

Smoking Cessation has no Influence on Quality of Life in Patients with Peripheral Arterial Disease 5 Years Post-vascular Surgery

M.T. Hoogwegt^{a,b}, S.E. Hoeks^c, S.S. Pedersen^{a,b},
W.J.M. Scholte op Reimer^d, Y.R.B.M. van Gestel^c,
H.J.M. Verhagen^e, D. Poldermans^{c,*}

^a CoRPS – Center of Research on Psychology in Somatic diseases, Tilburg University, The Netherlands

^b Department of Cardiology, Thorax Center, Erasmus Medical Center, Rotterdam, The Netherlands

^c Department of Anesthesiology, Erasmus Medical Center, 's-Gravendijkwal 230, 3015 GD Rotterdam, The Netherlands

^d Amsterdam University of Applied Sciences, School of Nursing, Amsterdam, The Netherlands

^e Department of Vascular Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

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Abstract *Objectives:* Smoking is an important modifiable risk factor in patients with peripheral arterial disease (PAD). We investigated differences in quality of life (QoL) between patients who quit smoking during follow-up and persistent smokers.

Design: Cohort study.

Methods: Data of 711 consecutively enrolled patients undergoing vascular surgery were collected in 11 hospitals in the Netherlands. Smoking status was obtained at baseline and at 3-year follow-up. A 5-year follow-up to measure QoL was performed with the EuroQol-5D (EQ-5D) and Peripheral Arterial Questionnaire (PAQ).

Results: After adjusting for clinical risk factors, patients, who quit smoking within 3 years after vascular surgery, did not report an impaired QoL (EQ-5D: odds ratio (OR) = 0.63, 95% confidence interval (CI) = 0.28–1.43; PAQ: OR = 0.76, 95% CI = 0.35–1.65; visual analogue scale (VAS): OR = 0.88, 95% CI = 0.42–1.84) compared with patients, who continued smoking. Current smokers were significantly more likely to have an impaired QoL (EQ-5D: OR = 1.86, 95% CI = 1.09–3.17; PAQ: OR = 1.63, 95% CI = 1.00–2.65), although no differences in VAS scores were found (OR = 1.17, 95% CI = 0.72–1.90).

* Corresponding author at: Department of Anesthesiology, Erasmus Medical Center, Room H805, 's-Gravendijkwal 230, 3015 GD Rotterdam, The Netherlands. Tel.: +31 10 7034613; fax: +31 10 7034957.

E-mail address: d.poldermans@erasmusmc.nl (D. Poldermans).

Conclusions: There was no effect of smoking cessation on QoL in PAD patients undergoing vascular surgery. Nevertheless, given the link between smoking, complications and mortality in this patient group, smoking cessation should be a primary target in secondary prevention.
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Peripheral arterial disease (PAD) is a progressive atherosclerotic disease that affects approximately 10–25% of adults older than 55 years.^{1,2} Smoking is an important modifiable risk factor for the development of PAD.³ In patients who smoke, the diagnosis of PAD is made, on average, a decade before the diagnosis of PAD in non-smokers, with an observed dose-response relationship between the amount of smoking and the development of PAD.⁴ Besides a higher prevalence of PAD among people who smoke and former smokers, those who smoke more heavily also have an increased incidence of symptomatic, rather than asymptomatic PAD.¹ In addition, smokers with PAD have a poorer survival rate than non-smokers with the disease, and are twice as likely to develop complications, such as critical limb ischaemia leading to surgery and amputation.⁵ Smoking cessation is thus of utmost importance for cardiac and vascular patients. This is subscribed by coronary artery bypass graft (CABG) surgery patients, who can gain up to 3 life-years after smoking cessation.^{6,7}

Recently, the impact of smoking and smoking cessation on quality of life (QoL) has received increasing attention. Health Related Quality of life (HRQoL) reflects the patients' evaluation of his/her physical, psychological and social functioning in relation to health. A number of studies have investigated the effect of smoking on HRQoL and health status (HS, the influence of disease on physical, emotional and social functioning⁸). However, these studies were restricted to the general population^{8–11} or patients with heart disease.^{12–15} Mostly, smoking was found to be associated with lower QoL.^{8–14} Once more, smoking was related to a lower HS and HRQoL, both in general and after revascularisation.^{12–14} The relationship between smoking (cessation) and QoL in PAD patients is less well established, although, as mentioned previously, smoking is an important predictor of prognosis in this patient group,^{1–3} and several studies have indicated that patients with PAD experience impaired QoL.^{15,16} Therefore, we investigated the effect of smoking and smoking cessation on QoL in a sample of PAD patients undergoing vascular surgery during a 5-year follow-up period. Our primary objective was to investigate differences in QoL between patients, who quit smoking, and persistent smokers. A secondary objective was to examine differences in QoL between persistent smokers and patients, who never smoked or quit smoking before or after baseline (non-smokers).

