Atherosclerotic Risk Factors Are Less Intensively Treated in Patients with Peripheral Arterial Disease Than in Patients with Coronary Artery Disease

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***OBJECTIVE*: To compare rates of therapy for atherosclerotic risk factors between patients with lower extremity peripheral arterial disease (PAD) and patients with coronary artery disease (CAD).**

***DESIGN*: Cross-sectional.**

***SETTING*: Academic medical center.**

***PATIENTS/PARTICIPANTS*: Three hundred forty-nine consecutive patients diagnosed with PAD or CAD identified from the blood flow and cardiac catheterization laboratories, respectively.**

***MEASUREMENTS AND MAIN RESULTS*: Participants were interviewed by telephone for medical history as well as therapies prescribed and recommended by their physicians. Among patients with hypercholesterolemia, more CAD patients were taking cholesterol-lowering drugs (58% vs 46%, $p = .08$) and more CAD patients recalled a physician's instruction to follow a low-fat, low-cholesterol diet (94% vs 83%, $p = .01$). CAD patients were more likely to exercise regularly (71% vs 50%, $p < .01$). Among patients not exercising, more CAD patients recalled a physician's advice to exercise (74% vs 47%, $p < .01$). In logistic regression analysis, hypercholesterolemic patients with exclusive CAD were more likely to be treated with drug therapy (odds ratio [OR] 2.3, $p = .05$). CAD patients were more likely to recall advice to exercise (OR 4.0, $p < .001$), and more likely to be taking aspirin or warfarin (OR 4.8, $p = .01$).**

***CONCLUSIONS*: Atherosclerotic risk factors are less intensively treated among PAD patients than CAD patients. A number of possible explanations could account for these disparities in therapeutic intensity.**

***KEY WORDS*: atherosclerotic risk factors; peripheral arterial disease; coronary artery disease.**
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Peripheral arterial disease (PAD) and coronary artery disease (CAD) are common among elderly patients, and both are associated with an increased risk of cardiovascular events.[1–8] Among patients with CAD, hyperlipidemia therapy, aspirin therapy, cardiac rehabilitation, and smoking cessation have been associated with a reduction in the number of cardiovascular events.[9–16] On the basis of such data, the American Heart Association and the American College of Cardiology have endorsed secondary prevention guidelines for CAD patients.[17,18]

Clinical trials have documented a favorable impact of exercise on the distance that PAD patients with intermittent claudication are able to walk without pain.[19–22] However, no large clinical trials have assessed the effects of aggressive atherosclerotic risk factor management on cardiovascular outcomes in patients with PAD. Because PAD is associated with a two-fold to six-fold increase in the risk of cardiovascular mortality,[6–8] aggressive treatment of atherosclerotic risk factors is recommended for PAD patients.[23–25]

Previous studies have documented undertreatment of atherosclerotic risk factors among CAD patients.[26,27] Rates of atherosclerotic risk factor therapy may be even lower in patients with PAD, in part because of the paucity of data relating such treatment to a reduction in cardiovascular events. Underappreciation of the strong association between PAD and cardiovascular mortality may also result in undertreatment. To evaluate the extent of atherosclerotic risk factor intervention in patients with PAD, we compared therapy between consecutive patients diagnosed with PAD and patients diagnosed with CAD at an academic medical center. We hypothesized that atherosclerotic risk factors are more aggressively treated among CAD patients than among PAD patients.

METHODS

Identification of Patients

The study was performed at an academic medical center in downtown Chicago. Computerized lists were used to identify consecutive patients diagnosed with PAD in the blood flow laboratory between May 1 and September 30, 1995. The PAD diagnosis was based on an ankle-brachial index less than 0.9 or an abnormal waveform in one or more arteries of either or both of the lower extremities. Using the cardiac catheterization logbook, we identified consecutive patients with an abnormal coronary angiogram between May 1 and October 31, 1995. CAD was defined as 70% or greater stenosis in one or more coro-

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nary arteries. We chose these diagnostic methods because they confirm significant CAD and PAD, respectively. Although only the CAD diagnosis required invasive testing, at our institution lower extremity arteriograms are used primarily to define the arterial anatomy of patients already selected for lower extremity revascularization, while coronary arteriograms are used predominantly for diagnostic purposes. Noninvasive testing for PAD is 95% sensitive and nearly 100% specific.[28]

