



Online article and related content
current as of July 5, 2009.

Peripheral Arterial Disease Detection, Awareness, and Treatment in Primary Care

Alan T. Hirsch; Michael H. Criqui; Diane Treat-Jacobson; et al.

JAMA. 2001;286(11):1317-1324 (doi:10.1001/jama.286.11.1317)

<http://jama.ama-assn.org/cgi/content/full/286/11/1317>

Correction	Contact me if this article is corrected.
Citations	This article has been cited 457 times. Contact me when this article is cited.
Topic collections	Primary Care/ Family Medicine; Cardiovascular System; Diagnosis; Cardiovascular Disease/ Myocardial Infarction Contact me when new articles are published in these topic areas.
Related Articles published in the same issue	Detection of Peripheral Arterial Disease in Primary Care Kenneth Ouriel. <i>JAMA</i> . 2001;286(11):1380. September 19, 2001 <i>JAMA</i> . 2001;286(11):1389. Peripheral Arterial Disease <i>JAMA</i> . 2001;286(11):1406.
Related Letters	Diagnosis and Treatment of Peripheral Arterial Disease Hyman Gaylis et al. <i>JAMA</i> . 2002;287(3):313.

Subscribe
<http://jama.com/subscribe>

Permissions
permissions@ama-assn.org
<http://pubs.ama-assn.org/misc/permissions.dtl>

Email Alerts
<http://jamaarchives.com/alerts>

Reprints/E-prints
reprints@ama-assn.org

Peripheral Arterial Disease Detection, Awareness, and Treatment in Primary Care

Alan T. Hirsch, MD

Michael H. Criqui, MD, MPH

Diane Treat-Jacobson, PhD, RN

Judith G. Regensteiner, PhD

Mark A. Creager, MD

Jeffrey W. Olin, DO

Susan H. Krook, PhD

Donald B. Hunninghake, MD

Anthony J. Comerota, MD

M. Eileen Walsh, RN, MSN, CVN

Mary M. McDermott, MD

William R. Hiatt, MD

PERIPHERAL ARTERIAL DISEASE (PAD) is a highly prevalent atherosclerotic syndrome that affects approximately 8 to 12 million individuals in the United States and is associated with significant morbidity and mortality.¹⁻⁴ Because of its high prevalence, high rates of nonfatal cardiovascular ischemic events (myocardial infarction [MI], stroke, and other thromboembolic events), increased mortality, and diminution of quality of life, the consequences of PAD in US communities are significant.¹⁻⁵ A regional pilot study of community screening for PAD demonstrated that patient awareness of the PAD diagnosis was low and associated with low atherosclerosis risk factor, antiplatelet, and claudication treatment intensity.⁵ There have been no national efforts in the United States to detect PAD in community-based office practice, to assess both physician and patient awareness of the diagnosis, or to assess the intensity of medical treatments. PAD has not emerged as a focus of public health ef-

See also p 1380 and Patient Page.

Context Peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis that is common and is associated with an increased risk of death and ischemic events, yet may be underdiagnosed in primary care practice.

Objective To assess the feasibility of detecting PAD in primary care clinics, patient and physician awareness of PAD, and intensity of risk factor treatment and use of antiplatelet therapies in primary care clinics.

Design and Setting The PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) program, a multicenter, cross-sectional study conducted at 27 sites in 25 cities and 350 primary care practices throughout the United States in June-October 1999.

Patients A total of 6979 patients aged 70 years or older or aged 50 through 69 years with history of cigarette smoking or diabetes were evaluated by history and by measurement of the ankle-brachial index (ABI). PAD was considered present if the ABI was 0.90 or less, if it was documented in the medical record, or if there was a history of limb revascularization. Cardiovascular disease (CVD) was defined as a history of atherosclerotic coronary, cerebral, or abdominal aortic aneurysmal disease.

Main Outcome Measures Frequency of detection of PAD; physician and patient awareness of PAD diagnosis; treatment intensity in PAD patients compared with treatment of other forms of CVD and with patients without clinical evidence of atherosclerosis.

Results PAD was detected in 1865 patients (29%); 825 of these (44%) had PAD only, without evidence of CVD. Overall, 13% had PAD only, 16% had PAD and CVD, 24% had CVD only, and 47% had neither PAD nor CVD (the reference group). There were 457 patients (55%) with newly diagnosed PAD only and 366 (35%) with PAD and CVD who were newly diagnosed during the survey. Eighty-three percent of patients with prior PAD were aware of their diagnosis, but only 49% of physicians were aware of this diagnosis. Among patients with PAD, classic claudication was distinctly uncommon (11%). Patients with PAD had similar atherosclerosis risk factor profiles compared with those who had CVD. Smoking behavior was more frequently treated in patients with new (53%) and prior PAD (51%) only than in those with CVD only (35%; $P < .001$). Hypertension was treated less frequently in new (84%) and prior PAD (88%) only vs CVD only (95%; $P < .001$) and hyperlipidemia was treated less frequently in new (44%) and prior PAD (56%) only vs CVD only (73%, $P < .001$). Antiplatelet medications were prescribed less often in patients with new (33%) and prior PAD (54%) only vs CVD only (71%, $P < .001$). Treatment intensity for diabetes and use of hormone replacement therapy in women were similar across all groups.

Conclusions Prevalence of PAD in primary care practices is high, yet physician awareness of the PAD diagnosis is relatively low. A simple ABI measurement identified a large number of patients with previously unrecognized PAD. Atherosclerosis risk factors were very prevalent in PAD patients, but these patients received less intensive treatment for lipid disorders and hypertension and were prescribed antiplatelet therapy less frequently than were patients with CVD. These results demonstrate that underdiagnosis of PAD in primary care practice may be a barrier to effective secondary prevention of the high ischemic cardiovascular risk associated with PAD.

