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Original Scientific Paper

Risk factor profiles and use of cardiovascular drug prevention in women and men with peripheral arterial disease

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Objective **To determine cardiovascular comorbidities and use of cardiovascular disease preventive drugs in patients with peripheral arterial disease (PAD), with special attention to sex differences.**
Design **A cross-sectional point-prevalence study.**
Patients **A population sample of patients that are 60–90 years old.**
Setting **Primary care areas in four Swedish regions.**
Main outcome measures **Prevalence of PAD stages, comorbidities and medication use.**
Results **The prevalence of any type of PAD was 18.0% (range 16–20), of asymptomatic peripheral arterial disease (APAD) was 11.1% (range 9–13), intermittent claudication was 6.8% (range 6.5–7.1), and of critical limb ischemia (CLI) was 1.2% (range 1.0–1.5). APAD and CLI were more common in women. Statins were used by 17.5% (range 16.9–18.2), 29.4% (range 29.0–30.1), and 30.3% (range 29.9–30.8) of the patients with APAD, intermittent claudication, and CLI, respectively, and antiplatelet therapy was reported by 34.1% (range 33.7–34.3), 47.6% (range 47.3–47.9), and 60.2% (range 59.1–60.7). The odds ratio for having APAD was 1.7 (range 1.2–2.4) for women with a smoking history of 10 years in relation to nonsmokers. This association was observed only in men who had smoked for at least 30 years or more. Preventive drug use was more common in men with PAD. Compared with women they had an odds ratio of 1.3 (range 1.1–1.5) for lipid-lowering therapy, 1.3 (range 1.0–1.7) for β-blockers or angiotensin-converting enzyme inhibitors, and 1.5 (range 1.2–1.9) for antiplatelet therapy.**
Conclusion **The patients' risk factor profiles differed among the PAD stages. Smoking duration already seemed to be a risk factor for women with PAD after 10 years of smoking, as compared with 30 years for men, and fewer women reported use of preventive medication. These observations may partly explain the sex differences in prevalence that were observed.**

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Keywords: ankle–brachial index, peripheral arterial disease, primary drug prevention, risk factors, sex differences

Introduction

Peripheral arterial disease (PAD) is defined by the presence of arteriosclerosis in the leg arteries and is diagnosed by ankle–brachial index (ABI) measurements. PAD afflicts a large proportion of the elderly population and recent observations have shown that the majority of the population with this disease comprises old women without symptoms [1,2]. The most well-known stage of PAD is intermittent claudication (IC). It restricts the patients' ability to walk and considerably diminishes their quality of life [3]. Critical limb ischemia (CLI) is the most severe stage, which, fortunately, is quite rare [1]. It is defined by the presence of rest pain and/or ulcers or gangrene and usually requires revascularization or amputation to relieve the pronounced symptoms [4]. Asymptomatic peripheral arterial disease (APAD) covers all patients with ABI of less than 0.9 without symptoms.

Patients with PAD face a three-to-seven times greater risk for early death because of cardiovascular events than a comparable population without PAD, and this elevated

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risk is also applicable for APAD patients who rarely come to medical attention [5]. For all PAD stages, cardiovascular risk prevention is important [6,7], but, in contrast to patients with coronary artery disease, less is known about PAD patients' state of risk factor burden and to what extent preventive measures are used [8]. Indications that PAD is underdiagnosed and undertreated in many populations have been observed [9]. One possible explanation for this is that up-to-date information on cardiovascular risk factors from a population perspective is lacking, and especially its implementation in patients with asymptomatic PAD and CLI. Knowledge about this is particularly important for patients that are unknown to healthcare providers and it could facilitate realization of focused disease awareness programs, including optimal use of preventive medication.

The principal aim of this study was to determine cardiovascular comorbidities associated with having PAD of different stages and to investigate the current use of pharmacological cardiovascular risk-reducing therapy in Sweden. The secondary aim was to assess sex differences in these two objectives.

