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Peripheral Arterial Disease in the Elderly
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Abstract—To assess the age- and sex-specific prevalence of peripheral arterial disease (PAD) and intermittent claudication (IC) in an elderly population, we performed a population-based study in 7715 subjects (40% men, 60% women) aged 55 years and over. The presence of PAD and IC was determined by measuring the ankle-arm systolic blood pressure index (AAI) and by means of the World Health Organization/Rose questionnaire, respectively. PAD was considered present when the AAI was <0.90 in either leg. The prevalence of PAD was 19.1% (95% confidence interval, 18.1% to 20.0%): 16.9% in men and 20.5% in women. Symptoms of IC were reported by 1.6% (95% confidence interval, 1.3% to 1.9%) of the study population (2.2% in men, 1.2% in women). Of those with PAD, 6.3% reported symptoms of IC (8.7% in men, 4.9% in women), whereas in 68.9% of those with IC an AAI below 0.90 was found. Subjects with an AAI <0.90 were more likely to be smokers, to have hypertension, and to have symptomatic or asymptomatic cardiovascular disease compared with subjects with an AAI of 0.90 or higher. The authors conclude that the prevalence of PAD in the elderly is high whereas the prevalence of IC is rather low, although both prevalences clearly increase with advancing age. The vast majority of PAD patients reports no symptoms of IC. **(*Arterioscler Thromb Vasc Biol*. 1998;18:185-192.)**

Key Words: atherosclerosis ■ elderly ■ intermittent claudication ■ peripheral arterial disease ■ cardiovascular risk

Peripheral arterial disease refers to the manifestation of atherosclerosis in the lower limb distal to the aortic bifurcation. When PAD becomes symptomatic, patients often present with complaints of IC: "cramping," "fatigue," or "aching" in the calf of the leg, induced by walking and relieved by standing still. In ≈25% of patients with IC, there is a progression to critical ischemia, eg, rest pain and gangrene, that may eventually necessitate amputation.[1,2]

Several studies have demonstrated that patients with PAD, both with and without symptoms of IC,[3–5] are at an increased risk of cardiovascular morbidity and mortality compared with subjects without PAD.[4,6–9] In comparison to the number of reports on other manifestations of atherosclerotic disease, however, relatively few population-based studies on the prevalence of PAD and IC have been performed. We assessed the prevalence of PAD and IC in a large population-based study including 7715 subjects aged 55 years and over.

Methods

This study is part of The Rotterdam Study, a prospective follow-up study designed to investigate determinants of the occurrence and progression of chronic diseases in the elderly. Emphasis is on four areas of research: cardiovascular diseases, neurogeriatric diseases, locomotor diseases, and ophthalmologic diseases. The rationale and design of the study have been described previously.[10]

All individuals aged 55 years and over living in a suburb of Rotterdam, the Netherlands (a total of 10 275 subjects), were invited to participate in the Rotterdam Study. Baseline measurements were compiled after an extensive interview at the participant's home and two visits to the research center. The overall response rate was 78% (7983 subjects; 3105 men and 4878 women). Of these, 879 subjects lived in nursing homes.

Intermittent claudication was diagnosed according to the criteria of the World Health Organization/Rose questionnaire,[11] which was included in the home interview. The prevalence of IC was assessed in 7715 participants in whom the answers to the Rose-questionnaire were available.

Blood pressure was calculated as the mean of two consecutive measurements with a random-zero sphygmomanometer at the right brachial artery while the patient was in a sitting position. The presence of PAD was evaluated by measuring the systolic blood pressure level of the posterior tibial artery at both the left and right leg using an 8-MHz continuous-wave Doppler probe (Huntleigh 500 D, Huntleigh Technology) and a random-zero sphygmomanometer.[12–16] For each leg, a single blood pressure reading was taken with the subject in the supine position. The ratio of the systolic blood pressure at the ankle to the systolic blood pressure at the arm (ie, AAI) was calculated for each leg. The lowest AAI in either leg was used in the analysis.[4] In agreement with the approach followed by Fowkes et al[4] and by Schroll and Munck,[17] PAD was considered present when the AAI was <0.90 in at least one leg. The AAI was not determined in 1533 participants: 824 subjects did

