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The Prevalence of Asymptomatic and Unrecognized Peripheral Arterial Occlusive Disease

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Stoffers H E J H (Department of General Practice, University of Limburg, PO Box 616, NL-6200 MD Maastricht, The Netherlands), Rinkens P E L M, Kester A D M, Kaiser V and Knottnerus J A. The prevalence of asymptomatic and unrecognized arterial occlusive disease. *International Journal of Epidemiology* 1996; **25:** 282–290.

Background. The prevalence of peripheral arterial occlusive disease (PAOD), including asymptomatic cases and cases unknown to the general practitioner (GP) was estimated in 18 884 men and women, aged 45–74 years, on the list of 18 general practice centres (GPC).

Methods. The study population (n = 3171) consisted of a stratified sample of the total population. In the GPC data were collected on intermittent claudication (IC), peripheral pulses, vascular risk factors, cardio- and cerebrovascular disease (CCVD) and the ankle brachial systolic pressure ratio (AB ratio) and PAOD was defined as an AB ratio <0.95 on two consecutive occasions. Results were recalculated for the total population.

Results. The prevalence of PAOD was 6.9% (95% confidence interval [CI] : 5.7–8.2%), of which one-third (2.2%) had an AB ratio <0.75. The prevalence of IC was 6.6% (95% CI : 5.2–7.9%), a quarter of which (1.6%) met the classic WHO criteria. Peripheral arterial occlusive disease did not occur significantly more often among men than among women but men suffered more often from an advanced stage of PAOD. Of all PAOD cases, 22% were symptomatic. The proportion of symptomatic cases correlated positively with higher age, male gender and lower AB ratio. Among asymptomatic PAOD cases the prevalence of concomitant CCVD was three to four times as high as in the group of subjects without PAOD. Of all PAOD cases 68% were unknown to the GP and this group mainly represented less advanced cases of atherosclerosis. However, among PAOD cases with an AB ratio <0.75, 42% were unknown to the GP.

Conclusions. Our data on asymptomatic and unknown PAOD cases show that GPs can still enhance their efforts towards (secondary) prevention of atherosclerosis.

Keywords: peripheral arterial occlusive disease, intermittent claudication, non-invasive testing, epidemiology, general practice, prevalence

Peripheral arterial occlusive disease (PAOD) is one of the many terms used to describe the manifestation of atherosclerosis below the bifurcation of the abdominal aorta. Due to ageing of the population in western societies, the prevalence of atherosclerotic disease will rise and the diagnostic and therapeutic management (adequate diagnosis, regular follow-up, conservative therapy, preventive measures, selection for referral, post-surgical follow-up) of this chronic disease will become more important to general practitioners (GPs).[1–4]

Figures on the prevalence of PAOD vary, depending on diagnostic criteria and the study population. In many studies on PAOD the WHO questionnaire on intermittent claudication has been used,[5–12] but in a number of population studies non-invasive diagnostic techniques were applied.[13–19] In the latter studies symptomatic as well as asymptomatic cases of PAOD were observed.

General practice registrations include patients who present with complaints of intermittent claudication to their GP.[20–22] Such figures depict the workload this chronic condition entails for primary health care. They also indicate the prior probability of intermittent claudication, which is an important diagnostic tool for the GP. On the other hand, data from population studies demonstrate the total extent of the burden a disease could impose on the health care system.

A review of these studies suggests that only a minority of all PAOD patients are recognized as such in primary health care (the tip of the iceberg).[2,23] It is unclear whether the unknown cases of PAOD represent a subcategory of patients with atherosclerosis to whom the GP should pay more attention, either for therapeutic or preventive reasons.

A second conclusion may be that there is a large group of asymptomatic or atypical patients with

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PAOD.[2,23] The prognostic importance of asymptomatic PAOD was recently demonstrated by the results of a longitudinal study showing that not only symptomatic patients, but also asymptomatic subjects had a higher cardiovascular mortality as compared to subjects without PAOD.[24]

Review of the literature also raised the question whether the idea that PAOD as a predominantly male disease is correct.[2,23] In this respect population studies using non-invasive methods appear to produce results that differ from the outcome of studies on intermittent claudication.