Methods

Study population

A point-prevalence study on PAD was performed in Sweden in 2005 (The Swedish PAD prevalence study, SPPS). A detailed description of the design and results of the SPPS has been published earlier [1]. Eight thousand individuals 60–90 years old were selected at random from the National Tax Registry and invited from four geographically and demographically different regions. These regions were selected to cover a wide range of demographics:

Region A (Karlstad): A mid-sized city with a dominance of white-collar workers.
Region B (Skellefteå): A rural area largely populated by farmers.
Region C (Malmö): A big city with a large population of immigrants.
Region D (Älvkarleby): A rural area with a small town and a large population of factory workers.

Of those invited, 5080 individuals agreed to participate giving a participation rate of 63%. The median age for the participants who were included was 71 years (interquartile range, 13 years). Validation and characterization of nonparticipants were performed and have been presented earlier [1].

Local ethics committees approved the study and informed consent was obtained from each participant.

Data collection

All enrolled participants answered a self-administered questionnaire covering weight, height, and morbidities that included hypertension (HTN), coronary artery disease, congestive heart failure, stroke, and diabetes mellitus (DM). They also reported present use and duration of any pharmacological treatment, and current and former smoking habits. The participants also answered a separate questionnaire that covered information about walking ability and pain at rest. Right brachial blood pressure and bilateral ankle blood pressure using both the posterior tibial and dorsal pedal artery for insonation were measured. All pressure values were recorded in a database, and the lowest ankle blood pressure value was used to calculate ABI [10].

For this report, 4926 participants from the entire cohort of 5080 participants were analyzed. Fifteen participants could not be assigned to a region and 139 participants lacked reliable blood pressure values and therefore could not be assigned as having PAD or not, giving a total population of 4926.

Diagnostic criteria and definitions

PAD was defined as having an ABI of less than 0.9, with or without symptoms. APAD was diagnosed when patients had ABI of less than 0.9 without reporting leg symptoms in the questionnaire. IC was defined as ABI of less than 0.9 and leg pain when walking with prompt relief at rest. For CLI, the definition of having an ankle pressure of less than 70 mmHg was used. In clinical practice, the term CLI includes having rest pain and/or ulcers or gangrene in addition to a low ankle blood pressure [11]. In the SPPS cohort less than 50 participants had CLI using the combined definition of an ankle blood pressure of less than 70 mmHg and rest pain. Ulcers or gangrene were not assessed. To enable a meaningful analysis, we therefore used a slightly wider definition of CLI for this study.

Coronary artery disease, congestive heart failure, stroke, DM, and HTN were considered present if reported in the questionnaire. Reported morbidities and drug use were up to the participants' discretion and only those listed were used in the analysis. Smoking status was also determined using self-reported answers from the questionnaire.

Body mass index (BMI) was calculated from questionnaire data and classified according to the standards proposed by WHO; underweight as having a BMI less than 18.5 kg/m^2, normal as BMI between 18.5 and 24.9 kg/m^2, overweight as BMI between 25.0 and 29.9 kg/m^2, and obesity as having a BMI greater than 30.0 kg/m^2 [12].

Statistics and analysis

To analyze associations between risk factors and different stages of PAD, multiple logistic regression models with

a likelihood ratio test were used. All collected risk factors and comorbidities (age, sex, regions, smoking history, history of coronary artery disease, diabetes, HTN, stroke, and BMI) were used in the models and the results expressed as odds ratios (ORs) with 95% confidence intervals (CI, Wald confidence limits). Interaction tests and tests for confounding among all factors were also addressed by logistic regression models. Sex and regions were identified as interacting factors and some amount of confounding was identified. To adjust for confounding, multivariate logistic regressions were used instead of univariate regressions. Accordingly, the first four models were created using the four stages of PAD as dependent variables and all the variables listed above including the interaction variables, region, and sex. Second, two new models, one for each sex, were developed using PAD (without separation into PAD stages) as a dependent variable and the risk factors mentioned above to assess regional differences in men and women independently, accounting for the interaction described above. Finally, we used four (one for each region) additional multivariate logistic models with PAD as dependent variable to assess how sex influences PAD prevalence in the regions.