JAMA. 2001;286:1317-1324

www.jama.com

Author Affiliations, PARTNERS Investigators, and Financial Disclosure are listed at the end of this article.
Corresponding Author and Reprints: Alan T. Hirsch, MD, Vascular Medicine Program, Minnesota

Vascular Diseases Center, Mayo Mail Code 508, University of Minnesota Medical School, 420 Delaware St, SE, Minneapolis, MN 55455 (e-mail: Hirsch005@umn.edu).

forts to improve quality of life nor to decrease the associated cardiovascular ischemic risk.

The PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) program was designed as a national investigation to assess the feasibility of detecting PAD using the ankle-brachial index (ABI) in office-based practices. Additional goals were to assess both patient and physician awareness of PAD, to evaluate the magnitude of the associated atherosclerosis risk factor burden, and to assess the intensity of use of risk-reduction strategies in community practice. The program evaluated the following hypotheses: (1) that PAD is prevalent but underdiagnosed in primary care practices and (2) that PAD is undertreated in terms of risk factor modification and use of antiplatelet therapies compared with that in other cardiovascular diseases (CVDs).

METHODS

Program Design

The program was designed by an interdisciplinary steering committee as a national, community-based PAD detection program. The program established physician-nurse partnerships at 27 regional coordinating centers selected for their expertise in PAD, which in turn identified a total of 350 local primary care sites for patient screening. The local study physician and coordinator identified their patients who met the study entry criteria. The local nurse administered standardized questionnaires; recorded the medical history, height, weight, blood pressure, and waist circumference; and measured each patient's ABI. The program design is shown in the FIGURE. The protocol was reviewed and approved by the institutional review boards at all study sites, and all patients provided written informed consent prior to participation.

Study Population

The survey population was identified prospectively by a predefined subject age and risk factor profile based on the known epidemiology of PAD.^{1-4,6,7} Pa-

tients were enrolled at each practice site if they were 70 years or older or if they were aged 50 through 69 years and had a history of diabetes or cigarette smoking (at least 10 pack-years), or both. We anticipated that these enrollment criteria would yield a PAD detection rate of 15% and a CVD detection rate of 15%. Therefore, we projected evaluating approximately 10000 individuals to identify 1500 patients with PAD and 1500 patients with CVD. This sample size was estimated to provide sufficient power to test the second hypothesis of a difference in treatment intensity for risk factors and use of antiplatelet therapy between patients with PAD who had no history of CVD vs patients with CVD who had no evidence of PAD. Data collection was conducted from June through October 1999. The survey was concluded after 6979 patients had been screened, for this sample had identified 1865 patients with PAD (825 with PAD only and 1040 with

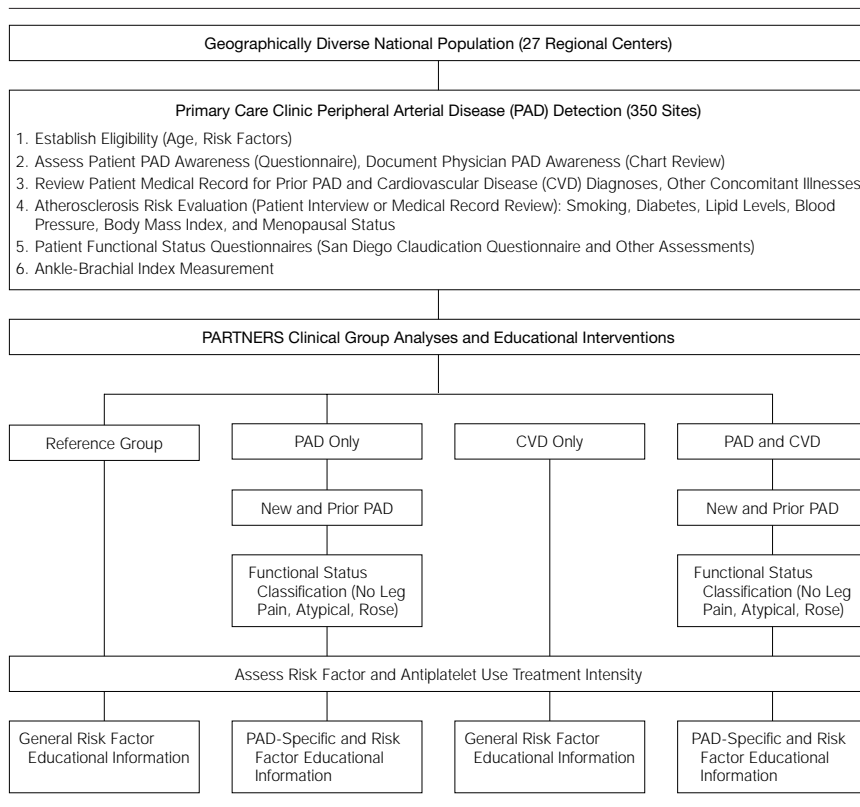
PAD and CVD). A total of 1527 patients were identified with CVD only.

Clinical Subgroups

The cohort was divided into 4 predefined, mutually exclusive clinical subgroups: (1) those without clinically recognized atherosclerosis in any vascular bed (reference group), (2) those with PAD only, (3) those with CVD only, and (4) those with both PAD and CVD. Individuals were considered to have previously established prior PAD if it was documented by chart review, if they had prior abnormal vascular laboratory studies confirming PAD, or they had prior limb arterial revascularization, regardless of their ABI value at the survey office visit. Patients with no previous chart documentation of PAD were considered to have new PAD if their ABI was 0.90 or less during the survey screening office visit.