Methods

Study population

Between May and December 2004, data of 711 consecutively enrolled patients with PAD were collected in 11 hospitals in the Netherlands. This survey was part of the Euro Heart Survey Programme.¹⁷ The enrolled patients

were seen at the vascular surgery departments at the participating hospitals. All patients were undergoing non-cardiac vascular surgery (open or endovascular procedures). Open procedures consisted of abdominal aortic surgery, carotid endarterectomy or infrainguinal arterial reconstruction. Endovascular procedures included aortic endograft procedures and peripheral angioplasties with or without stenting. All hospitals met the ethical requirements considered as necessary by the medical ethics committees of the participating hospitals.

Data collection

From the patients' hospital charts, data on patient characteristics, diagnostic procedures, cardioprotective treatment and the surgical procedure were collected by trained research assistants. All data were entered into the electronic case record form (CRF) and checked twice. Data were transferred via the Internet to the central database at the Erasmus Medical Center in Rotterdam, the Netherlands. Before each upcoming follow-up moment, survival status was obtained through the civil registries. Smoking status was assessed at baseline, and at 3- and 5-year follow-up. The QoL measured at 5-year follow-up was used in our study. Additional data concerning revascularisation, rehospitalisation, risk factors and several aspects of daily functioning, obtained at baseline through questionnaires, were used.

Quality of life

HRQoL and HS were combined to form QoL. HRQoL was measured with the Dutch version of the EuroQol Questionnaire (EQ-5D).¹⁸ The EQ-5D is a valid and reliable instrument for the measurement of HRQoL in cardiac patients that has also been shown to be responsive to changes.¹⁹ It is a standardised, generic measure that has been used to reflect HRQoL in patients with PAD²⁰ and cardiac patients, in general.^{19,21} The instrument consists of five items measuring aspects of HRQoL: mobility, self-care, daily activities, pain/discomfort and anxiety/depression. Each item consists of three statements: 'no problems', 'some problems' and 'severe problems'. Patients were asked which statement best described their health. Besides the five questions, the EQ-5D contains a Visual Analogue Scale (VAS), on which the respondents evaluate their health on a scale from 0 to 100, with 100 representing good health. In addition to the EQ-5D, the Dutch translation of the disease-specific Peripheral Arterial Questionnaire (PAQ) was used to measure HS. The PAQ contains 20 items, with one item identifying the most symptomatic leg and the other items being answered along equidistant variable Likert scales. The Dutch version of the PAQ is composed of three sub-domains: physical limitation, perceived disability and

treatment satisfaction.²² The PAQ is a valid, reliable and responsive disease-specific measure with good clinical validity.^{22,23}

Smoking status

Patients were characterised as quitters if they stopped smoking between baseline and 3 years of follow-up. Patients were considered as persistent smokers if they smoked from 1 year before surgery and still smoked at 5 years of follow-up; patients who never smoked were classified as never smokers, while patients who quit smoking before measurement at baseline were considered as previous smokers. To examine the effect of smoking on QoL, quitters, previous smokers and never smokers were combined to form the category of non-smokers.

Data analysis

Responders were compared with non-responders by means of the Pearson chi-square and Student's *t*-tests. Baseline demographic and clinical characteristics for the different categories of smokers were compared using the Pearson chi-square test and one-way analysis of variance (ANOVA), with a *post hoc* Bonferroni if the ANOVA showed a significant main effect. We determined a HRQoL score for each patient in our data set, as well as an HS score. To compute the five dimensions of the EQ-5D and form a utility score,