The test of equal proportions was used to analyze sex differences in the prevalence of cardiovascular diseases, medication use, and smoking habits, accounting for the two-stage cluster sample. Furthermore, three additional logistic regression models using lipid-lowering therapy, β-blockers, angiotensin-converting enzyme inhibitors, and antiplatelet therapy as dependent variables and region, sex, and PAD as independent variables to show the influence of medication on PAD prevalence. Beta-blockers and angiotensin-converting enzyme inhibitors were regarded as reducing cardiovascular events to a similar extent and were combined in the analyses [13,14].

All statistical analyses were performed using SPSS for Windows version 14.0 (SPSS Inc., Chicago, Illinois, USA). *P* values below 0.05 were considered statistically significant.

Results

Of the 5080 study participants 55% were women, and their median age was 71 years (interquartile range, 13 years). The prevalence of any type of PAD in the cohort was 18.0% (95% CI: 16–20), of APAD was 11.1% (9–13), of IC was 6.8% (6.5–7.1), and of CLI was 1.2% (1.0–1.5). The prevalence of APAD and CLI was significantly higher among women and the prevalence of IC was similar among women and men.

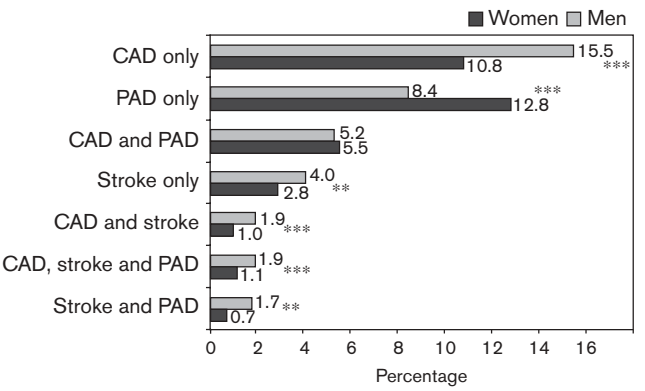
The participants in the cohort reported several cardiovascular morbidities and risk factors (Table 1). Fifty-eight percent were current or former smokers. Isolated coronary artery disease, PAD, and stroke were reported by 12.7, 10.3, and 3.4%, respectively, of the population (Fig. 1). Significantly ($P < 0.001$) more women had only PAD compared with men, who in turn reported more isolated coronary artery disease. Men also reported having multiple cardiovascular diseases more often than women.

Table 1 Baseline characteristics of participants with and without PAD (*N*=4926)

	No PAD (*N*=4046) Count (%)	Any PAD (*N*=880) Count (%)	Asymptomatic PAD (*N*=550) Count (%)	Intermittent claudication (*N*=330) Count (%)	Critical limb ischemia (*N*=65) Count (%)
Sex					
Women	2161 (53)	522 (59)	344 (63)	178 (54)	45 (69)
Men	1885 (47)	358 (41)	206 (37)	152 (46)	20 (31)
Age					
Median (IQR)	70 (12)	77 (13)	77 (12)	78 (12)	80 (8)
60–64 years	1095 (27)	89 (10)	56 (10)	33 (10)	4 (6)
65–69 years	924 (23)	113 (13)	75 (14)	38 (12)	4 (6)
70–74 years	791 (20)	128 (15)	78 (14)	50 (15)	4 (6)
75–79 years	631 (16)	206 (23)	133 (24)	73 (22)	19 (29)
80–84 years	441 (11)	195 (22)	119 (22)	76 (23)	24 (37)
85–90 years	164 (4)	149 (17)	89 (16)	60 (18)	10 (15)
BMI					
Normal weight	1638 (40)	382 (43)	260 (47)	122 (37)	27 (42)
Overweight	1654 (41)	325 (37)	204 (37)	121 (37)	22 (34)
Obese	589 (15)	121 (14)	60 (11)	61 (18)	13 (20)
Smoking					
Nonsmokers	1976 (49)	365 (41)	242 (44)	123 (37)	20 (31)
Smoked <10 years	544 (13)	88 (10)	53 (10)	35 (11)	8 (12)
Smoked 10–30 years	870 (21)	152 (17)	94 (17)	58 (18)	18 (28)
Smoked >30 years	656 (16)	275 (31)	161 (29)	114 (35)	19 (29)
Heart disease[a]	696 (17)	317 (36)	158 (29)	159 (48)	39 (60)
Hypertension	1392 (34)	413 (47)	231 (42)	182 (55)	26 (40)
Diabetes mellitus	350 (9)	151 (17)	78 (14)	73 (22)	17 (26)
Stroke	237 (6)	125 (14)	75 (14)	50 (15)	10 (15)

