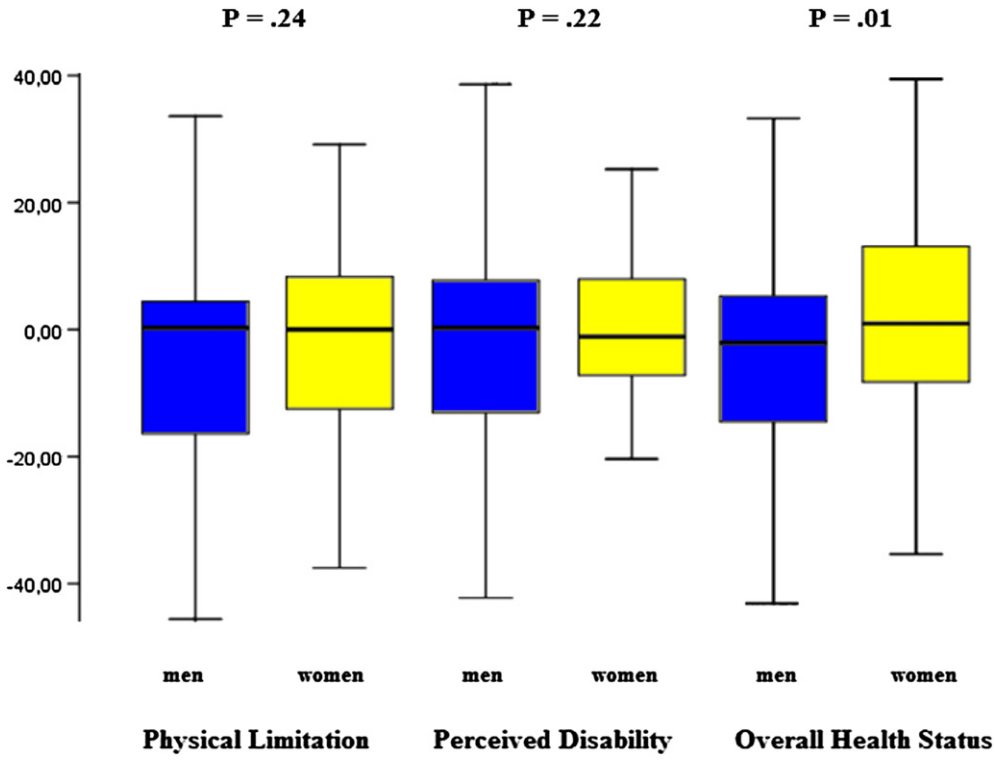


**Figure 3.** Mean PAQ domain and summary change scores for male and female PAD patients. Negative change scores signify a decline in HS from 3- to 5-year follow-up.

**Table 4**
General linear mixed model effects for PAQ summary.

| Effect | Men | Women | Men | Women |
|---|---|---|---|---|
| | $\beta$ (95% CI) | | *P*-value | |
| Intercept | 39.66 (−3.30 to 82.61) | 50.10 (−7.34 to 107.54) | 0.070 | 0.087 |
| Follow-up | 4.12 (1.64–6.60) | −1.69 (−5.61 to 2.23) | 0.001 | 0.393 |
| Age | −0.43 (−0.78 to −0.08) | −0.53 (−0.96 to −0.09) | 0.017 | 0.018 |
| IHD | 6.10 (−.059 to 12.78) | 5.52 (−9.78 to 20.82) | 0.074 | 0.476 |
| Heart failure | 13.72 (−10.12 to 37.57) | 10.74 (−16.69 to 38.18) | 0.258 | 0.439 |
| Stroke or TIA | 8.30 (−0.19 to 16.78) | −9.55 (−28.93 to 9.83) | 0.055 | 0.330 |
| Obesity | 6.72 (−3.45 to 16.89) | 9.93 (−6.11 to 25.97) | 0.194 | 0.222 |
| Hypertension | −4.75 (−11.09 to 1.59) | 7.16 (−3.96 to 18.28) | 0.142 | 0.204 |
| Diabetes | 8.30 (0.46–16.14) | 10.29 (−3.87 to 24.44) | 0.038 | 0.152 |
| Renal insufficiency | 10.63 (−1.88 to 23.15) | 16.05 (−13.19 to 45.29) | 0.096 | 0.278 |
| COPD | 5.58 (−4.17 to 15.34) | −0.77 (−21.18 to 19.64) | 0.261 | 0.941 |
| Endo | 2.53 (−3.58 to 8.64) | 0.29 (−13.23 to 13.81) | 0.416 | 0.966 |