a standard set of general population weights was used. To increase interpretability of our results in clinical practice, the utility scores were divided into equal tertiles. To investigate the effect of smoking and smoking cessation on HRQoL, these scores were dichotomised into 'low score' versus a combination of 'intermediate score' and 'high score'. The same procedure was followed to generate tertiles for the mean PAQ and VAS scores. These scores also were dichotomised into 'low score' versus a combination of 'intermediate score' and 'high score'. We categorised the different vascular surgery procedures into three main types: abdominal aortic, carotid and lower-limb surgery. By means of univariate and multivariate logistic regression, the effect of smoking cessation on QoL was assessed. Because QoL after 5 years could be determined by many factors besides smoking and smoking cessation, in multivariate regression analysis, we adjusted for the potential confounding effects of demographic variables such as age and gender, and clinical risk factors including ischaemia, angina pectoris (AP), myocardial infarction (MI), previous history of revascularisation, history of heart failure, cerebrovascular disease, renal failure, diabetes mellitus (DM) and type of surgery. Results of the logistic regression analyses are presented as odds ratios (OR) with 95% confidence intervals (CI). For all tests, a *P*-value <0.05 (two-sided) was considered significant. All statistical analyses were performed using SPSS 15.0 statistical software (SPSS Inc., Chicago, IL, USA).

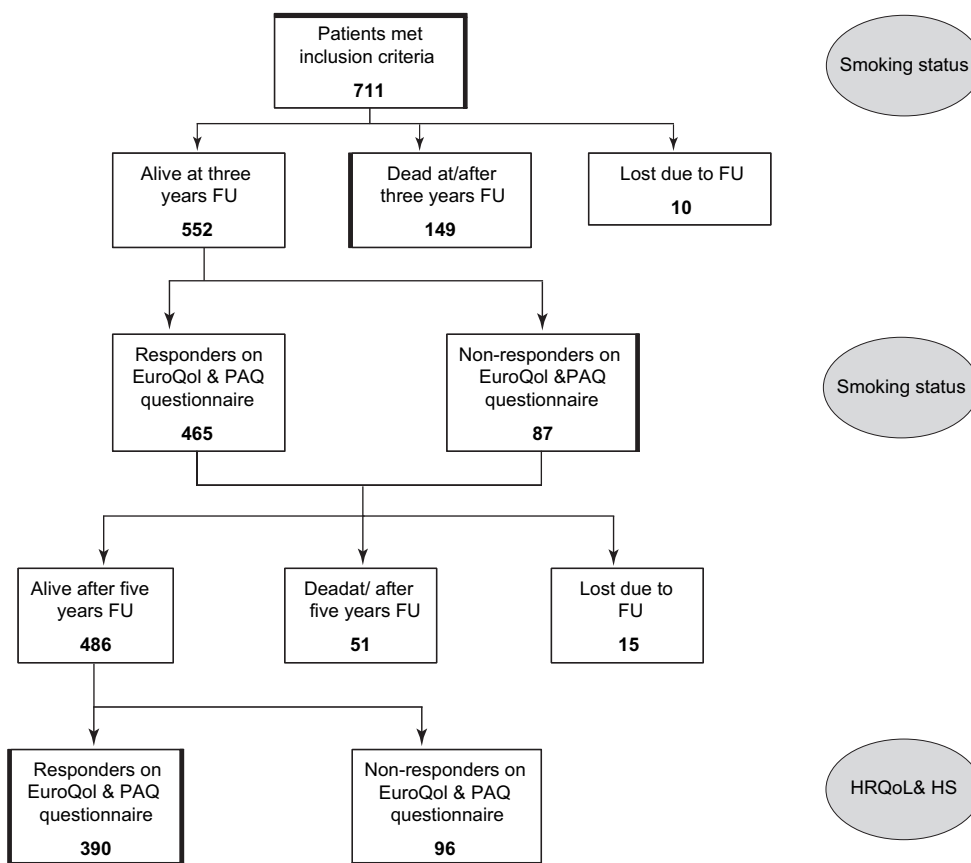


Figure 1 Flowchart FU, follow-up; PAQ, peripheral arterial questionnaire; HRQoL, health-related quality of life; HS, health status.

Results

Responders versus non-responders

The original sample consisted of 711 patients undergoing vascular surgery at baseline (Figure 1). After 3 years of follow-up, 552 patients were still alive, 149 patients died and 10 patients were lost to follow-up. A total of 200 (28.1%) patients died after 5 years of follow-up, of whom 72% were males. Their mean age was 76 ± 9 years. At baseline, 30% of these patients smoked. Of the remaining patients, four emigrated, five no longer wanted to participate in the study and 21 were lost to follow-up. All 486 surviving patients received a questionnaire, of which 390 (80.2%) responded. From these questionnaires, 364 contained sufficient information to generate HRQoL scores. With respect to the PAQ, from 384 questionnaires, an HS score could be obtained. To investigate response bias, responders were compared with non-responders. No differences were found in age, gender, cardiovascular history and clinical risk factors (all P -values > 0.05).