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Selected Abbreviations and Acronyms

AAI = ankle-arm systolic blood pressure index
CI = confidence interval
ECG = electrocardiogram
IC = intermittent claudication
LVH = left ventricular hypertrophy
PAD = peripheral artery disease
WHO = World Health Organization

not visit the research center; 4 subjects died before their visit to the center; and in 705 subjects the systolic arm blood pressure (n=7), the systolic ankle blood pressure (n=559), or both (n=139) were not measured. The characteristics of these 705 individuals did not differ appreciably from the population in which the AAI could be determined. Thus, the AAI was calculated for 6450 participants (2589 men and 3861 women). We excluded 41 participants (0.6%) with an AAI>1.50, because this AAI usually reflects arterial rigidity preventing arterial compression, leading to spuriously high ankle blood pressure values.

Established cardiovascular risk factors and the presence (or absence) of symptomatic cardiovascular diseases were recorded, and several noninvasive measures of atherosclerosis (notably ultrasound measurements of the carotid arteries and abdominal aorta) were performed.[10]

Hypertension was defined as a systolic blood pressure of 160 mm Hg or higher, a diastolic blood pressure of 95 mm Hg or higher, or current use of antihypertensive drugs for the indication hypertension.[18] Diabetes mellitus was defined as current use of antidiabetic drugs or a random or postload serum glucose level >11.0 mmol/L after an oral glucose tolerance test.[19,20] Subjects were categorized in as current smokers, former smokers, or those who had never smoked. Serum total cholesterol was determined by an automated enzymatic procedure in a nonfasting blood sample.[21] Serum HDL cholesterol was measured after precipitation of the non-HDL fraction with phosphotungstate-magnesium. Height and weight were measured and body mass index (kg/m^2) was calculated. A history of myocardial infarction and stroke was obtained through direct questioning and considered positive when confirmed by a physician. A history of angina pectoris was assessed using the World Health Organization/Rose questionnaire.[11] LVH was assessed using a 12-lead ECG, recorded with an ESAOTE-ACTA cardiograph with a sampling frequency of 500 Hz and stored digitally. ECG LVH was determined using an automated diagnostic classification system, the modular ECG analysis system (MEANS), based on voltage, shape, and repolarization criteria.[22,23] Ultrasonography of both carotid arteries was performed with a 7.5-MHz linear array transducer with a Duplex scanner (ATL

TABLE 1. General Characteristics of 7715 Men and Women Aged 55 Years or Older in Whom the Presence of PAD and IC Was Assessed

Characteristic	Men (n=3052)	Women (n=4663)
Age, y, mean (SD)	69.0 (8.7)	71.7 (10.3)
Body mass index, kg/m^2, mean (SD)	25.7 (3.7)	26.7 (4.1)
Systolic blood pressure, mm Hg, mean (SD)	139 (22)	140 (23)
Diastolic blood pressure, mm Hg, mean (SD)	75 (12)	73 (12)
Hypertension, %	26.3	33.2
Diabetes mellitus, %	10.0	9.9
Smoking, %		
Current	30.4	17.5
Former	61.5	27.1
Serum total cholesterol, mmol/L, mean (SD)	6.30 (1.18)	6.81 (1.22)
Serum HDL cholesterol, mmol/L, mean (SD)	1.22 (0.33)	1.43 (0.37)
Carotid artery*		
Intima-media thickness, mm, mean (SD)	0.82 (0.15)	0.78 (0.16)
Plaques (%)		
Common carotid	23.3	16.9
Carotid bifurcation	64.2	59.2
History of angina pectoris, %	6.8	6.9
History of myocardial infarction, %	12.2	4.3
History of stroke, %	5.0	4.3

*Data available for the first 1660 participants of the Rotterdam Study.[25]

