original article

Suboptimal use of risk reduction therapy in peripheral arterial disease patients at a major teaching hospital

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Ann Saudi Med 2011; 31(4): 371-375

DOI: 10.4103/0256-4947.83219

BACKGROUND AND OBJECTIVES: Current evidence suggests that modification of atherosclerosis risk factors plays an important role in reducing adverse cardiovascular outcomes in patients with peripheral arterial disease (PAD). This study was undertaken to determine whether patients in this high-risk group were adequately using risk factor modification therapy.

DESIGN AND SETTING: Prospective study of consecutive patients with PAD from a teaching hospital.

PATIENTS AND METHODS: The collected data included information about atherosclerotic risk factors and utilization of risk factor modification therapy

RESULTS: The 391 patients had a mean (standard deviation of 3 (1) atherosclerotic risk factors. Hypertension was identified in 56.8% of patients (222/391), of whom only 37.4% (83/222) had adequate blood pressure control (BP <140/90 mm Hg). The prevalence of diabetes mellitus (DM) was 35 % (137/391). Among patients with DM, only 49% (67/137) had adequate blood glucose control (glycosylated hemoglobin, HbA1c <7%). Statins were currently prescribed in 61% of patients (238/391), 38.7% (92/238) of whom continued to have low-density lipoprotein (LDL) >2.5 mmol/L, compared to a rate of 76.5% (117/153) among non-statin users (P<.001). The majority of patients of patients (72.4%; 283/391) were overweight/obese. Many patients (67.3%; 263/391) were nonsmokers; however, most (73.4%; 193/263) had a history of smoking. Antiplatelets were prescribed for 78.3% of patients (306/391), of whom 70.6% (216/306) were taking aspirin. Angiotensin converting enzyme (ACE) inhibitors were prescribed for 44.8% of patients (175/391). Among rampril users, only 36.8% of patients (53/144) were on an optimal dose.

CONCLUSION: Although atherosclerotic risk factors were prevalent in patients with PAD, we found that patients received sub-optimal use of risk reduction treatments. Effective strategies to encourage health professionals to use these adjunctive therapies need to be developed.

Peripheral arterial disease (PAD) is a marker for severe systemic atherosclerosis. Patients with PAD have widespread arterial disease and, therefore, are at a significantly increased risk of stroke, myocardial infarction (MI), and cardiovascular death.[1] The prevalence of coronary artery disease (CAD) and cerebrovascular disease (CVD) in these patients can reach 92% and 50%, respectively.[2,3] CAD is the most common cause of death in PAD patients, accounting for 40% to 60% of deaths, while stroke accounts for 10% to 20% of deaths.[1] Furthermore, patients with PAD have a sixfold-increased risk of cardiovascular disease mortality compared to patients without PAD.[4]

The risk factors for PAD are the same as those for atherosclerosis in general and include gender predilection (males at greater risk), advanced age, cigarette smoking, hypertension, diabetes mellitus, and hyperlipidemia.[5] Atherosclerotic risk factor identification and modification plays an important role in reducing the number of adverse outcomes among patients with atherosclerosis. Risk reduction therapy decreases the risk of cardiovascular mortality and morbidity in patients with PAD,[6-11] and is comprised of methods such as smoking cessation, blood sugar control, blood pres-

sure control, and medical intervention by antiplatelets, statins, and angiotensin-converting enzyme (ACE) inhibitors. Because of the efficacy of these techniques, several expert committees have recommended their use in patients with PAD.[12-14] Despite this, several studies have documented the underuse of risk reduction therapies in patients with PAD.[15-23]

The aim of this study was to explore the extent to which risk factors were managed, in accordance with the current recommendations of the American Heart Association and American College of Cardiology (AHA/ACC) for patients with PAD, which are highlighted in **Table 1**.[12,14]

PATIENTS AND METHODS

We prospectively collected data on the atherosclerotic risk factors and risk reduction therapies on consecutive PAD patients who were referred to the vascular surgery outpatient clinic at Toronto General Hospital, Toronto, Canada, between July 2004 and July 2006. This study was approved by the University Health Network Ethics Review Board in Toronto.