Baseline characteristics

General characteristics of the 390 patients at baseline are listed in Table 1. Patients were classified as smokers ($n = 151$), quitters ($n = 55$), previous smokers ($n = 166$) and never smokers ($n = 18$). The mean age of patients was 64.7 ± 9.7 years; 71.8% of the patients were males. Previous smokers were significantly older than persistent smokers and quitters ($P < 0.001$), reported a significantly higher prevalence of ischemic heart disease (IHD), MI, and previous revascularisation and were more likely to use beta-blockers ($P < 0.05$). Never smokers more often had

a prior history of cerebrovascular disease and more often had diabetes ($P < 0.05$).

The effect of smoking on QoL

First, we determined the impact of smoking on QoL. The mean scores of current smokers ($n = 151$) were compared with those of non-smokers ($n = 239$) after 5 years of follow-up. Impaired HRQoL and HS were defined as the lowest tertile of the EQ-5D summary and VAS scores, and the lowest tertile of the PAQ summary score, respectively. As shown in Table 2, there were no significant differences in the mean scores between the smoking categories ($P > 0.05$). The results of the univariate and multivariate analyses are displayed in Table 3. Analyses were adjusted for age, gender, clinical risk factors and type of surgery. Current smokers were significantly more likely to have an impaired HRQoL (EQ-5D summary score: OR = 1.84, 95% CI = 1.07–3.16). No differences in VAS (OR = 1.15, 95% CI = 0.70–1.87) and PAQ (OR = 1.60, 95% CI = 0.98–2.61) scores were found between patients, who smoked, and patients, who did not smoke. Furthermore, older age, DM ($P < 0.01$), previous ischaemia and renal failure ($P < 0.05$) were significant predictors of impaired HS and HRQoL.

Impact of smoking cessation on QoL

In relation to the main aim of our study, we compared the QoL scores between current smokers ($n = 151$) and quitters ($n = 55$). Again, we adjusted for the above-mentioned variables in multivariate regression analysis. As shown in Table 3, quitters were less likely to report an impaired PAQ summary score, but the predictive value of smoking category was not significant (OR = 0.84, 95% CI = 0.38–1.84).

Table 1 Baseline characteristics for the total study population and stratified by smoking status.^a

	Total	Current smokers	Quitters	Previous smokers	Never smokers	p -value
<i>N</i>	390 (100)	151 (38.7)	55 (14.1)	166 (42.6)	18 (4.6)	
Demographics						
Mean age (\pm SD)	64.7 (9.7)	62.2 (9.1)	61.1 (7.7)	68.3 (9.2)	64.2 (14.2)	<0.001
Men	280 (71.8)	106 (70.2)	38 (69.1)	129 (77.7)	7 (38.9)	0.005
Cardiovascular history						
IHD	107 (27.4)	31 (20.5)	9 (16.4)	63 (38.0)	4 (22.2)	0.001
Angina pectoris	54 (13.8)	17 (11.3)	5 (9.1)	30 (18.1)	2 (11.1)	0.213
Heart failure	9 (2.3)	2 (1.3)	1 (1.8)	5 (3.0)	1 (5.6)	0.591
MI	57 (14.6)	13 (8.6)	6 (10.9)	37 (22.3)	1 (5.6)	0.003
Stroke or TIA	50 (12.8)	11 (7.3)	10 (18.2)	24 (14.5)	5 (27.8)	0.023
Renal failure	18 (4.6)	4 (2.6)	3 (5.5)	10 (6.0)	1 (5.6)	0.532
Previous revascularisation	60 (15.4)	16 (10.6)	2 (3.6)	39 (23.5)	3 (16.7)	0.001
Hypertension	153 (39.2)	51 (33.8)	22 (40.0)	73 (44.0)	7 (38.9)	0.325
Diabetes mellitus	70 (17.9)	18 (11.9)	13 (23.6)	33 (19.9)	6 (33.3)	0.041
Medication use						
Aspirin	300 (76.9)	121 (80.1)	39 (70.9)	128 (77.1)	12 (66.7)	0.381
Statins	236 (60.5)	80 (53.0)	36 (65.5)	111 (66.9)	9 (50.0)	0.051
Beta-blockers	193 (49.5)	6 (43.0)	23 (41.8)	96 (57.8)	9 (50.0)	0.038

N, number; *SD*, standard deviation; *IHD*, ischemic heart disease; *MI*, myocardial infarction; *TIA*, transient ischemic attack.