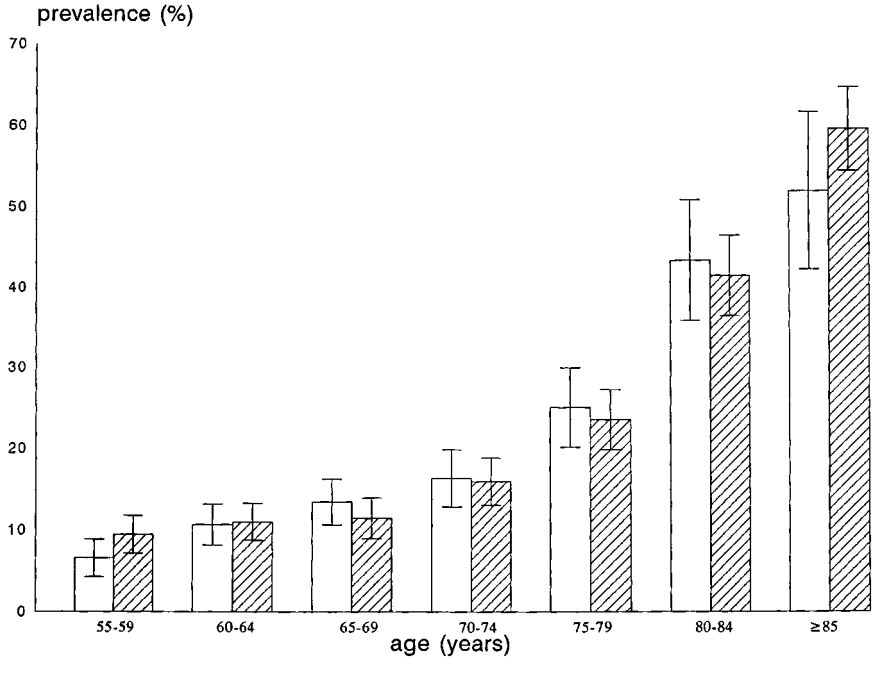

Figure 1. The age- and sex-specific prevalence of PAD (and 95% CI) according to age for men (white bars) and women (shaded bars).

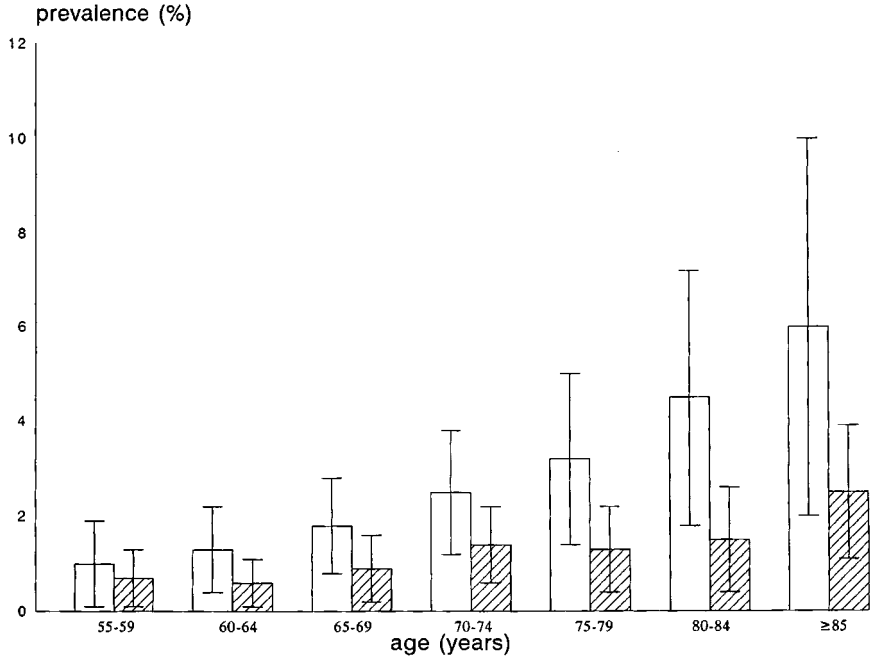

Figure 2. The age- and sex-specific prevalence of IC (and 95% CI) according to age for men (white bars) and women (shaded bars).