IQR, interquartile range; PAD, peripheral arterial disease. [a]Myocardial infarction, angina, or heart failure.

Fig. 1



The prevalence of vascular diseases, isolated and in combination by sex (*N*=4926 patients). CAD, coronary artery disease; PAD, peripheral arterial disease. **$P<0.01$; ***$P<0.001$.

Table 2 Relationship between selected risk factors and PAD stages (*N*=4926)

Risk factor	Any PAD OR (95% CI)	Asymptomatic PAD OR (95% CI)	Intermittent claudication OR (95% CI)	Critical limb ischemia OR (95% CI)
Age				
60–64 years	Reference	Reference	Reference	Reference
65–69 years	1.5 (1.1–2.1)	1.6 (1.1–2.3)	1.5 (0.9–2.5)	0.8 (0.2–3.7)
70–74 years	2.1 (1.5–2.8)	2.1 (1.4–3.0)	2.1 (1.1–3.5)	1.3 (0.3–5.1)
75–79 years	4.5 (3.4–6.0)	4.6 (4.0–8.2)	4.4 (2.8–7.1)	7.7 (2.5–23.4)
80–84 years	6.0 (4.4–8.1)	5.7 (3.4–8.2)	6.7 (4.2–10.8)	14.5 (4.7–44.3)
85–90 years	13.0 (9.2–18.3)	12.1 (8.0–18.2)	15.1 (18.9–25.6)	15.8 (4.5–55.3)
BMI				
Normal weight	Reference	Reference	Reference	Reference
Overweight	0.8 (0.7–1.0)	0.9 (0.7–1.1)	1.1 (0.7–1.6)	0.7 (0.4–1.3)
Obese	0.9 (0.7–1.2)	0.9 (0.6–1.0)	1.7 (1.0–2.9)	1.2 (0.6–2.6)
Smoking				
Nonsmokers	Reference	Reference	Reference	Reference
Smoked <10 years	1.0 (0.7–1.3)	1.0 (0.7–1.4)	1.3 (0.9–2.1)	1.7 (0.7–4.2)
Smoked 10–30 years	1.2 (0.9–1.5)	1.2 (0.9–1.5)	1.2 (0.8–1.8)	2.6 (1.3–5.1)
Smoked >30 years	3.6 (2.9–4.5)	3.0 (2.4–3.9)	4.9 (3.5–6.9)	4.3 (2.1–8.8)
Concomitant diseases				
No disease	Reference	Reference	Reference	Reference
Coronary artery disease[a]	1.9 (1.4–2.5)	1.9 (1.3–2.9)	2.4 (1.7–3.2)	6.3 (3.1–13.0)
Diabetes mellitus	1.8 (1.4–2.3)	1.6 (1.2–2.1)	2.6 (1.7–4.0)	2.7 (1.4–5.0)
Hypertension	1.6 (1.3–1.9)	1.5 (1.2–1.9)	2.3 (1.5–3.4)	1.4 (0.6–3.0)
Congestive heart failure	1.2 (0.8–1.9)	1.5 (1.2–1.9)	1.6 (0.9–2.8)	1.9 (0.6–3.0)

BMI, body mass index; CI, confidence interval; OR, odds ratio; PAD, peripheral arterial disease. [a]Myocardial infarction or angina.