A CVD diagnosis required a documented history of coronary artery dis-

Figure. PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) Program Design



ease, cerebrovascular disease, or abdominal aortic aneurysm repair. Coronary artery disease was established on the basis of a history of angina (stable or unstable), MI, percutaneous transluminal coronary angioplasty (PTCA), or coronary artery bypass graft surgery. Patients were considered to have cerebrovascular disease if they had a history of transient ischemic attack, stroke (ischemic or hemorrhagic), or carotid endarterectomy.

ABI Technique

All local sites received instruction on the accurate use of the Doppler technique and the ABI calculation prior to study initiation. A 5-mHz Doppler device (Elite-100R, Nicolet Vascular Inc, Golden, Colo) was used at each site to measure the ABI. This unit included a broad-beam ultrasound probe designed to facilitate performance of the ABI measurement. With each subject in the supine position, the systolic blood pressures were recorded in the upper extremities at the brachial arteries and in the lower extremities at the dorsalis pedis and posterior tibial arteries. The ABI for each leg was separately calculated by dividing the higher of the 2 ankle systolic pressures in that leg by the higher brachial systolic pressure. The subject was considered to have PAD if either leg ABI was 0.90 or less. The index leg was defined as the leg with the lower ABI. The sensitivity of the ABI is 90%, and the specificity is 98% for an angiographically defined stenosis of 50% or more in a major leg artery.⁸⁻¹⁰

Atherosclerosis Risk Factors

A smoking history (current or former) was established in patients who had 1 pack-year or more of tobacco use based on patient interview or chart documentation. Diabetes was determined from the clinical record (based on a chart diagnosis or use of diabetes medications), regardless of whether it was type 1 or type 2. Laboratory screening for new diabetes was not performed. In a similar fashion, hyperlipidemia was defined from the medi-

cal record as a total cholesterol concentration of 240 mg/dL (6.2 mmol/L) or more, low-density lipoprotein (LDL) cholesterol concentration of 160 mg/dL (4.1 mmol/L) or more, high-density lipoprotein (HDL) cholesterol concentration of 35 mg/dL (0.9 mmol/L) or less, triglyceride concentration of 200 mg/dL (2.26 mmol/L) or more, total cholesterol/HDL ratio of 5.0 or more,¹¹⁻¹³ or if the medical record included past or present use of lipid-lowering agents.¹¹ A fasting lipid profile was not obtained as part of this program and therefore not every patient could be evaluated for the presence of hyperlipidemia. Patients were designated as hypertensive if they had a systolic blood pressure of 140 mm Hg or more or a diastolic blood pressure of 90 mm Hg or more at the time of the office screening. Hypertension was also diagnosed from the chart by the use of calcium channel blockers, angiotensin-converting enzyme inhibitors, β -blockers, or diuretics for the indication of treatment of hypertension. Women were considered postmenopausal by self-report or the use of hormone replacement therapy.

Risk Factor Treatment and Antiplatelet Therapy

Smoking cessation therapy was defined as current participation in or previous referral to a smoking cessation program. Diabetes treatment was defined as current use of dietary interventions or use of diabetes medications, including insulin and oral hypoglycemic agents. Lipid-lowering therapy was defined as the prescription of agents used to treat lipid abnormalities (statins, niacin, fibrates, and bile acid binding resin agents). Treatment for hypertension was identified by the prescription of antihypertensive medications. In women, the use of estrogen and/or progesterone hormone replacement therapy was defined as treatment for menopause. The use of antiplatelet agents, including aspirin, clopidogrel, ticlopidine, and dipyridamole, was recorded.

Patient and Physician PAD Awareness and Educational Interventions

The PAD Awareness Questionnaire asked patients if any prior health care provider had informed them of a diagnosis of PAD or other limitations to lower extremity arterial blood flow. A positive response to any of 5 awareness questions was considered PAD aware. Primary care physician awareness of the PAD diagnosis was determined by his/her written response to a prior diagnosis question on the day of screening. Each participant received educational information regarding the impact of PAD as an atherosclerotic disease and the treatment of atherosclerosis risk factors, as well as a written record detailing ABI and blood pressure measurements. All participants received the *Fact Sheet on Heart Attack, Stroke and Risk Factors*.¹⁴ Patients diagnosed with PAD also received a newly written educational brochure, *Take Steps Against Peripheral Arterial Disease*.¹⁵

Claudication and Leg Symptoms

The San Diego Claudication Questionnaire, a modification of the Rose questionnaire, was used to identify the prevalence of claudication or other exertional leg pain.¹⁰ The questionnaire allows for lateralization of leg symptoms (right, left, or both) and categorizes leg symptoms as either classic claudication (meeting all Rose criteria, listed below), atypical leg pain that was exertional but did not meet all Rose criteria, or no leg pain. Rose claudication was defined as exercise-induced calf pain, not present at rest, which required stopping, and remitted in 10 minutes or less.

Statistical Analyses

The primary statistical analysis focused on the following contrasts: (1) comparisons between the reference group and the pooled clinical groups with atherosclerosis (PAD, CVD, or both), (2) comparisons between the prior PAD-only group and the CVD-only group, and (3) comparisons be-

tween the new PAD-only group and the prior PAD-only group.

Statistical analyses were performed by SAS version 6.12 (SAS Institute Inc, Cary, NC, 1990). Continuous variables were compared across the 4 clinical groups using analysis of variance with 2-tailed tests. For selected categorical variables, tests were conducted to see if proportions across clinical groups differed. The Mantel-Haenszel χ^2 test was used unless small cell sizes necessitated use of the Fisher exact test. Statistical significance was accepted at the .01 level given the multiple contrasts stated above.

RESULTS

Demographics: Prevalence of PAD and CVD

The data set was complete for 6417 patients, or 92% of the 6979 patients screened. PAD was detected in 1865 patients (29%). As shown in TABLE 1, 1527 patients (24%) had CVD only, 825

(13%) had PAD only, and 1040 (16%) had both PAD and CVD. Sixty-two percent of those screened were 70 years or older, and 38% of those screened were aged 50 through 69 years with a history of smoking, diabetes, or both.