Data Collection

The study was approved by the Institutional Review Board, and all participants were sent an "information letter" describing the research study. Approximately 2 weeks after the letters were sent, investigators telephoned the study patients. A standardized questionnaire was developed before beginning telephone calls. The questionnaires were identical for PAD patients and CAD patients with the exception that only CAD patients were asked whether they had ever been diagnosed with PAD ("a blood flow or circulatory problem in the arteries supplying the legs"), and only PAD patients were queried about complications of PAD such as a history of gangrene or leg ulcer. All patients were asked about their history of hypertension, diabetes, hypercholesterolemia, cigarette smoking, and cardiovascular disease. All patients were administered the Edinburgh claudication questionnaire.[29] Patients were asked about advice they recalled receiving from their physicians. Current smokers were asked whether they had been advised to quit smoking, and patients who reported a history of high cholesterol levels were asked whether they had been advised to follow a low-cholesterol, low-fat diet. Patients reporting hypercholesterolemia and hypertension were asked whether they were being treated with medications to lower their cholesterol level and blood pressure, respectively. All patients were asked whether they exercise and whether any physician had advised them to exercise.

Statistical Analyses

We used χ^2 tests of association for categorical variables and Student's t tests for continuous variables to compare characteristics between patients with PAD and those with CAD. Patients unable to walk were excluded from all exercise comparisons.

Coronary artery disease is common among patients with PAD and may confound comparisons between PAD patients and CAD patients. We therefore performed further analyses comparing patients with atherosclerotic disease limited to either the lower extremity or coronary arterial beds. Patients with exclusive PAD were PAD patients who had no history of myocardial infarction, cardiac arrest, angina, congestive heart failure, or coronary revascularization. Patients with exclusive CAD were patients with coronary atherosclerosis who did not have symptoms consistent with intermittent claudication as defined by the Edinburgh claudication questionnaire,[29] and who reported no history of blood flow problems to the legs or lower extremity revascularization. Although some patients categorized with exclusive disease may have had unidentified atherosclerotic disease in the other vascular bed, our aim was to classify patients according to established diagnoses recognized by the managing physicians.

Logistic regression analysis was used to determine whether cholesterol therapy was associated independently with exclusive CAD among patients with hypercholesterolemia, controlling for age, gender, race, and diabetes mellitus. Logistic regression was also used to determine whether exercise frequency and a physician's advice to exercise were associated independently with CAD, controlling for age, gender, race, and diabetes mellitus. The independent association between CAD and aspirin or warfarin therapy was tested using logistic regression analysis, controlling for age, gender, race, past coronary or lower extremity procedures, and history of atrial fibrillation. To determine the effect of physician specialty on therapy, patients were asked to identify their "primary" physician. Logistic regression analyses were repeated controlling for the specialty of each patient's main physician.

RESULTS

A total of 288 patients with CAD were identified from the cardiac catheterization laboratory. Of these, 12 patients (4%) died before telephone contact was made, 38 (13%) refused participation, 72 (25%) could not be reached, and 23 (4%) did not speak English. Among the 359 patients identified with PAD, 11 (3%) died before telephone contact was made, 56 (16%) refused participation, 73 (20%) could not be reached, and 10 (3%) did not speak English. A total of 363 interviews were conducted. Seven patients were interviewed both as part of the PAD cohort and as part of the CAD cohort. These seven patients, representing 14 interviews, were eliminated from analyses, leaving 349 patients. Of these 349 patients, 202 were PAD patients and 147 were CAD patients.

The majority of PAD patients and CAD patients had symptomatic disease, or previous procedures relevant to their atherosclerotic disease, or both. Among PAD patients, 60% had undergone a previous lower extremity procedure, and 93% had exertional leg pain, or a history of gangrene or ulcer, or a previous lower extremity procedure. Among CAD patients, 76% had undergone coronary revascularization and 93% had a history of myocardial infarction, cardiac arrest, angina, congestive heart failure, or coronary revascularization. Ninety-nine patients had PAD exclusively, and 104 patients had CAD exclusively.

Characteristics of Patients

Table 1 compares clinical characteristics between all PAD patients and CAD patients and between patients with exclusive PAD or CAD. PAD patients were older,

more frequently female, African American, diabetic, and more likely to currently smoke. Among patients who recalled having their cholesterol level checked, hypercholesterolemia was more common among those with exclusive CAD than those with exclusive PAD. Patients with CAD were significantly more likely to know their actual cholesterol level (51% vs 30%, $p < .001$).

Therapies for Patients

Table 2 compares therapies between CAD patients and PAD patients. Among patients reporting a history of hypercholesterolemia, those with CAD were more likely to be taking cholesterol-lowering drugs and more often recalled instruction by their physician to follow a low-cholesterol, low-fat diet. CAD patients were significantly more likely to report regular exercise. Among patients who were not exercising, those with CAD were more likely to recall a physician's advice to exercise.