The aim of the present study was to estimate the prevalence of PAOD in a population of middle-aged and elderly men and women. We were especially interested in the proportion of asymptomatic disease and in the number of PAOD cases 'unknown' to the GP. We also investigated the association of PAOD with cardio- and cerebrovascular disease.

METHODS

Background

The Limburg PAOD Study is a research project conducted by the University of Limburg in Maastricht (the Netherlands) and a number of general practice centres in the region. This project consists of three interrelated elements: a prevalence study, a diagnostic study and an intervention study (using aspirin).[3,25] The results of the prevalence study are presented here.

General Design

In the Netherlands every subject is registered in a general practice. Therefore, the registered population of a general practice is a segment of the general population. From a list of 18 general practice centres, all subjects were identified who were aged 40–75 years (source population). These subjects received a postal screening questionnaire with five yes/no questions: pain on walking, smoking $\geq$15 cigarettes per day, known high blood pressure, diabetes, heart disease or transient ischaemic attack (TIA)/stroke. Thus, the responders (base population) could be characterized by a 'prior risk score' between 0 and 5.

The study population was constructed through a complex stratified sampling procedure, which was necessary to meet the demands of the three studies mentioned above in an efficient way. First, a random sample was drawn from the category of responders with a prior risk score of 0 and another random sample was drawn from the subpopulation with a prior risk score of 1–5. Subsequently, from the remaining subjects in the latter category of responders, those with the highest risk score were selected (score 5, 4, 3 and sometimes 2). These three samples formed the population which was invited to participate in the study. Data were collected from those subjects who agreed to participate (study population). Results were recalculated for the base population.

Data Collection

Each participant filled in an extensive questionnaire which incorporated the WHO questionnaire on intermittent claudication.[5] The questionnaire also contained questions on smoking habits.

Subsequently, the participant visited his GP, who performed a physical examination (palpation of the pedal and femoral pulses, auscultation of the femoral artery) and copied relevant data from the patient record to the registration form (presence of peripheral, cardio- or cerebrovascular disease, hypertension, hypercholesterolaemia, diabetes mellitus). After this physical examination the GP had to state whether he thought PAOD (i.e. intermittent claudication) was currently present (GP's diagnosis).

Without knowing the results of the GP's examination, the practice assistant measured the ankle brachial systolic pressure ratio (AB ratio) of both legs using a hand-held Doppler device (Huntleigh Mini Dopplex D500, 8MHz) and a mercury sphygmomanometer.[1,26] Systolic pressures were recorded on both arms and ankles (posterior tibial artery or, if absent, the dorsalis pedis artery) with the subject lying in a supine position.

The AB ratio was defined as the systolic pressure at the ankle divided by the highest systolic arm pressure. If the AB ratio of at least one leg was $<$0.95, the patient was requested to return for a second measurement one week later. All sphygmomanometers were calibrated before the start of the study. The GPs and practice assistants had been trained in performing AB ratio measurements. In a previous study the reproducibility of these measurements had proved to be satisfactory.[27]

Further Definitions

PAOD according to patient record: a subject was already known to the GP as suffering from PAOD. *Specialist care*: known patients who had experienced percutaneous transluminal angioplasty (PTA), vascular surgery or an amputation. *Ischaemic heart disease (IHD)*: the patient record mentioned the diagnoses angina pectoris, coronary ischaemia or myocardial infarction. *Cerebral arterial disease (CeAD)*: the patient record mentioned carotid stenosis, TIA, or stroke.

Intermittent claudication (IC): (1) *definite IC*: pain or discomfort in the calf when walking (at an ordinary pace on the level or uphill or when in a hurry), never beginning when standing still or sitting.[28,29] This category included (1a) *Rose-IC*: definite IC, restricted to pain and meeting two extra criteria: 'pain not disappearing while walking' and 'you stop or slow down when you get it',[5] and (1b) *pain/discomfort, not Rose*: definite IC, not meeting both extra criteria. (2) *only non-calf IC*: absence of definite IC, but presence of non-radiating pain or discomfort in buttock, thigh or foot, and otherwise meeting the overall criteria for definite IC.