The study cohort reflected a national database, comprising 18% of patients from the Northeast, 27% from the Southeast, 25% from the Midwest, 16% from the Southwest, and 14% from the West Coast. Within the total cohort, 20% of the patients were employed, 73% were retired, and 7% were unemployed. The mean (SD) age of the population was 70 (10) years. There were approximately equal proportions of men (48%) and women (52%) overall, but more men were in the CVD-only group than in the reference and PAD-only groups ($P<.001$ for both contrasts). Black participants were overrepresented in the group with PAD only vs the reference and CVD-only groups (pooled reference group, $P<.005$; CVD only, $P<.001$; Table 1).

New vs Prior PAD and Other CVD Diagnoses

Of patients who had PAD only, 55% were newly diagnosed, whereas of patients who had PAD with CVD, 35% were newly diagnosed (Table 1). Thus, a diagnosis of new PAD at the time of this evaluation was more likely in patients without other evidence of CVD vs patients who had other evidence of CVD ($P<.001$). Congestive heart failure was more frequent in the CVD-only group vs the PAD-only and reference groups ($P<.001$ for both contrasts).

ABI and Leg Symptoms

The mean (SD) ABI in patients with PAD only was 0.78 (0.19) (the same in new or prior PAD groups), and in patients having PAD with CVD the mean (SD) ABI was 0.78 (0.20) ($P<.001$ for all pooled PAD groups compared with the reference group, [ABI, 1.09] TABLE 2). All patients without PAD, by definition, had an ABI of more than 0.90.

Table 1. Subject Demographics and Concomitant Cardiovascular Diseases (CVDs)*

Variables	All Atherosclerotic Disease Clinical Groups								P Value Comparisons	
	Reference Group	PAD Only			CVD Only	PAD and CVD		PAD Only Prior vs CVD Only	Reference Group vs All Atherosclerotic Disease Groups	
		New	Prior	P Value		New PAD	Prior PAD			
No. of patients	3025	457	368	...	1527	366	674	
Prevalence, %	47	7	6	...	24	6	10	
Age, mean (SD), y	68.9 (10.0)	70.8 (10.1)	71.5 (9.3)	.74	71.2 (8.9)	73.2 (9.2)	72.3 (9.1)	.74	<.001	
Men	1248 (41.3)	162 (35.4)	163 (44.3)	.008	886 (58.0)	189 (51.6)	389 (57.7)	<.001	<.001	
Race or ethnicity				.50				<.001	.005	
White	2437 (80.6)	347 (75.9)	274 (74.5)		1288 (84.3)	294 (80.3)	551 (81.8)			
Black	282 (9.3)	76 (16.6)	60 (16.3)		110 (7.2)	45 (12.3)	71 (10.5)			
Hispanic	137 (4.5)	14 (3.1)	16 (4.3)		47 (3.1)	9 (2.5)	17 (2.5)			
Other	114 (3.7)	11 (2.5)	14 (3.8)		51 (3.3)	10 (2.7)	22 (3.2)			
Concomitant Manifestations of CAD, CVD, and PAD										
Angina	0	0	0	...	802 (52.5)	169 (46.2)	361 (53.6)	
Myocardial infarction	0	0	0	...	619 (40.5)	152 (41.5)	304 (45.1)	
PTCA	0	0	0	...	383 (25.0)	88 (24.0)	156 (23.1)	
CABG	0	0	0	...	469 (30.7)	108 (29.5)	272 (40.4)	
CHF	115 (3.8)	23 (5.0)	27 (7.3)	.17	242 (15.8)	72 (19.7)	168 (24.9)	<.001	<.001	
TIA	0	0	0	...	238 (15.6)	52 (14.2)	119 (17.7)	
Stroke	0	0	0	...	253 (16.6)	67 (18.3)	127 (18.8)	
Revascularization of the lower extremities	0	0	86 (23.4)	...	0	0	179 (26.6)	

*All values are presented as numbers (percentages) unless otherwise indicated. PAD indicates peripheral arterial disease; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft surgery; CHF, congestive heart failure; TIA, transient ischemic attack; CAD, coronary artery disease; and ellipses, not applicable. Tests of significance were not performed to compare lower extremity revascularization nor cardiovascular history between clinical groups because these factors pre hoc defined the clinical group assignments.

In the PAD-only group, only 8.7% had classic Rose claudication. Although classic claudication was more common in patients with prior PAD than in those with newly diagnosed PAD (12.6% vs. 5.5%, $P < .001$) or in patients without atherosclerosis (1.7%, $P < .001$), it was distinctly uncommon overall (Table 2). Atypical leg symptoms were much more frequent in all groups.

Physician and Subject Awareness of Prior PAD

Eighty-three percent of the patients with a prior diagnosis of PAD were aware of the diagnosis, but only 49% of their phy-

sicians had recognized the PAD diagnosis at the time of screening ($P < .01$). This discrepancy between patient and physician PAD awareness was similar whether CVD was present or absent.

Atherosclerosis Risk Factor Prevalence and Treatment

Histories of smoking and diabetes were more common in all 3 clinical groups with atherosclerosis than in the reference group (TABLE 3, pooled comparison, $P < .001$). The prevalence of smoking was higher in the patients with prior PAD only than in those with CVD only ($P < .001$). Smoking cessation interventions were prescribed more frequently

in the prior PAD-only group and in the new PAD-only group compared with the CVD-only group and in the reference group. The diagnosis of diabetes was documented in more patients with prior PAD only vs CVD only ($P = .03$). Diabetes was treated to a similar extent in all patient groups.