Regression Analyses

In logistic regression analysis including patients with hypercholesterolemia and exclusive disease, CAD was associated independently with drug therapy for hypercholesterolemia (odds ratio [OR] 2.3, $p = .05$). In a separate analysis of the same cohort, CAD was associated independently with a physician's advice to follow a low-fat, low-cholesterol diet (OR 4.4, $p = .02$). Among patients with exclusive disease, CAD was associated independently with current exercise (OR 2.8 $p < .01$) and recollection of a physician's advice to exercise (OR 4.0, $p < .001$).

Warfarin, Aspirin, and Antioxidant Therapies

Prescribed drug therapies are shown in Table 3. CAD patients were significantly more likely to be prescribed aspirin or warfarin. In logistic regression analysis, CAD was associated independently with the prescription of aspirin or warfarin (OR 4.8, $p = .01$). Antioxidant vitamin use was not significantly different between CAD patients and PAD patients.

Estrogen Therapy Among Women

Among 115 women who did not have a history of breast or uterine cancer, rates of current and past estrogen use were comparable among women with PAD and those with CAD. Women with CAD were more likely to report that their physician had discussed estrogen therapy, but this difference was not significant (65% vs 51%, $p = .17$).

Effect of Managing Physician Specialty on Therapy

Thirty-five percent of CAD patients and 33% of PAD patients identified a general internist as their main physician. Fifty-six percent of CAD patients and 6% of PAD patients identified a cardiologist as their primary physician. Two percent of CAD patients and 44% of PAD patients identified a vascular surgeon as their primary physician. Seven percent of all patients identified a cardiac surgeon or other subspecialist as their main physician. The primary physician subspecialty could not be identified for 5% of patients.

Table 1. Characteristics of Patients with Peripheral Arterial Disease and Patients with Coronary Artery Disease*

	All Patients			Patients with Exclusive PAD or CAD†		
Characteristic	PAD ($n = 202$)	CAD ($n = 147$)	p Value	PAD ($n = 99$)	CAD ($n = 104$)	p Value
Mean age, years	68	64	<.01	67	64	.06
Male, %	55	75	<.001	47	75	<.001
White, %	75	84	.06	78	86	.15
African American, %	12	2	.001	21	2	<.01
Current smokers, %	17	8	.02	21	9	.01
Past smokers, %	72	66	.23	69	63	.37
Diabetes, %	41	23	.001	34	15	<.01
High cholesterol level, %	57	68	.09	48	75	<.001
Hypertension, %	66	63	.52	69	63	.35
Congestive heart failure, %	8	14	.08			
Coronary revascularization, %	27	76	<.001			
Atrial fibrillation, %	17	27	.03	13	28	<.01
Stroke or transient ischemic attack, %	17	15	.56	21	12	.10
Aortic aneurysm, %	9	8	.69	8	6	.52
Myocardial infarction, %	29	27	.76			
Angina, %	27	59	<.001			
Chronic lung disease, %	14	15	.88	10	13	.56

CAD indicates coronary artery disease; PAD, peripheral arterial disease.

†*By definition, patients with exclusive PAD did not have angina, past myocardial infarction, cardiac arrest, congestive heart failure, or prior coronary revascularization. Patients with exclusive CAD did not have a history of PAD or symptoms of intermittent claudication.*

Table 2. Therapeutic Management of Atherosclerotic Risk Factors Among Patients with Peripheral Arterial Disease and Patients with Coronary Artery Disease*

	PAD	CAD	*p* Value	Exclusive PAD	Exclusive CAD	*p* value
Patients with high cholesterol level, *n*	115	100		48	78	
Patients on medication, %	46	58	.08	40	56	.06
Patients advised to follow low-cholesterol diet, %	83	94	.01	79	92	.03
Patients with hypertension, *n*	134	92		68	65	
Patients who are currently taking medication, %	81	79	.82	80	79	.89
Patients who currently smoke, *n*†	34	12				
Physician has advised to quit, %	82	92	.44			
Physician advised to quit within past year, %	70	91	.16			
Patients not considering quitting, %	38	42	.83			
Patients who are able to walk, *n*	194	144		97	102	
Patients who exercise regularly, *n*‡ %	50	71	<.01	46	71	<.001
Patients who do not exercise regularly, *n*‡	97	42		52	30	
Physician has discussed exercise, %	47	74	<.01	35	83	<.001