Overall, the more severe the PAD stage was the larger the proportion of patients with at least one additional risk factor (Table 1). Among the patients without PAD, 34.4% had HTN, 7.1% had coronary artery disease, and 9.5% had DM. The corresponding figures for patients with PAD were 46.9, 19.5, and 17.0% (Table 2). Smoking habits and years of cigarette smoking, as well as medication use, were also associated with PAD stage. Statins were used by 17.5% (16.9–18.2), 29.4% (29.0–30.1), and 30.3% (29.9–30.8) of the patients with APAD, IC, and CLI, respectively, and antiplatelet therapy was reported by 34.1% (33.7–34.3), 47.6% (47.3–47.9), and 60.2% (59.1–60.7) of the patients.

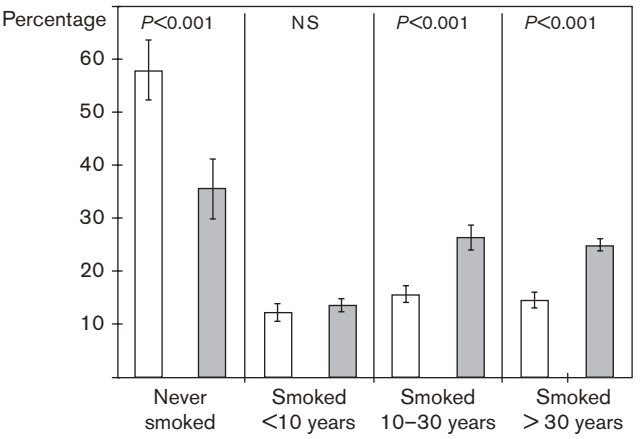
Men and women displayed differences in the extent of associated risk factors (Table 3). For example, the relationship between the presence of APAD and age appeared already at 66 years among men, whereas this association was not observed in women until the age of 75 years. Another example is that in CLI patients the odds ratio for the association with DM was 3.8 (1.2–11.7) in men, whereas it was 1.7 (0.7–4.1) in women. Sex differences in smoking habits are presented in Fig. 2. An association with smoking for less than or equal to 10 years in women with PAD was observed. For APAD the OR for

Table 3 Sex differences for selected risk factors in patients with PAD

Risk factor	Women OR (95% CI)	Men OR (95% CI)
Age		
60–64 years	Reference	Reference
65–69 years	1.5 (1.0–2.2)	1.7 (1.0–2.7)
70–74 years	2.1 (1.4–3.1)	2.3 (1.4–3.7)
75–79 years	4.7 (3.2–6.9)	4.4 (2.8–7.1)
80–84 years	5.1 (3.5–8.0)	7.2 (4.5–11.6)
85–90 years	11.7 (7.3–18.5)	16.3 (9.4–28.5)
BMI		
Normal weight	Reference	Reference
Overweight	0.9 (0.7–1.1)	0.9 (0.6–1.1)
Obese	0.9 (0.6–1.2)	1.0 (0.6–1.5)
Smoking		
Nonsmokers	Reference	Reference
Smoked <10 years	0.9 (0.6–1.3)	1.3 (0.8–2.1)
Smoked 10–30 years	1.5 (1.1–2.1)	1.1 (0.8–1.7)
Smoked >30 years	3.8 (2.8–5.2)	4.3 (3.1–6.1)
Concomitant diseases		
No disease	Reference	Reference
Coronary artery disease[a]	1.8 (1.2–2.8)	2.2 (1.5–3.3)
Diabetes mellitus	1.5 (1.1–2.1)	2.4 (1.7–3.4)
Hypertension	1.6 (1.2–2.0)	1.7 (1.2–2.4)
Congestive heart failure	1.2 (0.7–2.2)	1.1 (0.4–2.4)

BMI, body-mass index; CI, confidence intervals; OR, odds ratio; PAD, peripheral arterial disease. [a]Myocardial infarction or angina.