Low-density lipoprotein cholesterol values were available from 63% of new PAD-only and 65% of prior PAD-only patients compared with 73% of patients with CVD only ($P < .01$ for prior PAD-only compared with CVD-only groups). The prevalence of hyperlipidemia (derived from available data) was significantly greater in the 3 patient

Table 2. Ankle-Brachial Index and Leg Symptoms*

Variables	All Atherosclerotic Disease Clinical Groups							P Value Comparisons	
	Reference Group	PAD Only			CVD Only	PAD and CVD		PAD Only Prior vs CVD Only	Reference Group vs All Atherosclerotic Disease Groups
		New	Prior	P Value		New PAD	Prior PAD		
No. of patients	3017	457	366		1336	364	670
Prevalence, %	48	7	6		22	6	11
Leg symptoms, No. (%)†									
No pain	1105 (57.6)	193 (48.3)	84 (25.8)	<.001	689 (51.6)	149 (44.9)	146 (23.3)	<.001	<.001
Atypical	783 (40.8)	185 (46.3)	201 (61.7)	<.001	608 (45.5)	164 (49.4)	384 (61.3)	<.001	<.001
Classic Rose claudication	32 (1.7)	22 (5.5)	41 (12.6)	<.001	39 (2.9)	19 (5.7)	96 (15.3)	<.001	<.001
Ankle-brachial index, mean (SD)	1.09 (0.13)	0.78 (0.16)	0.78 (0.23)	<.001	1.09 (0.15)	0.77 (0.14)	0.78 (0.23)	<.001	<.001

*Ellipses indicate not applicable; PAD, peripheral arterial disease; and CVD, cardiovascular disease.
†Leg pain was evaluated using the San Diego Claudication Questionnaire.¹⁰

Table 3. Prevalence of Atherosclerosis Risk Factors and the Intensity of Risk Factor Treatment and Antiplatelet Medication Use in the Survey Population*

Variables	All Atherosclerotic Disease Clinical Groups							Reference Group vs All Atherosclerotic Disease Groups
	Reference Group	PAD Only			CVD Only†	PAD and CVD		
		New	Prior	P Value		New PAD	Prior PAD	
Current and former smoking	1499 (50)	274 (60)	235 (64)	.25	816 (53)	215 (59)	449 (67)	<.001
Proportion treated	607 (41)	146 (53)	120 (51)	.62	288 (35)	78 (36)	188 (42)	.66
Diabetes	1025 (34)	150 (33)	161 (44)	.001	572 (38)	155 (42)	304 (45)	<.001
Proportion treated	874 (85)	122 (81)	137 (85)	.38	467 (82)	128 (83)	257 (85)	.10
Hyperlipidemia	1672 (69)	243 (74)	225 (77)	.38	1059 (82)	264 (86)	482 (86)	<.001
Proportion treated	714 (43)	106 (44)	127 (56)	.006	768 (73)	174 (66)	366 (76)	<.001
Hypertension	2108 (70)	371 (81)	304 (83)	.60	1315 (86)	335 (92)	618 (92)	<.001
Proportion treated	1772 (84)	312 (84)	267 (88)	.17	1244 (95)	325 (97)	594 (96)	<.001
Postmenopausal	1537 (87)	261 (89)	174 (86)	.05	565 (91)	154 (89)	250 (90)	.08
Proportion treated	612 (40)	88 (34)	58 (33)	.98	187 (33)	36 (23)	73 (29)	<.001
Antiplatelet medication use	1043 (34)	151 (33)	199 (54)	<.001	1076 (71)	263 (71)	510 (74)	<.001

*All values are expressed as numbers (percentages). The proportion treated represents the fraction of those with each risk factor who were receiving treatment for that risk factor.
† $P < .01$ for those with prior peripheral arterial disease (PAD) alone vs those with cardiovascular disease (CVD) alone.

groups compared with the reference group ($P < .001$). However, patients with prior PAD only had a lower prevalence of hyperlipidemia (77%) compared with patients in the CVD-only group (82%, $P < .01$). The patients in the reference group were treated less frequently for their lipid disorders than were the patients with atherosclerosis ($P < .001$). Patients with a new PAD diagnosis were less intensively treated for hyperlipidemia than were patients with a prior PAD diagnosis ($P < .006$) and had a similar treatment intensity to the reference group. Importantly, prior PAD-only patients were less intensively treated for hyperlipidemia vs the CVD only group ($P < .001$).

Hypertension was more prevalent in the 3 pooled patient groups compared with the reference group ($P < .001$). Patients in the reference group were less frequently treated for their hypertension than were patients in the pooled groups with atherosclerosis ($P < .001$), whereas hypertension was treated more intensively in the patients with CVD than in those patients with new or prior PAD only ($P < .001$).

By definition all of the women in the study population were aged 50 years or older. Thus, most were postmenopausal and the postmenopausal state was equally prevalent across all diagnostic groups. Use of postmenopausal hormonal therapies was low overall, but it was higher in the reference group than in patients with atherosclerosis ($P < .001$).

Antiplatelet Therapies

Despite lack of a consistent national recommendation favoring the use of antiplatelet therapies as primary prevention,¹⁶ 34% of patients in the reference group were taking an antiplatelet drug (Table 3). This rate was significantly lower than in the patients with previously diagnosed atherosclerotic syndromes ($P < .001$). Among patients with PAD only, those with a new diagnosis were less intensively treated with antiplatelet therapy than were those with a prior diagnosis ($P < .001$). This low rate of use of antiplatelet treatments in those with

new PAD was similar to the reference group. Overall, patients who had CVD only were more likely to be receiving an antiplatelet agent than were patients with prior PAD only ($P < .001$). Patients with CVD and PAD used antiplatelet therapies at the highest level ($>71\%$). Use of specific antiplatelet medications within the total study population included aspirin (48%), clopidogrel bisulfate (2%), ticlopidine hydrochloride ($<1\%$), and dipyridamole ($<1\%$). In the survey population, 49% were not using any antiplatelet medication.