^a Presented as N (%), unless otherwise indicated.

Table 2 Mean scores on HRQoL and HS measures stratified by smoking status.

Mean	Total	Current smokers	Quitters	Previous smokers	Never smokers	<i>p</i> -value
EQ-5D						
<i>N</i>	364	143	51	155	15	
Score (\pm SD)	0.77 \pm 0.23	0.77 \pm 0.23	0.78 \pm 0.22	0.76 \pm 0.23	0.83 \pm 0.17	0.708
% impaired	26.60	28.70	23.50	27.10	13.30	0.587
VAS						
<i>N</i>	377	146	55	158	18	
Score (\pm SD)	68.65 \pm 18.67	69.25 \pm 18.22	68.11 \pm 18.57	68.14 \pm 19.85	69.89 \pm 11.59	0.942
% impaired	32.60	31.50	30.90	34.80	27.80	0.875
PAQ						
<i>N</i>	384	148	54	164	18	
Score (\pm SD)	61.24 \pm 26.73	62.69 \pm 27.52	62.29 \pm 27.01	59.69 \pm 26.27	60.31 \pm 24.71	0.780
% impaired	33.30	35.10	31.50	31.70	38.90	0.863

EQ-5D, EuroQoL; SD, standard deviation; VAS, visual analogue scale; PAQ, peripheral arterial questionnaire.

Quitting smoking neither had a significant impact on the EQ-5D summary score (OR = 0.64, 95% CI = 0.28–1.47) nor on the VAS score (OR = 0.92, 95% CI = 0.44–1.94). On the other hand, older age, having DM, ischaemia and renal failure were significant predictors of an impaired HRQoL and HS (all $P < 0.05$), and having had a previous revascularisation procedure was predictive for an impaired HS ($P < 0.05$).

Discussion

Our main finding is that there is no significant effect of smoking cessation on QoL in patients with PAD. Patients, who quit smoking within 3 years after vascular surgery, neither experienced a change in QoL compared to patients who kept smoking. To our knowledge, only a few studies have investigated the effect of smoking cessation in the high-risk population of PAD patients. Since smoking cessation is an enormous challenge for addicted patients, it is important to recognise that smoking cessation does not influence the QoL of patients with PAD negatively. Besides, the need for smoking cessation, which still receives very little attention, has to be emphasised both to the patients and to the physicians.²⁴ In CABG patients, smoking cessation had a greater effect on enhancing survival than any other form of intervention.^{6,25} Hence, patients should be encouraged to quit smoking, which could be facilitated by attending rehabilitation programmes. Through motivational counselling and behavioural therapy by a psychologist, the chances for successful quitting can be increased.²⁶ Besides these interventions, additional assistance including nicotine replacement therapy and pharmacological therapy, including varenicline²⁷ and bupropion,²⁸ can be applied.

Our results on the effect of smoking cessation on QoL do not fully match with some earlier findings. Several studies among university graduates, nurses and adults in the US found that smoking cessation resulted in a better HRQoL^{9,11} and less depressive symptoms and life dissatisfaction.²⁹ However, these studies were all conducted in segments of the general population. Although smokers are

expected to experience health benefits from cessation as compared with continued smokers, some of these health improvements may not directly be translated into perceptions of improvement of QoL. This could, in particular, be the case when chronic illnesses such as PAD are present. Other factors could be more important in determining QoL. Since PAD patients are mostly people smoking for a few decades, this could clarify the lack of significance in our study. In coronary artery disease (CAD), patients who stopped smoking at the time of revascularisation experienced more improvements in HRQoL than patients who continued to smoke.¹³ Nevertheless, the poor prognosis of PAD patients compared with CAD patients, partly explained by disease characteristics, receiving less cardiac medication than CAD patients, and more perioperative and long-term complications could possibly diminish the positive effect of smoking cessation on QoL in this vulnerable patient group.²⁵ Another explanation could be that smokers may quit after becoming symptomatic or getting a co-morbid condition related to tobacco use. The possibly positive effect of smoking cessation may diminish by the negative effect of the co-morbid disease. Finally, maybe the negative effects of smoking have already had their effect, and it could be too late for the quitters to improve their QoL.