The *pedal pulses* (posterior tibial artery and dorsalis pedis artery) were called abnormal if both pulses were absent or weak, or if one pulse was absent and the other one weak. Other positive test results were absence of the *femoral artery pulse* and presence of a *femoral bruit*.

PAOD: an AB ratio <0.95 on two consecutive occasions. This cutoff value was a balanced choice between the specific cutoff value of 0.90 and the sensitive cutoff value of 1.0 as reported in studies on the validity of the Doppler method.[30–35] This relatively high cutoff value was chosen because in primary care a sensitive cutoff value is more important than in the specialist's setting, where a high specificity (i.e. a lower cutoff value) is desired. *Symptomatic PAOD*: The combination of an AB ratio <0.95 with IC (definite and non-calf). *Asymptomatic PAOD*: the combination of an AB ratio <0.95 with no symptoms of IC. *Known PAOD*: the combination of an AB ratio <0.95 with 'PAOD according to patient record'.

Some analyses also were carried out at lower cutoff values for the AB ratio: <0.75, where a stenosis or occlusion is definitely present and PTA might be appropriate; values <0.50, which indicate that multiple occlusions are probable and surgical intervention might be considered.[1]

Statistical Analysis

Due to the time period that had passed between the postal questionnaire and GP's examination, the youngest 40–44 years) and oldest age category (≥75 years) were incomplete. These age categories were excluded from the analysis.

The study population and the base population were divided into strata defined by the variables age (45–54, 55–64, 65–74), gender (male, female) and prior risk score (0–5). Prevalence figures for the base population were recalculated as appropriately weighted means of stratum-specific prevalences. The 95% confidence intervals (CI) were based on normal approximation and *P*-values for differences in prevalence figures were calculated using an unpaired two-sample t-test.

RESULTS

Populations

The source population consisted of 26 620 subjects (male: 47.5%) with a mean age of 56.5 years (SD: 9.8 years). The number of subjects that returned the postal questionnaire was 23 004 (86.4%). The distribution of age and gender in the population of responders was the same as in the source population.

As a result of the sampling procedure 5301 subjects were invited to partake in the study. The participation rate was 68.9% (3654 participants aged 40.7–78.3 years). Non-participation had various reasons: subjects had died, had moved, or were absent due to protracted admission to a hospital or nursing home (17.5% of the non-participants); there were medical or practical reasons according to the GP (11%); or subjects showed no interest (48%). For a quarter of the non-participants the reason remained unknown.

Data analysis was restricted to the 3171 participants (male: 47.2%) aged 45–74 years (mean: 59.8 years, SD: 8.0 years). Frequencies found in this population were used to calculate the prevalence figures for the 18 884 subjects (male: 47.3%) in the base population, who were aged 45–74 years (mean: 58.6 years, SD: 8.1 years).

Registered Atherosclerotic Morbidity

Table 1 presents the recalculated prevalence of various manifestations of atherosclerotic disease as registered in the patient records of the GPs. Among men the prevalence of registered atherosclerotic morbidity was significantly higher than among women. The proportion of cases of PAOD according to the patient record, who had experienced PTA, vascular surgery or an amputation was 52% among men and 25% among women.

Current Signs and Symptoms of PAOD

Table 2 shows the prevalence figures of clinical signs and symptoms associated with PAOD, as recalculated based on the population survey.

The prevalences of IC, abnormal pedal pulses and a femoral bruit increased with rising age. Women more often met the Rose criteria for IC than men. The figures on clinical signs and symptoms did not demonstrate an unequivocal male predominance.