COMMENT

Epidemiologic and natural history studies have determined that PAD is prevalent and confers a high risk of fatal and nonfatal cardiovascular ischemic events.^{1,17-21,34} This national study demonstrates that PAD is highly prevalent in primary care settings and is easily detected by the ABI examination during routine primary care office visits. The high 29% PAD prevalence documented in this community survey supported our hypothesized underdiagnosis, because a new PAD diagnosis was established in approximately half of those with the disease. Despite the prevailing notion that PAD is a disease with a predilection for men,^{2,18,19} PAD was as common in women in our investigation, especially in those without CVD. Furthermore, PAD was detected at high rates in all national regions and all races, although these data indicate that isolated PAD is particularly common in black persons, as has been previously observed.²⁰⁻²²

These data demonstrate that although more than half of the patients with PAD have leg symptoms, relatively few reported classic Rose claudication. The presence of typical leg symptoms was more common in those patients whose PAD diagnosis was previously established, and asymptomatic patients were more likely to have their PAD diagnosis established only by the survey's ABI measurement. These data suggest that clinicians who utilize a classic history of claudication alone to detect PAD are likely to miss 85% to 90% of the PAD diagnoses.

These data corroborate that the PAD population carries a high atherosclerosis risk factor burden and ischemic risk. In the PAD-only cohort, patients had the same ABI as patients having PAD with CVD. More strikingly, new PAD-only patients had the same ABI as prior PAD-only patients. Even in patients without CVD, an ABI value of 0.78 portends an approximate 30% 5-year risk of MI, ischemic stroke, and vascular death.²²⁻²⁴ This increased mortality risk could presumably be reduced by appropriate lifestyle and pharmacological interventions within a primary care setting. Such interventions would preferably be initiated by each patient's primary care provider, who is best able to establish the PAD diagnosis and to maintain a long-term therapeutic relationship.

A second study hypothesis was that patients with a prior diagnosis of PAD only would be less intensively treated for their atherosclerosis risk factors and less frequently prescribed antiplatelet therapies than patients with a prior diagnosis of CVD.^{5,25} Recognition of the role of tobacco in the pathogenesis of PAD has been widespread, and smoking cessation reduces disease progression and mortality risk in PAD patients.^{26,27} While PAD patients were referred to smoking cessation programs at a higher rate than patients with CVD or in the reference group, even in PAD patients smoking cessation therapies only were prescribed approximately 50% of the time.

Diabetes was a risk factor treated at a similar intensity in all of the clinical groups, including the reference group. Thus, the diagnosis of diabetes was adequate to initiate treatment in almost all patients with this disorder, regardless of the presence or absence of clinically evident CVD. A similar pattern of treatment was observed for the use of hormone replacement therapy in women with atherosclerosis although the role of hormone replacement therapy remains controversial.²⁸

Patients with prior PAD only were less intensively managed for hyperlipidemia and hypertension and were less

often prescribed antiplatelet therapies than were patients with CVD. Current lipid-lowering guidelines of the National Cholesterol Education Program suggest that patients with PAD should achieve an LDL cholesterol concentration of 100 mg/dL (2.59 mmol/L) and treatment for elevated serum triglyceride levels.¹² Despite these recommendations, lipid measurements were obtained less often in PAD-only patients. In addition, these patients were less intensively treated, findings that support our undertreatment hypothesis.

Guidelines published for the detection and treatment of hypertension recognize PAD as evidence of clinical CVD requiring drug therapy for all stages of hypertension.²⁹ In this survey, hypertension was generally treated at high levels in all patients evaluated in office practice. Nevertheless, patients with PAD only were less frequently treated than patients with documented CVD.

In patients with atherosclerosis, antiplatelet agents have been shown to reduce the risks of MI, ischemic stroke, and vascular death.³⁰⁻³² Antiplatelet therapy is therefore recommended for secondary disease prevention in patients with CVD.³³ This survey also demonstrated lower rates of administration of antiplatelet therapy in patients with both new and prior PAD compared with CVD patients without PAD.

Study Limitations

This national study was not designed to evaluate the epidemiology and natural history of PAD because this has been performed in many previous studies.^{3,4,20,34-37} Rather, the primary goal was to determine the yield of routinely measuring ABI in the primary care setting to detect previously undiagnosed PAD. Potential biases could have occurred in that clinicians at the practice sites were aware of the goals of the study and therefore may have preferentially over-enrolled patients with known PAD. Also, patients with leg symptoms may have been more willing to participate. Despite this possibility, 44% of the PAD patients were newly diagnosed at the time of the study.

A critical goal of this research program was to identify the prevalence of atherosclerosis risk factors in the clinical groups. Although standard clinical criteria were used to define cigarette smoking, diabetes, and hyperlipidemia, we did not validate the application of these criteria by using biochemical markers for each condition. It was impractical to obtain plasma cotinine, or fasting glucose or lipid panels from each survey participant. Consequently, the true prevalence of these risk factors in PAD-only patients was therefore likely underestimated, thus potentially magnifying the undertreatment findings.

Conclusion

PAD is a prevalent atherosclerotic syndrome and is associated with a very high risk of MI, stroke, and death. In the absence of a national program of PAD education and detection, many patients will not receive a diagnosis of PAD prior to the occurrence of a morbid or mortal ischemic event. The PARTNERS program demonstrated that PAD is easily detected with the ABI technique by both nurses and physicians in the primary care setting. Despite the known benefits of antiplatelet therapy and treatment of hypertension and hyperlipidemia to reduce ischemic event rates, PAD patients were less intensively treated than patients with CVD. The underdiagnosis of PAD and subsequent exposure of this large cohort to ischemic risk would be expected to adversely affect their clinical outcome, increasing rates of MI and stroke, cardiovascular mortality, long-term costs, and diminishing quality of life. In as much as PAD affects between 8 and 12 million US residents, effective long-term care of patients with PAD will require increased diagnostic efforts and appropriate medical interventions in community-based, primary care settings to decrease limb-specific symptoms, improve quality of life, and decrease systemic cardiovascular risk.