**CAD indicates coronary artery disease; PAD, peripheral arterial disease.*
†*The number of patients with exclusive PAD or CAD who were current smokers was too low to allow a meaningful comparison.*
‡*Excludes patients who are unable to walk.*

Among smokers and patients with hypercholesterolemia and hypertension, therapy rates did not vary by physician specialty. Among patients who did not exercise, physician specialty did not influence whether a patient recalled advice to exercise. However, patients who identified a cardiologist as their main physician were more likely to exercise and be treated with aspirin or warfarin. Among patients who identified a cardiologist, generalist, or vascular surgeon as their main physician, rates of regular exercise were 71%, 48%, or 51%, respectively ($p < .01$), and for those without a history of coronary revascularization or lower extremity procedures, rates of aspirin or warfarin therapy were 93%, 52%, or 64%, respectively ($p = .02$).

To further assess the effect of physician specialty on therapies, the logistic regression analyses reported above were repeated adjusting for physician specialty. In these analyses, CAD remained independently associated with aspirin or warfarin therapy (OR 4.4, $p = .03$), exercise (OR 3.9, $p < .001$), and recollection of advice to exercise (OR 5.7, $p < .001$). Among hypercholesterolemic patients, CAD was no longer independently associated with pharmacologic therapy of hypercholesterolemia (OR 1.8, $p = .22$) or recollection of advice to follow a low-cholesterol, low-fat diet (OR 1.8, $p = .45$). Physician subspecialty was not independently associated with therapy in any analysis.

Previous Procedures and Atherosclerotic Risk Factor Management

Our selection criteria necessitated that all CAD subjects had undergone at least one invasive procedure because of suspected coronary atherosclerosis. Because an

Table 3. Medications Prescribed to Patients with Peripheral Arterial Disease Versus Patients with Coronary Artery Disease*

	PAD *n* = 202	CAD *n* = 147	*p* Value	Exclusive PAD* *n* = 99	Exclusive CAD† *n* = 104	*p* Value
All patients						
Aspirin, %	47	76	<.001	37	82	<.001
Warfarin, %	28	13	<.001	23	12	.03
Aspirin or warfarin, %	66	88	<.001	57	88	<.001
Vitamin E, vitamin C, or beta-carotene, %	30	37	.13	31	43	.08
Patients without atrial fibrillation or prior leg or coronary revascularization procedures, *n*	71	96		43	72	
Aspirin, %	49	81	<.001	42	83	<.001
Warfarin, %	10	8	.73	9	7	.65
Aspirin or warfarin, %	56	87	<.001	49	86	<.001

**CAD indicates coronary artery disease; PAD, peripheral arterial disease.*
†*By definition, patients with exclusive PAD did not have angina, past myocaridal infarction, cardiac arrest, congestive heart failure, or prior coronary revascularization. Patients with exclusive CAD did not have a history of PAD or symptoms of intermittent claudication.*

invasive procedure for known or suspected atherosclerotic disease may affect a patient's recall of physician advice or therapy, we compared atherosclerotic risk factor treatment between subjects with exclusive CAD or PAD who had undergone lower extremity revascularization or amputation. The resultant therapy discrepancies were comparable to those shown in Table 2 for all subjects with exclusive CAD or PAD. Among patients with hypercholesterolemia, 56% of CAD patients and 39% of PAD patients were taking cholesterol-lowering drugs. Ninety-two percent and 82%, respectively, recalled a physician advising them to follow a low-cholesterol, low-fat diet. The greatest differences were observed in exercise practices and recall of exercise advice. Seventy percent of CAD subjects and 51% of PAD subjects reported regular exercise ($p = .02$), while 84% of nonexercising PAD subjects and 30% of nonexercising CAD subjects recalled a physician's advice to exercise.

DISCUSSION

Peripheral arterial disease is common. Recent data suggest that the prevalence of PAD is as high as 23% among men and women aged 55 years and older in a general medicine practice.[30] Most interventions to lower atherosclerotic risk factors have not been tested in clinical trials of patients with PAD. However, because of the strong and independent relation between PAD and cardiovascular mortality, publications by the American Heart Association, the National Cholesterol Education Program, and others recommend that patients with PAD be targeted for aggressive atherosclerotic risk factor therapy. [23–25,31]

A comparison of atherosclerotic risk factor therapy between PAD patients and CAD patients has not been previously reported to our knowledge. Our results show that PAD patients were significantly less likely to recall a physician's advice to exercise, less likely to recall dietary advice for hypercholesterolemia, and less likely to be taking aspirin or warfarin.