Nonetheless, GPs diagnosed PAOD more often among men than among women (Table 2). This difference was significant in the two oldest age categories. A preliminary analysis showed that GPs more

TABLE 1 *Prevalence of atherosclerotic disease as registered by general practitioners (recalculated to n = 18 884, 47.3% men; age 45–74 years, mean age 58.6 years)*

Atherosclerotic disease	Prevalence (95% CI) %	Prevalence by gender (95% CI) %	Male/ female ratio
PAOD according to patient record[a]	3.8 (2.9–4.6)	m 5.9 (4.2–7.6) f 2.1 (1.3–2.9)	2.8
—of which had experienced specialist care[a]	1.6 (1.0–2.2)	m 3.0 (1.6–4.5) f 0.5 (0.1–0.9)	5.8
Ischaemic heart disease (IHD)[a]	10.8 (9.5–12.1)	m 15.6 (13 0–18.1) f 6.9 (5.6–8.2)	2.3
Cerebral arterial disease (CeAD)[a]	3.4 (2.4–4.4)	m 5.2 (3.2–7.3) f 2 0 (1.0–2.9)	2.6

[a] For definitions: see text.

TABLE 2 *Prevalence of clinical signs and symptoms associated with peripheral arterial occlusive disease (PAOD) (recalculated to n = 18 884, 47.3% men; age 45–74 years, mean age 58.6 years)*

Signs and symptoms[a]	Prevalence (%), total (95% CI)	Male/female ratio	Prevalence in % (95% CI)		
			45–54 years (m = 3474, f = 3590)	55–64 years (m = 3381, f = 3735)	65–74 years (m = 2071, f = 2633)
Intermittent claudication questionnaire, all	6.6 (5.2–7.9)	1 2	m 3.7 (1.0–6.4) f 5.7 (2.4–9 1)	9.2 (5 5–12 8)[b] 4.9 (2.6–7.3)	10.1 (5.7–14.6) 8 2 (4.3–12 1)
definite	5.3 (4.2–6.5)	1.3	m 2.8 (0.4–5.3) f 2.8 (0.7–4 9)	8.4 (4.7–12 0)[b] 4.6 (2.3–6.9)	8.8 (4.4–13.2) 7.5 (3.6–11.4)
Rose	1.6 (0 9–2 2)	0.6	m 0.5 (0.2–0.9) f 0.3 (0.1–0.5)	0.9 (0.5–1 3) 2.2 (0.4–4.1)	2.4 (1.5–3.3) 3.7 (0.3–7.0)
pain/discomfort not Rose	3.7 (2.7–4.7)	1.8	m 2.3 (0–4.7) f 2.5 (0.4–4.6)	7.5 (3.9–11.1)[b] 2.3 (0.9–3.7)	6.4 (2.1–10.8) 3.8 (1 6–5.9)
only non-calf	1 2 (0.6–1.9)	0.7	m 0 9 (0–2.0) f 2.9 (0.3–5.6)	0.8 (0.4–1.2) 0.4 (0.1–0.7)	1.3 (0.6–2.0) 0.7 (0.2–1.2)
Abnormal pedal pulses	8.0 (6.5–9.5)	0.8	m 2.7 (0.2–5.1) f 5.6 (2.6–8.6)	6.6 (3.8–9.4) 8 3 (4 9–11 6)	17.6 (11.3–23.8) 13.8 (8.4–19.2)
Absent femoral pulse	1.0 (0.5–1.5)	0.5	m 0.2 (0–0.5) f 1.8 (0–3 5)	0.3 (0.1–0.6) 1.3 (0.2–2.3)	2.1 (0–4.7) 0.8 (0.3–1.3)
Femoral bruit	4.5 (3.6–5.9)	1.4	m 2.0 (0.8–3 3) f 2.2 (0.4–4.0)	6.2 (3.2–9 2) 4.3 (1.9–6.8)	9.5 (5.3–13 7) 6.8 (2.6–11.1)
GP's diagnosis	2.7 (2.0–3.3)	3 0	m 1.4 (0.2–2.6) f 0.8 (0–1.9)	3.7 (1.8–5.6)[b] 1.0 (0.6–1.4)	10.6 (5 6–15.5)[b] 2.9 (2.0–3.7)

[a] For definitions: see text.
[b] $P < 0.05$ for differences between men and women in the same age category (unpaired two sample t-test).

often established a positive GP's diagnosis among men with registered IHD than among women with a diagnosis of IHD: 11% versus 8%. The sensitivity of a positive GP's diagnosis for the presence of an AB ratio <0.95 appeared to be 42% for men and 13% for women (overall 27%); for an AB ratio <0.75 these figures were 54% and 40% respectively (overall 51%).