IHD, ischaemic heart disease; TIA, transient ischaemic attack; COPD, chronic obstructive pulmonary disease; Endo = type of intervention.

Furthermore, we were not able to define intra-individual changes from pre- to post-intervention. Second, since participants who completed HS questionnaires at 3- and 5-year follow-up probably comprise a relatively healthy subpopulation, our findings might not generalise to all PAD patients. Death might have led to a selection bias, with the possibility that these patients would have experienced poorer HS, given that HS has proven to be an independent predictor of prognosis in PAD patients.[5]

The study also has several strengths. To measure HS we used the PAQ, a disease-specific instrument. As it taps into limitations specific to PAD, it is a sensitive measure with respect to detecting small but clinically meaningful differences in HS.[4] In addition, besides defining group mean changes, we examined intra-individual changes by determining the percentage of male and female patients who experienced a clinically meaningful decline in HS from 3- to 5-year follow-up. Moreover, we conducted GLMM analyses that acknowledge both group and individual differences. Furthermore, we focussed on gender disparities in perceived HS, which is of clinical importance since arterial disease in terms of anatomy, physiology and clinical manifestations has shown to differ according to sex.[21]

In conclusion, this study shows that gender differences in perceived HS do exist in postoperative PAD patients. Future studies are warranted to replicate the findings of the current study. Furthermore, we encourage other researchers to examine intra-individual changes in HS in addition to group mean changes, as it allows us to get a better estimate of the likelihood that patients will benefit from a vascular intervention. Finally, attention should be paid to gender disparities in postoperative PAD patients, since men and women seem to experience different levels of HS over time.

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## Conflicts of Interest

None.