Fig. 2



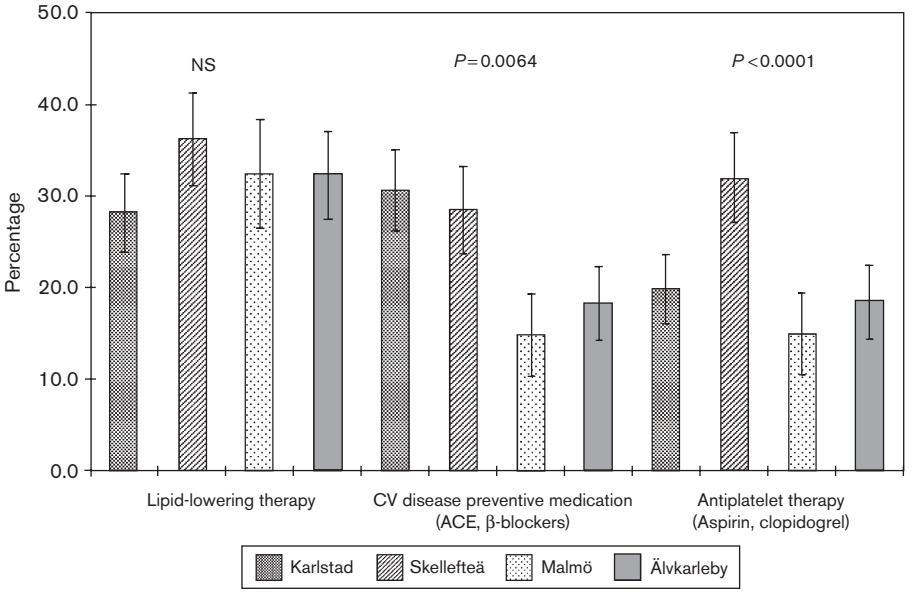
Prevalence (95% confidence interval) of smoking habits in the total study cohort (*N*=4926, open bars represent women and filled bars men, *P* values according to test of equal proportions comparing men and women). NS, nonsignificant.

Table 4 Relationship between sex medication use adjusted for age and PAD

	Lipid-lowering therapy, OR (95% CI)	Cardiac preventive therapy, OR (95% CI)	Antiplatelet therapy, OR (95% CI)
Sex	Reference category		
Women			
Men	1.3 (1.1–1.5)**	1.4 (1.1–1.8)*	1.6 (1.3–2.1)***

CI, confidence intervals; OR, odds ratio; PAD, peripheral arterial disease. *0.05> *P* value >0.01; **0.01> *P* value >0.001; ***P value <0.001.

Fig. 3



Medication use among patients with peripheral arterial disease and/or coronary artery disease separated by region ($N=1379$, P values according to χ^2 test comparing regions). ACE, angiotensin-converting enzyme; CV, cardiovascular; NS, nonsignificant.

this association was 1.7 (1.2–2.4) and for CLI it was 4.2 (1.7–10.6). The association between smoking and PAD did not appear for men unless their smoking habits continued for at least 30 years.

Use of drugs with a potential of preventing cardiovascular disease was more common among men than women, with an OR of 1.3 (range 1.1–1.5) for lipid-lowering therapy, 1.3 (range 1.1–1.8) for β-blockers and/or ACE inhibitors and 1.6 (range 1.3–2.1) for antiplatelet therapy (asprin or clopidogrel); an OR of 1.4 (range 1.1–1.8) for β-blockers and/or ACE inhibitors and 1.6 (range 1.3–2.1) for antiplatelet therapy (Table 4).