Non-invasive Testing

The mean AB ratio in the base population was 1.08 (men: 1.10, women: 1.07). The total prevalence of PAOD (an AB ratio <0.95 on two occasions) among women (6.5%; 95% CI : 4.8–8.2) was not significantly lower than the prevalence in men (7.2%; 95% CI : 5.5–9.0). Table 3 provides the prevalence figures of PAOD for the various ages and gender categories.

TABLE 3 *Prevalence of peripheral arterial occlusive disease (PAOD) according to non-invasive testing (recalculated to n = 18 884, 47.3% men; age 45–74 years, mean age 58.6 years)*

Category	Prevalence in % (95% CI)	Male/female ratio		Prevalence in % (95% CI)		
				45–54 years (m = 3474, f = 3590)	55–64 years (m = 3381, f = 3735)	65–74 years (m = 2071, f = 2633)
PAOD, total[a]	6.9 (5.7–8.2)	1.1	m	1.6 (1.0–2.1)	7.7 (4.9–10.6)	16.4 (10.6–22.3)
			f	3.1 (1.0–5.2)	6.8 (3.8–9 7)	11.2 (7.0–15.3)
symptomatic cases (IC[c] present)	1.5 (1.1–1.9)	3.3	m	0.5 (0.1–0.8)	3.1 (1.3–5.0)[b]	4.8 (2 0–7 5)[b]
			f	0.3 (0–0.5)	0.6 (0.2–0.9)	1 7 (1 0–2.4)
concomitant IHD[d]/CeAD[e]	2.4 (1.9–3.0)	2.6	m	0.6 (0.3–1.0)[b]	3.4 (1.9–4.8)[b]	8.9 (4.9–13.0)[b]
			f	0.1 (0–0.3)	1.6 (0.6–2.7)	3.0 (1.4–4.7)
known cases	2.2 (1.6–2.8)	2.5	m	0.7 (0.3–1.1)	2.8 (1.4–4.2)[b]	8.7 (4 0–13.4)[b]
			f	0.7 (0–1 7)	0.9 (0 5–1.3)	2.9 (1.3–4.5)

[a] 2 × AB ratio <0.95. The AB ratio was defined as the systolic pressure at the ankle divided by the highest systolic arm pressure.
[b] $P < 0.05$ for differences between men and women in the same age category (unpaired two sample t-test).
[c] Intermittent claudication.
[d] Ischaemic heart disease.
[e] Cerebral arterial disease.

The prevalence of PAOD increased with rising age. In the youngest age group the prevalence among women was higher, in the oldest age category the prevalence among men was higher. These gender differences were not statistically significant. However, the figures on symptomatic cases, cases with concomitant IHD or CeAD and known cases, indicated that the proportion of cases with manifest atherosclerosis was evidently higher among men. Also the proportion with an AB ratio <0.75 was larger among men (Table 4).

Table 4 shows the proportions of symptomatic cases, cases with concomitant IHD or CeAD and known cases at two cutoff values for the AB ratio (0.95 and 0.75). All proportions were larger at the cutoff value of 0.75.

The prevalence of PAOD was higher in patients with a registered diagnosis of hypertension, hypercholesterolaemia or diabetes mellitus. Smoking, currently or in the past, also increased the probability of PAOD being present (Table 5).

Symptomatic and Asymptomatic PAOD

Of all PAOD cases 22% were symptomatic. Of these symptomatic cases 75% were male, 49% belonged to the oldest age group, 69% had an AB ratio <0.75, 12% had an AB ratio <0.50. The proportion having concomitant IHD was 33%, CeAD 6%.