Author Affiliations, PARTNERS Investigators, and Financial Disclosure: Vascular Medicine Program, University of Minnesota Medical School, Minneapolis (Drs

Hirsch, Treat-Jacobson, Krook, and Hunninghake); Department of Family and Preventive Medicine, University of California, San Diego, School of Medicine, San Diego (Dr Criqui); University of Colorado Health Sciences Center (Dr Regensteiner) and Divisions of Geriatrics and Cardiology, University of Colorado Health Sciences Center (Dr Hiatt), Denver; Brigham and Women's Hospital, Boston, Mass (Dr Creager); Heart and Vascular Institute, Morristown, NJ (Dr Olin); Temple University Hospital, Philadelphia, Pa (Dr Comerota); Jobst Center, Toledo, Ohio (Ms Walsh); and Northwestern University Medical School, Chicago, Ill (Dr McDermott).

Members of the PARTNERS Steering Committee are: Drs Hirsch and Hiatt (cochairs), Dr Criqui (study epidemiologist), and Drs Treat-Jacobson, Regensteiner, Creager, Olin, Krook, Hunninghake, Comerota, and McDermott, and Ms Walsh.

Financial Disclosure: All authors served as consultants to and Drs Hirsch, Treat-Jacobson, Creager, Olin, Comerota, and Hiatt, and Ms Walsh, have received speakers' bureau honoraria from the Bristol Myers Squibb/Sanofi-Synthelabo Partnership.

Author Contributions: The steering committee, which includes all the authors of this study, supervised creation of all data collection forms, created the data analysis plan, had access to all data, reviewed all data analyses, and prepared the manuscript.

Study concept and design: Hirsch, Criqui, Treat-Jacobson, Creager, Olin, Krook, Hunninghake, Comerota, Walsh, McDermott, Hiatt.

Acquisition of data: Hirsch, Criqui, Treat-Jacobson, Regensteiner, Olin, Comerota, Walsh, Hiatt.

Analysis and interpretation of data: Hirsch, Criqui, Treat-Jacobson, Regensteiner, Olin, Comerota, Walsh, McDermott, Hiatt.

Drafting of the manuscript: Hirsch, Criqui, Hiatt.

Critical revision of the manuscript for important intellectual content: Hirsch, Criqui, Treat-Jacobson, Regensteiner, Creager, Olin, Krook, Hunninghake, Comerota, Walsh, McDermott, Hiatt.

Statistical expertise: Criqui.

Obtained funding: Hirsch, Criqui, Hiatt.

Administrative, technical, or material support: Criqui, Regensteiner, Krook, Hunninghake.

Study supervision: Hirsch, Criqui, Treat-Jacobson, McDermott, Hiatt.

Funding/Support: Dr Hirsch received additional support during the course of this research program from grant 1-K07-HL03435-01, an academic award from the Vascular Diseases from the National Heart, Lung, and Blood Institute. This program was sponsored by the Bristol-Myers Squibb-Sanofi Synthelabo Partnership, which provided financial support for the Program and contracted PPD Inc (Morrisville, NC) to conduct data collection and analysis. Dr Hiatt is the Novartis Foundation Professor of Cardiovascular Research at the University of Colorado School of Medicine.

Acknowledgment: We thank Wayne Wilson, MPH, for his aid in managing the database, Robert L. Boggs, PhD, for statistical support, and Chitra Sekaran, MD, and Joan Stagers, PhD, for their contributions to the manuscript.

PARTNERS Investigators: *Arizona:* Kent Smith, Phoenix; *California:* John P. Cooke, Stanford, Michael Criqui, San Diego, and Thomas McNamara, Los Angeles; *Colorado:* William Hiatt, Denver; *Florida:* David Bernstein, Clearwater, and Gerald Zemel, Miami; *Illinois:* Jeffrey Buckman and Mary M. McDermott, Chicago; *Louisiana:* Tyrone Collins, New Orleans; *Maryland:* Michael Lilly, Baltimore; *Massachusetts:* Marie Gerhard, Boston; *Michigan:* James Froehlich, Ann Arbor; *Minnesota:* Alan T. Hirsch, Minneapolis; *Missouri:* Catherine Wittgen, St Louis; *New York:* Jonathan Halperin, New York; *North Carolina:* Pavel Levy, Winston-Salem; *Ohio:* Steven Gale, Toledo, and Jeffrey Olin, Cleveland; *Oklahoma:* Thomas Whitsett, Oklahoma City; *Pennsylvania:* Anthony Comerota and Emile

Mohler III, Philadelphia, and David Steed, Pittsburgh; Tennessee: Mitchell Goldman, Knoxville; Texas: Kenneth McIntyre, Dallas; Washington: Eugene Zierler, Seattle; and Washington, DC: John Laird.