UltraMark IV, Advanced Technology Laboratories) to assess intima-media thickness of the distal part of the common carotid artery and the presence of plaques in the common and internal carotid arteries and carotid bifurcation, as detailed elsewhere.[24,25] Common carotid intima-media thickness was calculated as the mean of the near and far wall measurements of both left and right carotid arteries. Ultrasound measurements of the diameter of the abdominal aorta were taken by way of B-mode ultrasound recordings using a 3.5-MHz linear-array probe (Toshiba SSH 60A, Toshiba Medical Systems) with the patient in the supine position.[26]

To compare our prevalence data for PAD and IC with those reported in other population-based screening surveys, adjusted prevalences were calculated by applying the age and gender distributions and definitions of PAD in these other studies to the Rotterdam Study data set. Prevalence rates were calculated with exact 95% confidence limits. One-way ANCOVAs were applied to determine the statistical significance of the differences in cardiovascular risk indicators and noninvasive measures of atherosclerosis between subjects with and without PAD, adjusted for differences in age between these two groups. All analyses were performed using BMDP software (BMDP Statistical Software, Inc).

Results

In Table 1, selected characteristics of the study population are given separately for men and women. PAD was present in 19.1% (95% CI, 18.1% to 20.0%) of all participants. The prevalence of PAD in women (20.5%; 95% CI, 19.2% to 21.8%) was higher than that in men (16.9%; 95% CI, 15.4% to 18.3%). The age difference between men and women accounted for most of this difference in prevalence, because the prevalences in 5-year age categories for men and women were similar. In both men and women, a clear increase in the prevalence of PAD with age was observed, ranging from 6.6% in the age category 55 to 59 years to 52.0% in the age category 85 years or over in men, and from 9.5% to 59.6% in the corresponding age categories in women (Fig 1).

IC was reported by 1.6% (95% CI, 1.3% to 1.9%) of all participants, whereas the prevalence of IC in men (2.2%; 95% CI, 1.7% to 2.8%) was higher than in women (1.2%; 95% CI, 0.9% to 1.5%). In both men and women, a clear increase in prevalence of IC with increasing age was present, ranging from 1.0% in the age category 55 to 59 years to 6.0% in the age category 85 years or over in men, and from 0.7% to 2.5% in the corresponding age categories in women (Fig 2).

Of the 1166 subjects with PAD, 73 (6.3%) reported symptoms of IC (Table 2). Interestingly, men with PAD more often complained of symptoms of intermittent claudication (8.7%) than women with PAD (4.9%). Of the 106 subjects with symptoms of IC according to the Rose criteria, 73 (68.9%) had PAD, defined as an AAI$<$0.90. This proportion was similar in men and women.

The mean AAI was 1.05 (standard deviation [SD], 0.23): 1.08 (SD, 0.24) in men and 1.03 (SD, 0.23) in women. The AAI decreased sharply with advancing age (Fig 3). The distribution of AAI values (Fig 4) is skewed to the left. In 41 participants (0.6%), an AAI $>$1.50 was measured. These 41 participants were not included in the other tables or figures.

TABLE 2. PAD and IC in Subjects Aged 55 Years or Older

	PAD*		
IC†	Present (AAI$<$0.90)	Absent (AAI$\geq$0.90)	Total
Men			
Present	37	18	55
Absent	387	2117	2504
Women			
Present	36	15	51
Absent	706	3008	3714
Total			
Present	73	33	106
Absent	1093	5125	6218

*Assessed by measuring the AAI.
†According to the criteria of the WHO/Rose questionnaire.