On the other hand, of the asymptomatic cases only 43% were male, 22% had an AB ratio <0.75 and 2% had an AB ratio <0.50. The age distribution was shifted only slightly to the younger age groups (oldest age group 47%) as compared to the symptomatic cases. The proportion having concomitant atherosclerosis also did not differ much from the symptomatic cases (IHD 29%, CeAD 12%).

PAOD and Concomitant Arterial Disease

The total prevalence of ischaemic heart disease in the base population was 10.8% (Table 1). If PAOD was present (AB ratio <0.95) the probability of IHD increased to 29.6%. In the subcategory of PAOD patients with an AB ratio <0.75, the prevalence of IHD was 49.6%. If PAOD was absent (AB ratio ≥0.95) the probability of IHD was 9.3%.

The total prevalence of cerebral arterial disease was 3.4% (Table 1). If PAOD was present the probability of CeAD increased to 11.0%. In the subcategory of PAOD patients with an AB ratio <0.75, the prevalence of CeAD was 13.1%. If PAOD was absent the probability of CeAD was 2.8%.

In reverse, the prevalence of (symptomatic and asymptomatic) PAOD was 19.1% among patients with IHD and 22.5% among patients with CeAD. If IHD or CeAD were absent these figures were 5.4% and 6.3% respectively.

Known and Unknown Cases of PAOD

Of all cases of PAOD (AB ratio <0.95), 32% were known as such to their GP; in general this proportion was larger when the AB ratio was lower (Tables 3 and 4). Of these known cases, 69% were male, 60% were ≥65 years and 60% had concomitant cardio- or cerebrovascular disease. Complaints of intermittent claudication (symptomatic PAOD) were present in 37% of the known cases of PAOD. The proportion of known

TABLE 4 *Characteristics of peripheral arterial occlusive disease (PAOD) at two cutoff values[a] for the AB ratio[b] (recalculated to n = 18 884, 47.3% men; age 45–74 years, mean age 58.6 years)*

Gender	Cutoff value AB ratio	Prevalence in % (95% CI)	Proportion		
			symptomatic	concomitant IHD[c]/CeAD[d]	known
Men	0.75	3 4 (2.2–4.6)	53%	57%	58%
	0.95	7.2 (5.5–9.0)	34%	50%	46%
Women	0.75	1 3 (0.8–1.8)	32%	46%	57%
	0.95	6 5 (4.8–8.2)	11%	22%	20%
All	0.75	2.2 (1.7–2.8)	47%	54%	58%
	0.95	6 9 (5 7–8.2)	22%	35%	32%

[a] Due to sparse data in the study population for the age categories 45–54 years and 55–64 years, the results for an AB ratio <0.50 are not presented.
[b] The AB ratio is the systolic pressure at the ankle divided by the highest systolic arm pressure.
[c] Ischaemic heart disease.
[d] Cerebral arterial disease.

TABLE 5 *Prevalence of peripheral arterial occlusive disease (PAOD) in various vascular risk groups (recalculated to n = 18 884, 47.3% men; age 45–74 years, mean age 58.6 years; prevalence of PAOD 6.9%)*

Risk indicator	Prevalence of risk indicator in % (95% CI)	Probability of PAOD in % if		Relative risk[a]
		indicator present	indicator absent	
Hypertension	24.2 (22.0–26.4)	13.3	4.8	2.8
Hypercholesterolaemia	8.7 (7 1–10.3)	12.4	6.2	2.0
Diabetes mellitus	5.6 (4.6–6.7)	20.5	6.2	3.3
Smoking				
ever	65.4 (62.3–68.4)	8.0		1.7
current	36.7 (33 8–39.5)	8.7	4.8	1.8
stopped	28.7 (25.8–31.6)	7 2		1.5

[a] Bivariate relative risk.

cases with an AB ratio of ≤0.75 was 59%, while an AB ratio of ≤0.50 occurred in 5% of known cases.

Of the unknown PAOD cases, 60% were female, 58% were <65 years, only 24% had concomitant cardio- or cerebrovascular disease and only 15% were symptomatic. The proportion of unknown cases with an AB ratio of ≤0.75 was 20% and an AB ratio of ≤0.50 occurred in 4% of the unknown PAOD cases.