The discrepancy between the PAD and CAD groups in rates of exercise and recollection of a physician's advice to exercise is noteworthy. Clinical trials have clearly demonstrated a favorable impact of exercise on pain-free walking distance for PAD patients with intermittent claudication.[19–22] Ironically, the discrepancies in exercise frequency and recollection of a physician's advice to exercise were among the greatest observed between PAD patients and CAD patients. These findings suggest that the reasons for undertreatment of atherosclerotic risk factors in patients with PAD may be multifactorial and not only a result of absent clinical trial data supporting the interventions. Physicians may be unaware of literature documenting the benefits of walking exercise for patients with intermittent claudication. Alternatively, physicians may perceive improved walking as a relatively unimportant outcome. Although only 30% of PAD patients in this cohort had symptoms consistent with intermittent claudication, the data show that physicians were not reserving exercise advice for patients with intermittent claudication. Fifty-nine percent of PAD patients without claudication and 57% of PAD patients with claudication recalled physician advice to exercise.

Physician Specialty and Atherosclerotic Risk Factor Therapy

Our data show an effect of physician specialty on some of the observed differences between therapies for CAD patients and those for PAD patients. Most patients identified a general internist, cardiologist, or vascular surgeon as their main physician. The independent relation between CAD patients and aspirin or warfarin therapy and exercise was maintained in regression analyses controlling for physician specialty. However, CAD was no longer associated independently with therapies for hypercholesterolemia after controlling for physician specialty.

Several factors limit our ability to ascertain the full impact of physician specialty on prescribed therapies. First, because CAD was highly associated with identifying a cardiologist as the main physician, and PAD with identifying a vascular surgeon as the main physician, even regression analyses may not fully adjust for the effect of physician specialty on therapy. Second, the number of patients cared for by generalists was too small to allow meaningful comparisons between PAD patients and CAD patients who identified a generalist as their main physician. Finally, we did not ascertain whether patients were cared for by more than one physician. Approximately half of all study participants were primarily cared for by "experts" in their respective diseases. The profile of physicians caring for PAD patients suggests that interventions to increase rates of atherosclerotic risk factor therapy in these patients should be aimed primarily at vascular surgeons and primary care physicians.

Higher Rates of Atherosclerotic Risk Factor Therapy

Patients with CAD at our institution were more likely to be treated for hypercholesterolemia than patients in previously reported studies of secondary prevention. [26,32] The higher rates of therapy in this study may be attributable to improved rates of atherosclerotic risk factor therapy over time, perhaps because of increasing emphasis on secondary prevention in the literature. Relatively recent data describing aspirin prescription rates for patients with CAD are comparable to rates of aspirin or warfarin therapy documented in the present study.[33] Although rates of atherosclerotic risk factor therapy may be higher in academic medical centers, a previous study did not show differences between community and academic health centers.[33] If similar discrepancies in atherosclerotic risk factor treatment between PAD patients and CAD patients exist at other institutions, rates of risk factor

therapy for PAD patients may be even lower in other settings than those reported here.

Study Limitations

Our study has weaknesses, including the reliance on patient report for medical history and therapeutic management. However, lack of medical record documentation was a potential confounder for both PAD patients and CAD patients. Furthermore, physicians may not consistently document advice, such as dietary recommendations. Patient recall is a reasonable proxy for the emphasis placed by physicians on specific therapies. Although approximately half of identified patients could not be reached or refused participation, these rates were comparable between PAD patients and CAD patients, suggesting that our data are useful for comparative purposes.

Because more effective interventions exist for CAD than for PAD, patients referred to the blood flow laboratory for diagnostic testing may have had more severe atherosclerotic disease than patients referred for cardiac catheterization. If this selection bias was operating, our findings may underestimate the true differences in atherosclerotic risk factor therapy for all PAD patients and CAD patients. Our results did not significantly change when we compared therapies between patients in the two groups who had undergone invasive procedures for the atherosclerotic disease, suggesting that invasive procedures were unlikely to have introduced recall bias into our findings.

Future Directions

Our results suggest that despite their significant risk of cardiovascular mortality and the established benefit of exercise, PAD patients receive less aggressive therapy for certain atherosclerotic risk factors. Further investigation is needed to determine whether physicians are aware of the association between PAD and cardiovascular mortality and the beneficial effects of exercise for PAD patients with intermittent claudication. Physician education may be necessary to improve cardiovascular mortality and quality of life for the growing number of patients with PAD.

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