The prevalence of PAD differed between the regions used in the study. It ranged from 14.0% (12.6–15.5) in region B to 21.8% (20.0–23.6) in region A. The extent of reported risk factors associated to PAD also displayed regional differences. Significantly ($P < 0.001$) more participants in region D with BMI greater than 25 (45.2%, 42.5–47.9) and DM (13.3%, 11.4–15.1) than in region A (38.1%, 35.6–40.6, and 7.8%, 6.4–9.2, respectively) were observed. The proportion of participants with a smoking history longer than 30 years varied from 14.0% (12.2–15.7) in region B to 23.7% (20.9–26.5) in region C. Antiplatelet drug use was much more widespread in region B than in the other regions, and use of lipid-lowering therapy was reported more frequently by individuals in region B and region A than in regions C and D (Fig. 3).

Discussion

This analysis, to our knowledge the first ever reported covering all three PAD stages, has identified certain features that may explain the rather high prevalence of 18% in elderly populations. It also provides new information on concomitant vascular diseases, medication use and gives some indirect evidence that pharmacological cardiovascular risk prevention may be beneficial in reducing PAD occurrence.

Information on whether PAD occurs in an isolated condition or in combination with other manifestations of cardiovascular disease is important when trying to increase PAD awareness and prevent cardiovascular events [15,16]. In this study other manifestations of cardiovascular disease were twice as common in PAD patients compared with those without, emphasizing the well-known link between PAD and atherosclerosis. Our data also suggest that a large proportion of participants with PAD may be unknown to primary care physicians. Almost half of the PAD patients did not have known cardiovascular disease and only a minority reported use of preventive medication. Accordingly, despite a high cardiovascular risk a large proportion of the patients do not present with a history pointing toward a PAD diagnosis or other cardiovascular manifestations. These findings can thus be interpreted as support for a screening program using ABI measurements to identify individuals in need of preventive measures [17].

Overall, the risk factors with an association with PAD in this study were consistent with an earlier report [2]. The higher prevalence of DM (37 vs. 17% in our) and HTN (62 vs. 47% in our) in PAD patients in that study can probably be explained by differences in populations. The cohort in Diehm *et al.*'s study came from patients seeking care for other diseases at primary care centers and was not strictly population based. Compared with the National Health and Nutrition Examination survey we observed twice as many patients with coronary artery disease, a difference that can be explained by our patients being older. That DM was rare in our cohort compared with the National Health and Nutrition Examination survey could be a consequence of their intended over-sampling of Mexican–American and African–American populations known to have a high prevalence of DM [18].

We expected that multiple and higher proportions of cardiovascular risk factors would be observed in patients with more severe PAD. In line with this, long-time smoking, high age, and concomitant coronary artery disease were strongly associated with CLI. For APAD and IC our data were similar to findings from the Limburg study [19]. Interestingly, our IC patients had a stronger association with DM than the other stages. This finding could be because of over-reporting of leg symptoms caused by neuropathy among DM patients or a higher awareness of leg problems among patients and physicians. It could also be a finding by chance because only a few patients had IC and DM.

A remarkable finding, not reported earlier, to our knowledge, was that smoking for less than 30 years was not associated with having PAD in the total population. Depending on predisposition for arteriosclerosis development it may take a certain number of years of smoking to develop PAD when the age factor is accounted for. Another explanation is that the duration of tobacco use was under-reported in our cohort. Surprisingly, the relationship between smoking duration and PAD is not clear in the literature. A recent study from Norway focusing on CLI, for example, reported no relationship between having PAD and current or former cigarette smoking habits [20].

In our patients HTN was associated with APAD and IC but not with CLI. Very old patients with multiple diseases using numerous medications dominated the CLI group. This suggests that under-reporting explains the low frequency of HTN for this group. Furthermore, CLI was the only stage with a strong association with congestive heart failure, indicating that a substantial number of the participants in this group had a low systemic blood pressure, which could contribute to both less HTN and decreased leg perfusion.