The probability that a patient with PAOD was known as such to his GP was higher when he had complained of IC (53% of the symptomatic cases were known against 26% of the asymptomatic cases), also suffered from other atherosclerotic disease (53% of the cases with concomitant IHD or CeAD were known against 20% of cases without concomitant manifestations of atherosclerosis) and was older than 65 (40% of the cases who were 65–74 years of age were known against 28% in the age group 45–54 and 24% in the age group 55–64). The proportion of known cases of PAOD among men was higher than among women (Table 4).

DISCUSSION

In this population study the prevalence of PAOD (an AB ratio <0.95 on two occasions) in the age group 45–74 years was 6.9% of which one-third (2.2%) had an AB ratio <0.75. About two-thirds of all PAOD cases appeared to be unknown to the GP. In only one-fifth of all PAOD patients IC was present. The overall prevalence of PAOD was only slightly higher among men, but symptomatic PAOD and concomitant IHD or CeAD occurred significantly more often in the male subpopulation. Prevalence figures were higher when clinical risk indicators were present.

Prevalence Figures

Our figures for the prevalence of IC (Table 2) were in the range of results reported by others (0.6–6.1%; men 1.1–7.0%, women 0.7–7.4%).[7,10–14,16–18,36,37] Our results for Rose IC were on the low side of this range. Our figures for the prevalence of abnormal pedal pulses (8%) were also within the range reported by others (3.2–18%).[13–15]

We demonstrated how prevalence figures for IC can vary when different definitions of IC are applied to the same population. Our definitions permit comparison with studies in which the classic WHO/Rose questionnaire or a modern version of this questionnaire was used.[5,28,29] There is a need for an international consensus on the use of questionnaires on IC for epidemiological research on PAOD.

Population-based prevalence studies on PAOD applying non-invasive testing can be divided in two groups: those in which a certain cutoff value of the AB ratio was used as the criterion for PAOD (cutoff values between 0.75 and 0.95) and those in which more extensive tests were performed. This study is an example of the first category. We did not use the reactive hyperaemia test. Its application on a large scale is less feasible in general practice: one session takes about 30–45 minutes and is often painful for the patient. Furthermore, its reproducibility was reported to be less than the reproducibility of the measurement of the resting AB ratio.[4,15,38–42] Our prevalence figures (Tables 3 and 4) were within the range of results found by other authors (3.4–14.3%).[13,15,17,18,43,44] In the study by Coni *et al.*, the prevalence of an AB ratio <0.75 was 9.1% among 264 subjects aged 66–96 years.[17] Using this cutoff value in our younger population a prevalence of 5.5% was found.

In a second group of studies prevalence figures were reported to be 11.7%, 13.7% and 8% (grossly abnormal) to 25% (moderately and grossly abnormal).[14–16] It should also be noted that in Hiatt *et al.*'s study 87% of all PAOD cases were discovered using only the AB ratio at rest (cutoff value 0.94).[15]

(A)symptomatic Cases

The overall proportion of symptomatic cases was 22% and correlated with age, gender (women: 11%) and AB ratio (Tables 3 and 4). Asymptomatic cases of PAOD differed from symptomatic PAOD cases with regard to gender (more women) and AB ratio (more higher values), but age distribution and prevalence of concomitant arterial disease did not differ much. Compared to the subpopulation of subjects without PAOD the prevalence of concomitant arterial disease was three to four times as high in the subpopulation with asymptomatic PAOD.