Our secondary objective was to determine possible differences in QoL between current smokers and non-smoking patients. Current smokers were more likely to have an impaired QoL than patients, who did not smoke, indicating that smoking had a negative impact on QoL in our group of PAD patients. These results are in line with the earlier findings, showing a poorer HRQoL and more mental and physical distress among current smokers.^{14,29} In addition, smokers were more likely to have activity limitations due to greater impairments. Among heart failure patients, those who smoked were found to have a significant lower HS score than former smokers or patients who never smoked.¹² Taira and colleagues found that revascularisation in patients with symptomatic CAD leads to improved HRQoL, although patients who smoked improved substantially less (up to 75%) than patients who did not smoke.¹³ In our study, no effect of smoking on the domains of the PAQ

Table 3 Univariate and multivariate regression analyses; current smokers compared to non-smokers and current smokers compared to quitters.

Smoking status	Impaired HRQoL EQ-5D ^a			EQ VAS ^b			Impaired HS PAQ ^c		
	N (%)	Univariate OR (95%CI)	Multivariate ^d OR (95%CI)	N (%)	Univariate OR (95%CI)	Multivariate ^d OR (95%CI)	N (%)	Univariate OR (95%CI)	Multivariate ^d OR (95%CI)
Non-smokers	221 (60.7)	1	1	231 (61.3)	1	1	236 (61.5)	1	1
Current smokers	143 (39.3)	1.18 (0.74–1.90)	1.84 (1.07–3.16)	146 (38.7)	0.95 (0.61–1.47)	1.15 (0.70–1.87)	148 (38.5)	1.14 (0.74–1.76)	1.60 (0.98–2.61)
Quitters	143 (73.7)	1	1	146 (72.6)	1	1	148 (73.3)	1	1
	51 (26.3)	0.77 (0.37–1.61)	0.64 (0.28–1.47)	55 (27.4)	0.95 (0.49–1.86)	0.92 (0.44–1.94)	54 (26.7)	0.85 (0.44–1.65)	0.84 (0.38–1.84)

HRQoL, health-related quality of life; HS, health status; EQ-5D, EuroQol; EQ VAS, EuroQol visual analogue scale; PAQ, Peripheral arterial questionnaire; N, number; OR, odds ratio; CI, confidence interval.

^a 7% and 6% missing respectively.

^b 3% and 2% missing respectively.

^c 1% and 2% missing respectively.

^d Adjusted for age, gender, ischemia, angina pectoris, myocardial infarction, previous history of revascularisation, heart failure, cerebrovascular disease, renal failure and diabetes mellitus.

and EQ-5D was found in the unadjusted analysis. This may be explained by the relatively large group of previous smokers, which is older and more often has a history of cardiovascular disease than current smokers, quitters and never smokers. When comparing scores on the domains of the QoL questionnaires, the impaired QoL of previous smokers due to older age and a burden of previous cardiovascular history^{30–32} may suppress the negative effect of smoking on QoL. By adjusting these variables in multivariate analysis, we did find a significant negative effect of smoking on QoL.

Another important finding of our study is that never smokers more often had a prior history of cerebrovascular disease and had diabetes. At first sight, this may seem puzzling, but when considering the group of never smokers in detail, the explanation might be quite logical. In our group of patients, only 4.2% had a history of never having smoked. The other 95.8% still smoked or had been smoking for a great part of their life. Based on these percentages, and since smoking has proved to be a major risk factor for the development of PAD, the non-smokers are likely to develop PAD due to reasons other than smoking. This conclusion is further supported by other results of our study, which display a higher frequency of IHD, MI and previous revascularisation among previous smokers, than among current smokers. Maybe for this subgroup of patients, these events have motivated them to quit smoking.

This study has some limitations. First, all patients underwent a vascular intervention, which may limit generalisability to the general PAD population. Moreover, confounding might have played a role, as smoking is associated with a variety of other conditions such as pulmonary disease, cancer and psychiatric conditions, which we were unable to adjust for statistically.^{32,33} A third limitation is the low number of patients, who quit smoking after revascularisation. With a larger group of quitters, we potentially would have been able to determine a clearer effect of smoking cessation on QoL. Another limitation is that smoking status was based on self-report, rather than an objective measure, such as exhaled carbon monoxide, which could lead to underestimation of the actual amount of smoking patients.³⁴ Fifth, there might be a selection bias due to non-response and death, with the likelihood that these patients would have had a worse QoL, given that HS has proven to be an independent predictor of prognosis in patients with PAD,³⁵ or with the likelihood that only the current smokers with best health and better QoL survived. A final limitation is related to the study design, as we had no information on the baseline QoL.