REFERENCES

- Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, Gabriel S, Goodman D. The prevalence of peripheral arterial disease in a defined population. *Circulation*. 1985;71:510-515.
- Criqui MH, Denenberg JO, Langer RD, Fronek A. The epidemiology of peripheral arterial disease: importance of identifying the population at risk. *Vasc Med*. 1997;2:221-226.
- Meijer WT, Hoes AW, Rutgers D, Bots ML, Hofman A, Grobbee DE. Peripheral arterial disease in the elderly: the Rotterdam Study. *Arterioscler Thromb Vasc Biol*. 1998;18:185-192.
- Fowkes FG, Housley E, Cawood EH, Macintyre CC, Ruckley CV, Prescott RJ. Edinburgh Artery Study: prevalence of asymptomatic and symptomatic peripheral arterial disease in the general population. *Int J Epidemiol*. 1991;20:384-392.
- Hirsch AT, Halverson SL, Treat-Jacobson D, et al. The Minnesota Regional Peripheral Arterial Disease Screening Program: toward a definition of community standards of care. *Vasc Med*. 2001;6:87-96.
- Fowkes FGR. Epidemiology of peripheral vascular disease. *Atherosclerosis*. 1997;131(suppl):S29-S31.
- Papademetriou V, Narayan P, Rubins H, Collins D, Robins S, for the HIT Investigators. Influence of risk factors on peripheral and cerebrovascular disease in men with coronary artery disease, low high-density lipoprotein cholesterol levels, and desirable low-density lipoprotein cholesterol levels. *Am Heart J*. 1998;136:734-740.
- Ouriel K, McDonnell AE, Metz CE, Zarins CK. Critical evaluation of stress testing in the diagnosis of peripheral vascular disease. *Surgery*. 1982;91:686-693.
- Yao ST, Hobbs JT, Irvine WT. Ankle systolic pressure measurements in arterial disease affecting the lower extremities. *Br J Surg*. 1969;56:676-679.
- Criqui MH, Denenberg JO, Bird CE, Fronek A, Klauber MR, Langer RD. The correlation between symptoms and non-invasive test results in patients referred for peripheral arterial disease testing. *Vasc Med*. 1996;1:65-71.
- Ansell BJ, Watson KE, Fogelman AM. An evidence-based assessment of the NCEP Adult Treatment Panel II guidelines: National Cholesterol Education Program. *JAMA*. 1999;282:2051-2057.
- Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486-2497.
- Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA*. 1998;279:1615-1622.
- American Heart Association. *Fact Sheet on Heart Attack, Stroke and Risk Factors*. Dallas, Tex: American Heart Association; 1999. Publication. 55-0532991118 D.
- Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership. *Take Steps Against Peripheral Arterial Disease*. New York, NY; Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership; 1999. Available at: <http://www.takestepsagainstPAD.com>.
- Department of Health and Human Services, Food and Drug Administration. Internal analgesic, antipyretic, and antirheumatic drug products for over-the-counter human use; final rule for professional labeling of aspirin, buffered aspirin, and aspirin in combination with antacid drug products [21 CFR Part 343]. *Federal Register*. 1998;63:56802-56819.
- Dormandy JA, Rutherford RB. Management of peripheral arterial disease (PAD). TransAtlantic Inter-Society Consensus (TASC). *J Vasc Surg*. 2000;31(1 pt 2):S1-S296.
- Aronow WS, Ahn C. Prevalence of coexistence of coronary artery disease, peripheral arterial disease, and atherothrombotic brain infarction in men and women 62 years of age. *Am J Cardiol*. 1994;74:64-65.
- Kannel WB, Skinner JJJ, Schwartz MJ, Shurtleff D. Intermittent claudication. Incidence in the Framingham Study. *Circulation*. 1970;41:875-883.
- Newman AB, Sutton-Tyrrell K, Rutan GH, Locher J, Kuller LH. Lower extremity arterial disease in elderly patients with systolic hypertension. *J Clin Epidemiol*. 1991;44:15-20.
- Newman AB, Siscovick DS, Manolio TA, et al. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. *Circulation*. 1993;88:837-845.
- Newman AB, Tyrrell KS, Kuller LH. Mortality over four years in SHEP participants with a low ankle-arm index. *J Am Geriatr Soc*. 1997;45:1472-1478.
- McDermott MM. Ankle brachial index as a predictor of outcomes in peripheral arterial disease. *J Lab Clin Med*. 1999;133:33-40.
- McKenna M, Wolfson S, Kuller L. The ratio of ankle and arm arterial pressure as an independent predictor of mortality. *Atherosclerosis*. 1991;87:119-128.
- McDermott MM, Mehta S, Ahn H, Greenland P. Atherosclerotic risk factors are less intensively treated in patients with peripheral arterial disease than in patients with coronary artery disease. *J Gen Intern Med*. 1997;12:209-215.
- Jonason T, Bergstrom R. Cessation of smoking in patients with intermittent claudication: effects on the risk of peripheral vascular complications, myocardial infarction and mortality. *Acta Med Scand*. 1987;221:253-260.
- Hirsch AT, Treat-Jacobson D, Lando HA, Hatsukami DK. The role of tobacco cessation, antiplatelet, and lipid-lowering therapies for the treatment of peripheral arterial disease. *Vasc Med*. 1997;2:243-251.
- Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA*. 1998;280:605-613.
- Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [published erratum appears in *Arch Intern Med*. 1998;158:573]. *Arch Intern Med*. 1997;157:2413-2446.
- Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy. I: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *BMJ*. 1994;308:81-106.
- CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel vs aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet*. 1996;348:1329-1339.
- Jackson MR, Clagett GP. Antithrombotic therapy in peripheral arterial occlusive disease. *Chest*. 1998;114(suppl 5):666S-682S.
- Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). *J Am Coll Cardiol*. 2000;36:970-1062.
- Criqui MH, Langer RD, Fronek A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med*. 1996;326:381-386.
- Newman AB, Shemanski L, Manolio TA, et al. Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. *Arterioscler Thromb Vasc Biol*. 1999;19:538-545.
- Vogt MT, Cauley JA, Newman AB, Kuller LH, Hulley SB. Decreased ankle/arm blood pressure index and mortality in elderly women. *JAMA*. 1993;270:465-469.
- Zheng ZJ, Sharrett AR, Chambless LE, et al. Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study. *Atherosclerosis*. 1997;131:115-125.