Obesity was common among patients with IC. Obesity could be a consequence of impaired walking ability, and it may *per se* also have contributed to more extensive arteriosclerosis because of patients' reduced ability to exercise [21].

Use of cardiovascular risk preventive medication is generally well accepted in the health-care community [6,22,23]. Already in 1997, Mc Dermott *et al.* [24] reported more intensive drug treatment in patients with coronary artery disease than in PAD patients, despite their similar risk for cardiovascular disease. In our report this discrepancy still remains and only a minority of patients with PAD used drugs preventing cardiovascular risk, emphasizing a continued need for improvement in this area. Several possible explanations for the rather low rate of medication use are observed. The strong relation between PAD and cardiovascular morbidity may not be evident to all physicians [15] and understanding of PAD is still limited [9]. Implementation of preventive programs may also be inadequate because of lack of resources.

Sex differences in risk factors related to PAD were apparent in our cohort. Although APAD and CLI were more common among women, the prevalence of IC was similar or slightly more common among men [1]. The explanation may be that IC is the only stage relying on perception of symptoms for diagnosis [25]. The latter can be sex-specific and women may not be diagnosed because a higher frequency of atypical IC symptoms [26]. In concordance with the ARIC Study men with APAD displayed a stronger association with stroke and coronary artery disease than women [27]. More men are known to have atherosclerotic manifestations than women and it is possible that the awareness of women's risk for cardiovascular disease in PAD is low [28,29]. Women also seemed to be more sensitive to tobacco exposure. We observed a strong age-independent relationship with PAD after 10 years of smoking for women, an association that did not appear until after 30 years in men. This finding seems plausible considering differences in body size and composition, as well as the influence of hormonal status that is known to play a role in the atherosclerotic process. For example, it is reported that women smoking even for short periods of time are at risk for early menopause, a known risk factor for arteriosclerosis and PAD development [30,31]. Accordingly, it is possible that smoking influences PAD development in a sex-dependent manner [32]. This information is important considering the smoking habits in many countries today, where young women are the most common smokers [20,33]. Although many PAD patients in this study did not use appropriate risk preventive medication, this observation was particularly valid for women. Men used medication more frequently, a difference that showed in all PAD stages, except for antiplatelet therapy in the CLI group. A similar sex difference has also been reported in patients with coronary artery disease [34].

The variation in PAD prevalence between the regions used in SPPS may be explained by demographic differences other than age and sex differences, which were accounted for [1]. The mid-sized city that consisted of patients with a large proportion of white-collar workers had the largest prevalence of APAD, whereas the area with a high proportion of immigrants (region C) and the small town of factory workers (region D) had a high prevalence of IC and CLI, respectively. These regions also displayed disproportionate rates of concomitant DM and patients with a smoking history. The rural area (region B) had the lowest PAD prevalence in SPPS. In this area cardiovascular risk awareness programs were initiated in the mid 1980s [35]. Increased awareness in this region may have improved diets and exercise habits, and use of more preventive medication therapy may explain this. Together, these observations encourage awareness programs and aggressive risk factor management.

Several limitations of this study are observed. Risk factors and medications were self-reported, which could lead to underestimations of occurrence and use. This could certainly influence the reported smoking habits, but the notion of poor reliability of self-reported smoking history is contradicted by data from a meta-analysis in which the sensitivity was found to be 88% and the specificity 89% [36].

In conclusion, the patients' risk factor profile differed among the PAD stages and 40% of those with PAD did not report any cardiovascular risk factor. Smoking duration seemed to be a risk factor after less extensive smoking for women than men; fewer women used preventive medication. These observations may explain the observed sex differences in PAD prevalence. Aggressive use of preventive measures seems to have resulted in less PAD. The clinical implications of these findings are several. The data emphasize that the classical PAD patient – a male smoker with additional known risk factors – is not very common. A large proportion consists of rather healthy females who never have smoked. Furthermore, PAD patients, in particular women, seem to be undertreated with preventive drugs and increased awareness and more aggressive management is desirable.

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