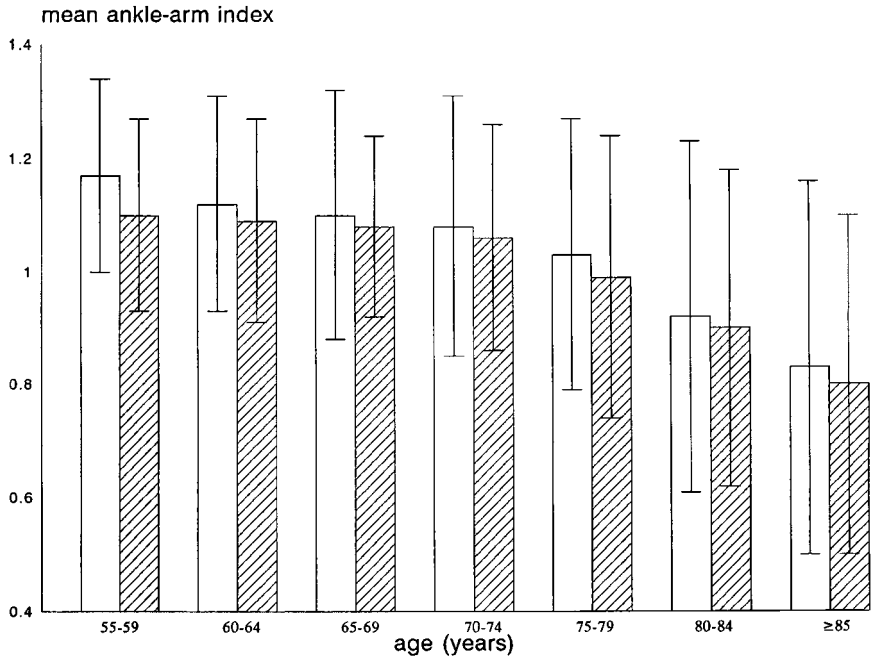

Figure 3. AAI (and 95% CI) according to age for men (white bars) and women (shaded bars).

In Table 3, subjects with and without PAD are compared with respect to the presence of cardiovascular risk factors and disease and noninvasive measures of atherosclerosis. Subjects with an AAI<0.90 had a more unfavorable cardiovascular risk profile than did subjects with an AAI≥0.90. In both men and women, hypertension, cigarette smoking, and a history of stroke were significantly more frequent among subjects with an AAI<0.90. LVH was more frequent in those with an AAI<0.90, and similarly, these subjects had an increased common carotid intima-media thickness, a higher frequency of carotid plaques, and a larger distal abdominal aortic diameter.

Tables 4 and 5 show a comparison between the results of previous large screening surveys assessing the prevalence of PAD and IC and findings from the Rotterdam Study. When the definitions for PAD and IC and the population characteristics of these other studies were applied to our own data set, no major differences in the prevalence estimates were found.

Discussion

In the population-based Rotterdam Study, the prevalence of PAD was 19.1%, varying from 6.6% in women aged 55 to 59 years to 59.6% in men aged 85 years or older. Intermittent