## References

1 Stehouwer CD, Clement D, Davidson C, Diehm C, Elte JW, Lambert M, et al. Peripheral arterial disease: a growing problem for the internist. *Eur J Intern Med* 2009 Mar;**20**(2):132–8.
2 Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med* 1992 Feb 6;**326**(6):381–6.
3 Spertus JA. Evolving applications for patient-centered health status measures. *Circulation* 2008 Nov 11;**118**(20):2103–10.
4 de Vries M, Ouwendijk R, Kessels AG, de Haan MW, Flobbe K, Hunink MG, 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 Feb;**41**(2):261–8.
5 Issa SM, Hoeks SE, Scholte op Reimer WJ, Van Gestel YR, Lenzen MJ, Verhagen HJ, et al. Health-related quality of life predicts long-term survival in patients with peripheral artery disease. *Vasc Med* 2010 Jun;**15**(3):163–9.
6 Treat-Jacobson D, Halverson SL, Ratchford A, Regensteiner JG, Lindquist R, Hirsch AT. A patient-derived perspective of health-related quality of life with peripheral arterial disease. *J Nurs Scholarsh* 2002;**34**(1):55–60.
7 Ponte E, Cattinelli S. Quality of life in a group of patients with intermittent claudication. *Angiology* 1996 Mar;**47**(3):247–51.
8 de Graaff JC, Ubbink DT, Kools EI, Chamuleau SA, Jacobs MJ. The impact of peripheral and coronary artery disease on health-related quality of life. *Ann Vasc Surg* 2002 Jul;**16**(4):495–500.
9 Breek JC, Hamming JF, De Vries J, van Berge Henegouwen DP, van Heck GL. The impact of walking impairment, cardiovascular risk factors, and comorbidity on quality of life in patients with intermittent claudication. *J Vasc Surg* 2002 Jul;**36**(1):94–9.
10 Holtzman J, Caldwell M, Walvatne C, Kane R. Long-term functional status and quality of life after lower extremity revascularization. *J Vasc Surg* 1999 Mar;**29**(3):395–402.
11 Feinglass J, Morasch M, McCarthy WJ. Measures of success and health-related quality of life in lower-extremity vascular surgery. *Annu Rev Med* 2000;**51**:101–13.
12 Slovacek L, Slovakova B, Chovanec V, Vackova P, Kaslikova M, Bohutinska H, et al. The effect of selected health, demographic and psychosocial aspects on quality of life in patients with peripheral arterial occlusive disease – a prospective analysis. *Acta Med (Hradec Kralove)* 2007;**50**(2):125–7.
13 Dick F, Grobety V, Immer FF, Do DD, Savolainen H, Carrel TP, et al. Outcome and quality of life in patients treated for abdominal aortic aneurysms: a single center experience. *World J Surg* 2008 Jun;**32**(6):987–94.
14 Pell JP, Lee AJ. Impact of angioplasty and arterial reconstructive surgery on the quality of life of claudicants. The Scottish Vascular Audit Group. *Scott Med J* 1997 Apr;**42**(2):47–8.
15 Bosch JL, van der Graaf Y, Hunink MG. Health-related quality of life after angioplasty and stent placement in patients with iliac artery occlusive disease: results of a randomized controlled clinical trial. The Dutch Iliac Stent Trial Study Group. *Circulation* 1999 Jun 22;**99**(24):3155–60.
16 Safley DM, House JA, Laster SB, Daniel WC, Spertus JA, Marso SP. Quantifying improvement in symptoms, functioning, and quality of life after peripheral endovascular revascularization. *Circulation* 2007 Feb 6;**115**(5):569–75.
17 Cassar K, Bachoo P, Brittenden J. The effect of peripheral percutaneous transluminal angioplasty on quality of life in patients with intermittent claudication. *Eur J Vasc Endovasc Surg* 2003 Aug;**26**(2):130–6.
18 Slovacek L, Slovackova B, Chovanec V. The effect of femoral and popliteal percutaneous transluminal balloon angioplasty on patients' quality of life. *Sao Paulo Med J* 2007 Jul 5;**125**(4):250–2.
19 Aquarius AE, Denollet J, de Vries J, Hamming JF. Poor health-related quality of life in patients with peripheral arterial disease: type D personality and severity of peripheral arterial disease as independent predictors. *J Vasc Surg* 2007 Sep;**46**(3):507–12.
20 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 Mar;**41**(3):436–42.
21 Vouyouka AG, Egorova NN, Salloum A, Kleinman L, Marin M, Faries PL, et al. Lessons learned from the analysis of gender effect on risk factors and procedural outcomes of lower extremity arterial disease. *J Vasc Surg* 2010 Jul 29.
22 Collins TC, Suarez-Almazor M, Bush RL, Petersen NJ. Gender and peripheral arterial disease. *J Am Board Fam Med* 2006 Mar–Apr;**19**(2):132–40.
23 Oka RK, Szuba A, Giacomini JC, Cooke JP. Gender differences in perception of PAD: a pilot study. *Vasc Med* 2003 May;**8**(2):89–94.
24 Wann-Hansson C, Hallberg IR, Risberg B, Lundell A, Klevsgard R. Health-related quality of life after revascularization for peripheral arterial occlusive disease: long-term follow-up. *J Adv Nurs* 2005 Aug;**51**(3):227–35.
25 Brevetti G, Bucur R, Balbarini A, Melillo E, Novo S, Muratori I, et al. Women and peripheral arterial disease: same disease, different issues. *J Cardiovasc Med (Hagerstown)* 2008 Apr;**9**(4):382–8.
26 Voudris V, Ong AT, Serruys PW, Sianos G, Stavrides G, Lindeboom W, et al. Sex differences and their impact on clinical outcome after percutaneous or surgical