In conclusion, in the current study, we found no effect of smoking cessation on QoL in PAD patients undergoing vascular surgery. Nevertheless, smoking cessation should still be a primary target in secondary prevention, given that smoking enhances the risk of severe complications and mortality in this patient group. Future studies are warranted to replicate the findings of the current studies; however, in the meantime, more attention should be paid to lifestyle changes and risk factor management in this patient group, both by the physicians and by the patients themselves.

Conflicts of Interest

None.

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References

- Watson K, Watson BD, Pater KS. Peripheral arterial disease: a review of disease awareness and management. *The American Journal of Geriatric Pharmacotherapy* 2006;4(4): 365–79.
- Stehouwer CDA, Clement D, Davidson C, Diehm C, Elte JW, Lambert M, et al. Peripheral arterial disease: a growing problem for the internist. *European Journal of Internal Medicine* 2009; 20(2):132–8.
- Criqui MH. Peripheral arterial disease – epidemiological aspects. *Vascular Medicine* February 1, 2001;6(Suppl. 3):3–7.
- Willigendael EM, Teijink JAW, Bartelink M-L, Kuiken BW, Boiten J, Moll FL, et al. Influence of smoking on incidence and prevalence of peripheral arterial disease. *Journal of Vascular Surgery* 2004;40(6):1158–65.
- Bartholomew JR, Olin JW. Pathophysiology of peripheral arterial disease and risk factors for its development. *Cleveland Clinic Journal of Medicine* October 2006;73(Suppl. 4):S8–14.
- van Domburg RT, Meeter K, van Berkel DFM, Veldkamp RF, van Herwerden LA, Bogers AJJC. Smoking cessation reduces mortality after coronary artery bypass surgery: a 20-year follow-up study. *Journal of the American College of Cardiology* 2000;36(3):878–83.
- van Domburg RT, op Reimer WS, Hoeks SE, Kappetein AP, Bogers AJJC. Three life-years gained from smoking cessation after coronary artery bypass surgery: a 30-year follow-up study. *American Heart Journal* 2008;156(3):473–6.
- Breek JC, de Vries J, van Heck GL, van Berge Henegouwen DP, Hamming JF. Assessment of disease impact in patients with intermittent claudication: Discrepancy between health status and quality of life. *Journal of Vascular Surgery* 2005;41(3): 443–50.
- Gutiérrez-Bedmar M, Seguí-Gómez M, Gómez-Gracia E, Bes-Rastrollo M, Martínez-González MA. Smoking status, changes in smoking status and health-related quality of life: findings from the SUN (“Seguimiento Universidad de Navarra”) cohort. *International Journal of Environmental Research and Public Health* 2009;6(1):310–20.
- Sales MPU, Oliveira MI, Mattos IM, Viana CMS, Pereira EDB. The impact of smoking cessation on patient quality of life. *Jornal Brasileiro de Pneumologia* 2009;35:436–41.
- Sarna L, Bialous SA, Cooley ME, Jun H, Feskanich ME. Impact of smoking and smoking cessation on health-related quality of life in women in the Nurses’ Health Study. *Quality of Life Research* 2008;17(10):1217–27.
- Conard MW, Haddock CK, Walker SCP, John AS. The impact of smoking status on the health status of heart failure patients. *Congestive Heart Failure* 2009;15(2):82–6.
- Taira DA, Seto TB, Ho KKL, Krumholz HM, Cutlip DE, Berezin RM, et al. Impact of smoking on health-related quality of life after percutaneous coronary revascularization. *Circulation* 2000;102 (12):1369–74.
- Strine TW, Okoro CA, Chapman DP, Balluz LS, Ford ES, Ajani UA, et al. Health-related quality of life and health risk behaviors among smokers. *American Journal of Preventive Medicine* 2005;28(2):182–7.
- Breek JC, Hamming JF, De Vries J, Henegouwen DPvB, van Heck GL. The impact of walking impairment, cardiovascular risk factors, and comorbidity on quality of life in patients with intermittent claudication. *Journal of Vascular Surgery* 2002;36 (1):94–9.