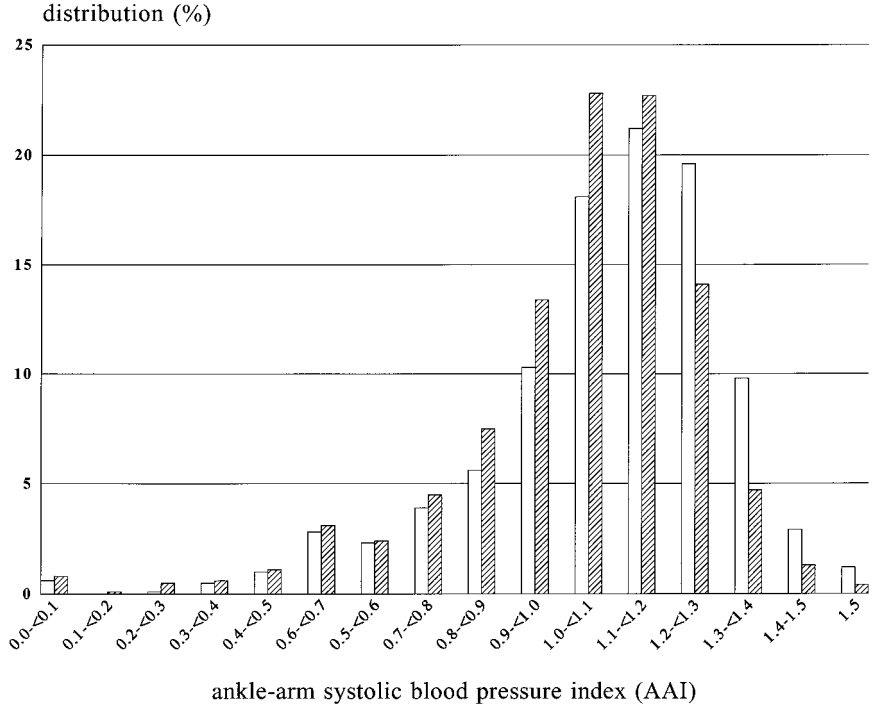

Figure 4. The distribution of the AAI for men (white bars) and women (shaded bars).

TABLE 3. Cardiovascular Risk Indicators in Subjects with an AAI <0.90 or an AAI ≥0.90, Adjusted for Differences in Age

	Men			Women		
	AAI			AAI		
	<0.90	≥0.90	*P*	<0.90	≥0.90	*P*
Cardiovascular risk factors						
Body mass index, kg/m^2, mean	25.2	25.8	.43	26.6	26.7	.02
Systolic blood pressure, mm Hg, mean	148	137	.07	150	137	<.01
Diastolic blood pressure, mm Hg, mean	74	75	.02	74	73	<.01
IC, %*	9.5	.9	<.01	5.0	.5	<.01
Hypertension, %†	39.4	23.8	<.01	48.1	29.1	<.01
Serum total cholesterol, mmol/L, mean	6.28	6.32	.60	6.97	6.81	<.01
Serum HDL cholesterol, mmol/L, mean	1.19	1.21	.06	1.38	1.46	.63
Diabetes mellitus, %	11.9	6.7	.08	16.0	6.3	<.01
Smoking, %						
Current	37.9	21.4	<.01	21.5	17.1	<.01
Former	46.7	62.2	<.01	25.8	29.0	.91
Cardiovascular disease or measures of atherosclerosis						
History of angina pectoris, %	9.3	5.9	.12	9.2	6.4	.24
History of myocardial infarction, %	29.9	17.0	<.01	15.2	7.4	.34
History of stroke, %	9.0	3.6	<.01	8.4	2.0	<.01
Carotid artery‡						
Intima-media thickness, mm	.880	.804	<.01	.830	.756	<.01
Plaques, %						
Common carotid	34.4	20.2	<.01	35.4	10.8	<.01
Carotid bifurcation	74.2	59.8	.01	66.7	52.3	<.01
Distal abdominal aortic diameter, mm	23.1	19.3	<.01	16.8	16.0	<.01
LVH by ECG, %	17.3	9.5	.05	11.4	4.9	.01

*According to the criteria of the WHO/Rose questionnaire.

†Defined as a systolic blood pressure of 160 mm Hg or higher, or a diastolic blood pressure of 95 mm Hg or higher, or current use of antihypertensive drugs for the indication hypertension.

‡Data available for the first 1660 participants of the Rotterdam Study.[25]

claudication was reported by 1.6% of the participants, varying from 0.7% in women aged 55 to 59 years to 6.0% in men aged 85 years or older. Of those with PAD, only 6.3% reported symptoms of IC. Compared with those with an AAI ≥0.90, subjects with an AAI<0.90 clearly had an unfavorable cardiovascular risk profile, also with regard to other noninvasive measures of atherosclerosis.

The response rate in the Rotterdam Study of 78% is within the range of similar surveys, with response rates varying from 59% to 98%.[3–5,17,27–31] Because of a lower response rate in the very old in the Rotterdam Study, the prevalence of PAD and IC may have been underestimated for this age group, although in a study by Aronow et al[32] among 1886 persons with a mean age of 82 years who were living in a nursing home, the prevalence of PAD was 29% among men and 23% among women.