A similar observation was made in the Edinburgh artery study, where ischaemic heart disease occurred 1.6 times as often among asymptomatic PAOD cases as compared to subjects without PAOD.[16]

Newman *et al.* demonstrated that asymptomatic patients with modest reductions in the AB ratio (0.8–1.0) appeared to be at increased risk of cardiovascular disease. They found that the occurrence of a carotid plaque, major ECG abnormality, angina pectoris and myocardial infarction was significantly higher among subjects with an AB ratio between 0.9 and 1.0 as compared to subjects with an AB ratio above 1.0.[18]

Gender

In two studies no significant gender differences were found with regard to AB ratio.[13,17] The results of Fowkes *et al.* were similar to ours: a higher mean AB ratio but a larger proportion with an AB ratio <0.80 for men.[16]

In our study the overall prevalence of PAOD among men was slightly higher than among women but in the age category 65–74 years the gender difference was more apparent. The results of non-invasive testing in two other studies were comparable to ours: PAOD occurred about 1.3 times more often among men.[14,16] An Italian study using non-invasive testing revealed a gender ratio of 1.4–2.0.[43] In the age group 65–74 years Criqui *et al.*, using extensive non-invasive testing, found a prevalence among men of 12–19%, among women of 12%.[14]

However, we could demonstrate that manifest atherosclerosis (i.e. symptomatic PAOD, IHD, CeAD) and an advanced stage of PAOD (more lower AB ratios, more surgical interventions) occurred significantly more often in men than in women. A higher prevalence of symptomatic PAOD (AB ratio <0.90, IC, pulses absent) among men was also found in a Scandinavian study (3.3% versus 1.0%).[13]

Unknown Cases

In their review Dormandy *et al.* concluded that probably at least half of all patients with intermittent claudication are unknown.[45] In our study two-thirds of all PAOD cases were not known in primary care. A British population study in which the patients of two general practices were asked to participate, disclosed that only half of all those with complaints of claudication had consulted a doctor.[6]

As compared to the subpopulation, 'known' cases of PAOD, the group 'unknown' PAOD cases could be characterized as having more females, was younger, and was associated with less complaints of IC, higher

AB ratios and less concomitant arterial disease. It follows that this 'unknown' group mainly represents less advanced cases of PAOD. However, even in the group of PAOD cases with an AB ratio <0.75, two-fifths of all cases appeared to be unknown to the GP.

Practical Implications

Should the GP pay more attention to his unknown PAOD patients? Possibly many patients accept leg complaints as a normal feature of ageing or adapt their activities to their capabilities. Furthermore, complaints of IC may improve in the course of time.

Certainly PAOD is known to have a favourable prognosis in many cases, but life expectancy is reduced owing to the increased risk of cardio- and cerebrovascular mortality. Therefore presence of PAOD should be regarded as an important indicator of this risk. The group of unknown cases mainly represented less advanced PAOD. This group of patients was younger and included a relative large proportion of women. Since conservative treatment of PAOD has been proven effective, this offers an opportunity to GPs to enhance their efforts towards primary and secondary prevention of PAOD (and symptomatic atherosclerosis in general).

Firstly, GPs should try to achieve a complete picture of the vascular risk profile of their middle-aged patients. Smoking, hypertension, hypercholesterolaemia and diabetes mellitus are vascular risk indicators that can be influenced by lifestyle advice and medication.

Secondly, since asymptomatic cases of PAOD are highly correlated with concomitant IHD and CeAD, we think that active case finding, e.g. by performing a measurement of the AB ratio, is a tenable option in high-risk patients. Longitudinal studies are required to reveal the effectiveness of such a strategy.

Thirdly, signs and symptoms are inadequate diagnostic tests to establish the diagnosis PAOD. Therefore, when history and vascular examination yield ambiguous results, non-invasive testing might be appropriate.

Further, our results suggest that in female patients the possibility of PAOD might be considered more often. Although the occurrence of signs and symptoms associated with PAOD was not unequivocally lower among women, GPs less often concluded that PAOD was present among women, even when IHD was present. As a consequence the sensitivity of the GP's diagnosis regarding the presence of PAOD was lower for women. Further (multivariable) analysis of the factors that GPs consider relevant for their diagnosis is required to throw light on this matter.

Finally, when the diagnosis PAOD is established, whether symptomatic or asymptomatic, advice on stopping smoking and dietary measures should be given and, when appropriate, hypertension and diabetes should be regulated adequately. In many patients this will prevent progression of PAOD to the point where vascular surgery becomes inevitable. It also will decrease their risk of manifest cardio- and cerebrovascular disease.

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