- Smolderen KG, Hoeks SE, Pedersen SS, van Domburg RT, de Liefde II, Poldermans D. Lower-leg symptoms in peripheral arterial disease are associated with anxiety, depression, and anhedonia. *Vascular Medicine* 2009;14(4):297–304.
- Hoeks SE, Scholte op Reimer WJM, van Gestel YRBM, Smolderen KG, Verhagen H, van Domburg RT, et al. Preoperative cardiac risk index predicts long-term mortality and health status. *The American Journal of Medicine* 2009;122(6):559–65.
- EuroQol—a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy* 1990;16(3): 199–208.
- Schweikert B, Hahmann H, Leidl R. Validation of the EuroQol questionnaire in cardiac rehabilitation. *Heart* January 1, 2006; 92(1):62–7.
- de Vries M, Ouwendijk R, Kessels AG, de Haan MW, Flobbe K, Hunink MGM, et al. Comparison of generic and disease-specific questionnaires for the assessment of quality of life in patients with peripheral arterial disease. *Journal of Vascular Surgery* 2005;41(2):261–8.
- Ellis JJ, Eagle KA, Kline-Rogers EM, Erickson SR. Validation of the EQ-5D in patients with a history of acute coronary syndrome. *Current Medical Research and Opinion* 2005;21(8):1209–16.
- Hoeks SE, Smolderen KG, Scholte op Reimer WJM, Verhagen HJM, Spertus JA, Poldermans D. Clinical validity of a disease-specific health status questionnaire: the peripheral artery questionnaire. *Journal of Vascular Surgery* 2009;49(2):371–7.
- 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. *American Heart Journal* 2004;147(2):301–8.
- Oka RK, Umoh E, Szuba A, Giacomini JC, Cooke JP. Suboptimal intensity of risk factor modification in PAD. *Vascular Medicine* May 1, 2005;10(2):91–6.
- Welten GMJM, Schouten O, Hoeks SE, Chonchol M, Vidakovic R, van Domburg RT, et al. Long-Term prognosis of patients with peripheral arterial disease: a comparison in patients with coronary artery disease. *Journal of the American College of Cardiology* 2008;51(16):1588–96.
- Hall S, Humfleet G, Muñoz R, Reus V, Robbins J, Prochaska J. Extended treatment of older cigarette smokers. *Addiction* 2009;104(6):1043–52.
- Hays JT, Ebbert JO, Sood A. Efficacy and safety of varenicline for smoking cessation. *The American Journal of Medicine* 2008; 121(4, Suppl. 1):S32–42.
- Piper ME, Smith SS, Schlam TR, Fiore MC, Jorenby DE, Fraser D, et al. A randomized placebo-controlled clinical trial of 5 smoking cessation pharmacotherapies. *Archives of General Psychiatry* November 1, 2009;66(11):1253–62.
- McClave AK, Dube SR, Strine TW, Mokdad AH. Associations between health-related quality of life and smoking status among a large sample of U.S. adults. *Preventive Medicine* 2009; 48(2):173–9.
- Rumsfeld JS, Ho PM, Magid DJ, McCarthy M, Shroyer ALW, MaWhinney S, et al. Predictors of health-related quality of life after coronary artery bypass surgery. *The Annals of Thoracic Surgery* 2004;77(5):1508–13.
- Lee GA. Determinants of quality of life five years after coronary artery bypass graft surgery. *Heart and Lung: The Journal of Acute and Critical Care* 2009;39(2):91–9.

- 32 Correa P, Barreto S, Passos V. Smoking-attributable mortality and years of potential life lost in 16 Brazilian capitals, 2003: a prevalence-based study. *BMC Public Health* 2009;9(1):206.
- 33 Lineberry TW, Allen JD, Nash J, Galardy CW. Population-based prevalence of smoking in psychiatric inpatients: a focus on acute suicide risk and major diagnostic groups. *Comprehensive Psychiatry* 2009;50(6):526–35.
- 34 Gorber SC, Schofield-Hurwitz S, Hardt J, Levasseur G, Tremblay M. The accuracy of self-reported smoking: a systematic review of the relationship between self-reported and cotinine-assessed smoking status. *Nicotine and Tobacco Research* January 1, 2009;11(1):12–24.
- 35 Issa SM, Hoeks SE, Scholte op Reimer WJM, Van Gestel YRBM, Lenzen MJ, Verhagen HJM, et al. Health-related quality of life predicts long term survival in patients with peripheral artery disease. *Vascular Medicine* 2010;15(3):163–9.