We used the AAI at rest as an indicator of PAD. In a number of surveys, an AAI measurement during exercise or a reactive hyperemia test was used.[16,31,33] Hiatt et al[31] concluded that these tests are not as useful as the AAI measured at rest. By analogy with other studies, we used a single measurement of the AAI to define PAD. Taking the mean of consecutive measurements, as for example in the Limburg PAOD Study,[27] would likely have reduced the prevalence estimates.

There is no consensus regarding the cutoff value for the AAI to define PAD. Most of the published surveys have used a cutoff value between 0.80 and 0.95,[3–5,17,27,28,30,31] whereas in one, a cutoff value of 0.75 was used.[29] Different cutoff values result in different prevalences for PAD between the individual surveys, as is clearly illustrated by comparing the crude and adjusted prevalence rates in Table 4. Other reasons for reported differences in prevalence estimates between published studies are differences in the age and sex distribution of the screened populations or the restriction to populations with a higher risk for PAD (such as dyslipidemic,[5] hypertensive,[30] or diabetic[31] patients).

TABLE 4. Prevalence of PAD in Nine Population-Based Screening Surveys and in the Rotterdam Study

Study	Age, y	Sex	No.	Definition of AAI	Prevalence		Adjusted Prevalence,* %
					%	95% CI	
Rotterdam Study	≥55	Men	2589	<0.90	16.9	15.4–18.3	16.9
		Women	3861		20.5	19.2–21.8	20.5
Stoffers et al[27]	55–75†	Men	1719	<0.95	11.0	9.5–12.5	16.5
		Women	1935		8.6	7.4–9.8	17.0
Newman et al[3]	≥65	Men	2214	<0.90	13.9	12.5–15.3	22.3
		Women	2870		11.4	10.2–12.6	26.5
Vogt et al[28]	≥65	Women	1492	≤0.90	5.5	4.3–6.7	26.5
Coni et al[29]	>65	Men	112	<0.75	9.1‡	5.6–12.6	14.0§
		Women	153		9.1‡		14.0§
Fowkes et al[4]	55–74	Men	809	≤0.90	18.3‡	16.4–20.2	11.6§
		Women	783		18.3‡		11.6§
Newman et al[30]	≥60	Men	82	<0.90	26.7‡	20.4–33.0	21.4§
		Women	105		26.7‡		21.4§
Hiatt et al[31]	44–68	Men	410	<0.94	11.9‡	9.8–13.9	13.4§
		Women	540		11.9‡		13.4§
Criqui et al[5]	38–82	Men	275	≤0.80§	11.7‡	9.2–14.2	8.7§
		Women	338		11.7‡		8.7§
Schroll/Munck[17]	60	Men	360	<0.90	16.0	12.2–19.8	9.7
		Women	306		13.0	9.2–16.8	9.2

*The prevalence was adjusted by applying the age and gender distributions and definitions of PAD in the other studies to the Rotterdam Study data set.

†The age group 45–55 years was not considered in this comparison; the actual studied age group was 45 to 75 years or over.

‡Prevalence in the total population; no separate estimates according to gender were reported.

§Criqui et al[5] used a different approach to assess the prevalence of peripheral arterial disease; the standard AAI was not used, but 4 different noninvasive measurements of limb perfusion in the lower extremities.

Only a minority of the participants with PAD in the Rotterdam Study (6.3%) reported symptoms of IC. Other studies reported figures in the range of 5.3% to 18.9%,[3–5,17,27,28,30,31] with the exception of one study, reporting a prevalence as high as 37.5%.[29] This prevalence of 37.5% observed by Coni et al[29] should be interpreted with caution because in this study the strict Rose criteria were not used to assess the number of subjects with IC.