revascularisation: a report from the Arterial Revascularisation Therapies Study (ARTS). *EuroIntervention* 2006 Aug;**2**(2):175–80.
27 Redzek A, Susak S, Zecevic D. Long term survival and quality of life after myocardial revascularization with respect to age and sex distribution. *Med Pregl* 2007 Jul–Aug;**60**(7–8):317–21.
28 Koch CG, Khandwala F, Cywinski JB, Ishwaran H, Estafanous FG, Loop FD, et al. Health-related quality of life after coronary artery bypass grafting: a gender analysis using the Duke Activity Status Index. *J Thorac Cardiovasc Surg* 2004 Aug;**128**(2):284–95.
29 Norris CM, Spertus JA, Jensen L, Johnson J, Hegadoren KM, Ghali WA, et al. Sex and gender discrepancies in health-related quality of life outcomes among patients with established coronary artery disease. *Circ Cardiovasc Qual Outcomes* 2008 Nov;**1**(2):123–30.
30 Hawkes AL, Mortensen OS. Up to one third of individual cardiac patients have a decline in quality of life post-intervention. *Scand Cardiovasc J* 2006 Aug;**40**(4):214–8.
31 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 Feb;**49**(2):371–7.
32 Spertus J, Jones P, Poler S, Rocha-Singh K. The peripheral artery questionnaire: a new disease-specific health status measure for patients with peripheral arterial disease. *Am Heart J* 2004 Feb;**147**(2):301–8.
33 Sloan JA, Symonds T, Vargas-Chanes D, Fridley B. Practical guidelines for assessing the clinical significance of health-related quality of life changes within clinical trials. *Drug Inf J* 2003;**37**(1):23–31.
34 Krueger C, Tian L. A comparison of the general linear mixed model and repeated measures ANOVA using a dataset with multiple missing data points. *Biol Res Nurs* 2004 Oct;**6**(2):151–7.
35 Vaccarino V, Lin ZQ, Kasl SV, Mattera JA, Roumanis SA, Abramson JL, et al. Sex differences in health status after coronary artery bypass surgery. *Circulation* 2003 Nov 25;**108**(21):2642–7.
36 Peric V, Borzanovic M, Stolic R, Jovanovic A, Sovtic S, Djikic D, et al. Quality of life in patients related to gender differences before and after coronary artery bypass surgery. *Interact Cardiovasc Thorac Surg* 2010 Feb;**10**(2):232–8.
37 Herlitz J, Brandrup-Wognsen G, Evander MH, Libungan B, Sjoland H, Caidahl K, et al. Quality of life 15 years after coronary artery bypass grafting. *Coron Artery Dis* 2009 Sep;**20**(6):363–9.
38 Pedersen SS, Ong AT, Lemos PA, Erdman RA, Serruys PW, van Domburg RT. Risk factors for impaired health status differ in women and men treated with percutaneous coronary intervention in the drug-eluting stent era. *J Psychosom Res* 2006 Jul;**61**(1):11–7.
39 Hoeks SE, op Reimer WJ, van Gestel YR, Smolderen KG, Verhagen H, van Domburg RT, et al. Preoperative cardiac risk index predicts long-term mortality and health status. *Am J Med* 2009 Jun;**122**(6):559–65.
40 Oka RK, Sanders MG. The impact of type 2 diabetes and peripheral arterial disease on quality of life. *J Vasc Nurs* 2005 Jun;**23**(2):7–8. 61–6; quiz.
41 Engelhardt M, Bruijnen H, Scharmer C, Jezdinsky N, Wolfle K. Improvement of quality of life six months after infrageniculate bypass surgery: diabetic patients benefit less than non-diabetic patients. *Eur J Vasc Endovasc Surg* 2006 Aug;**32**(2):182–7.