The relatively low proportion of PAD patients with complaints of IC can partly be explained by the fact that many elderly people do not walk far enough to experience symptoms of IC, because of either impaired vascularization of the extremities or other typical disorders, such as osteoarthritis. Of interest is that women with PAD less often reported symptoms of IC (4.9%) than men with PAD (8.7%). Possibly, women more frequently present atypical symptoms from ischemic disease than men, by analogy with observations of coronary heart disease.[34,35]

PAD is often considered an indicator of generalized atherosclerosis and as such is associated with a poor cardiovascular prognosis. This association seems to be true for participants of this study, as illustrated by the relatively unfavorable cardiovascular risk profile of those with an AAI <0.90. From other studies similar findings have been reported,[3,4,6–8,27,28] especially for the association between PAD and hypertension, diabetes mellitus, and smoking. The finding of an increased common carotid intima-media thickness, a higher frequency of carotid plaques, and a larger diameter of the abdominal aorta (as measures of atherosclerosis) supports the relatively poor prognosis of subjects with an AAI<0.90.

We conclude that the prevalence of PAD in the elderly is high whereas the prevalence of reported IC is relatively low. Both prevalences sharply increase with advancing age. The vast majority of PAD patients reported no symptoms of IC. This, together with the high prevalence of PAD and unfavorable cardiovascular risk profile of patients with PAD, illustrates the need to explore the use of the AAI as a risk indicator in cardiovascular screening and risk profiling in medical practice.

Acknowledgments

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TABLE 5. Prevalence of IC in 13 Population-Based Screening Surveys and in the Rotterdam Study

Study	Age, y	Sex	No.	Population	Prevalence		Adjusted Prevalence,* %
					%	95% CI	
Rotterdam Study	≥55	Men	3052	General	2.2	1.7–2.8	2.2
		Women	4663		1.2	0.9–1.5	1.2
Stoffers et al[27]	55–75†	Men	1719	General	1.5	0.9–2.1	1.6
		Women	1935		2.8	2.1–3.5	0.9
Newman et al[3]	≥65	Men	2214	General	2.0‡	1.6–2.4	2.0‡
		Women	2870		2.0‡		2.0‡
Vogt et al[28]	≥65	Women	1492	Rural	7.4	6.1–8.7	1.5
Coni et al[29]	>65	Men	112	Rural	6.1‡	3.2–9.0	2.0‡
		Women	153		6.1‡		2.0‡
Fowkes et al[4]	55–74	Men	809	General	4.6‡	3.6–5.6	1.2‡
		Women	783		4.6‡		1.2‡
Newman et al[30]	≥60	Men	82	Systolic hypertension	6.4‡	2.9–9.9	1.8‡
		Women	105		6.4‡		1.8‡
Hiatt et al[31]	44–68	Men	410	General/diabetic	0.6‡	0.1–1.1	1.0‡
		Women	540		0.6‡		1.0‡
Smith et al[8]	40–64	Men	18 388	Civil servants	0.8	0.7–0.9	0.8
Hale et al[36]	≥65	Men	621	General	14.4	11.6–17.2	2.9
		Women	1082		14.1	12.0–16.2	1.5
Criqui et al[5]	38 –82	Men	275	General/dyslipidemic	2.2	0.5–3.9	2.0
		Women	338		1.7	0.3–3.1	1.0
Reunanen et al[37]	30–59	Men	5738	General	2.1	1.7–2.5	1.0
		Women	5224		1.8	1.4–2.2	0.6
Schroll/Munck[17]	60	Men	360	General	5.8	3.4–8.2	1.0
		Women	306		1.3	0.0–2.6	0.6
Hughson et al[38]	45–69	Men	1716	General	2.2	1.5–2.9	1.4
	50–69	Women	1535		1.2	0.7–1.7	0.7

*The prevalence was adjusted by applying the age and gender distributions and definitions of PAD in the other studies to the Rotterdam Study data set.

†The age group 45–55 was not considered in this comparison; the actual studied age group was 45 to 75 years or older.

‡Prevalence in the total population; no separate estimates according to gender were reported.

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