Table 1. Current recommendations of the American Heart Association and American College of Cardiology (AHA/ACC) for risk reduction in patients with peripheral arterial disease12,14

	Recommendation	Class of recommendation	Level of evidence
	Medication use		
Antiplatelets	All patients	I	A
Statins	All patients	I	B
ACE inhibitors	Symptomatic patients Asymptomatic patients	I IIa	B B
	Management goals		
Blood pressure	Systolic <140 mm Hg in all patients <130 mm Hg in diabetic patients Diastolic <90 mm Hg in all patients <80 mm Hg in diabetic patients	I	A
LDL-C	LDL <2.5 mmol/L in all patients	I	A
Diabetes	HbA1c <7% in diabetic patients	I	B
Smoking	Complete cessation in all patients	I	B
BMI	18.5-24.9 kg/m^2 in all patients	I	B

ACE: Angiotensin-converting enzyme; LDL-C: low-density lipoprotein-cholesterol; HbA1c: glycosylated hemoglobin A1c; BMI: body mass index. Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective; Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment; Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy. Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses; Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.

Patients were defined as having PAD if they had previously undergone lower limb revascularization (bypass surgery and/or percutaneous transluminal angioplasty [PTA]) or a lower limb amputation for lower limb ischemia, or had received a clinical diagnosis of intermittent claudication, ischemic rest pain, or tissue loss in conjunction with ankle brachial index (ABI) <0.9.

We collected data on the following atherosclerotic risk factors: age, gender, family history, smoking habits (current and former), diabetes mellitus (defined as a fasting blood sugar (FBS) >7 mmol/L when measured on two separate occasions), hypertension (defined as systolic blood pressure [BP] >140 mm Hg and/or diastolic BP >90 mm Hg), hyperlipidemia (defined as a low-density lipoprotein cholesterol level (LDL-C) >2.5 mmol/L and/or triglyceride levels (TG) >1.7 mmol/L), and being overweight (defined as having a body mass index [BMI] >25 kg/m^2) or obese (BMI >30 kg/m^2). In addition, HbA1c was measured in diabetic patients to assess whether they had achieved optimal control for diabetes. We also investigated the use of the following risk reduction pharmacotherapies: antiplatelet medications (e.g., aspirin and clopidegrol), statins, ACE inhibitors, oral hypoglycemic medications, insulin, and antihypertensive medications. Finally, we noted whether patients had any comorbidities, such as a history of coronary artery disease (CAD), cerebrovascular disease (CVD), and any other major diseases.

Values were expressed as frequencies and percentages, for categorical variables, and as means and standard deviations (SD), for continuous variables. Chi-square tests t tests were used, where appropriate, to make comparisons between groups. All reported P values are two tailed. Significance was defined as $P<.05$.

RESULTS

Data was collected on 391 PAD patients. Baseline characteristics are shown in **Table 2**. The mean (SD) number of atherosclerotic risk factors was 3 (1). Hypercholesterolemia was diagnosed in 29.7% (116/391) patients, and hypertriglyceridemia in 40% (157/391) patients. Overall, patients did not adequately control their atherosclerotic risk factors (**Table 3**). Of the 56.8% (222/391) of patients with hypertension, only 37.4% (83/222) had adequate blood pressure control (e.g., had BP <140/90 mm Hg). Furthermore, among patients who were not known to have hypertension, 67.5% (114/169) had BP >140/90 mm Hg, as measured on two separate occasions at the clinic. Therefore, 64.7% of patients (253/391) either had in-

Table 2. Baseline characteristics of peripheral arterial disease patients (n=391).

Characteristics	Values
Mean age (standard deviation), years	67 (10)
Female, n (%)	137 (35.0%)
Diabetes, n (%)	137 (35.0%)
Hypertension, n (%)	222 (56.8%)
Current smoker, n (%)	128 (32.7%)
Current or ex-smoker, n (%)	321 (82.1%)
Hyperlipidemia, n (%)	272 (69.6%)
BMI >25 kg/m^2, n (%)	283 (72.4%)
CAD, n (%)	135 (34.5%)
CABG, n (%)	72 (18.4%)

BMI: body mass index; CAD: coronary artery disease; CABG: coronary artery bypass graft

Table 3. Achievement of the current recommendations of the American Heart Association and American College of Cardiology (AHA/ACC) for control of atherosclerotic factors in patients with peripheral arterial disease in the study.

	Recommendations	Achievement rates among patients in the current study n (%)
	Medication use	
Antiplatelets	All patients	78.3% (306/391)
Statins	All patients	61.0% (238/391)
ACE inhibitors	All patients	44.8% (175/391)
	Management goals	
Blood pressure	Systolic <140 mm Hg in all patients <130 mm Hg in diabetic patients Diastolic <90 mm Hg in all patients <80 mm Hg in diabetic patients	 21.2% (83/391) 21.5% (30/137) 77.8% (304/391) 48.4% (66/137)
LDL-C	LDL <2.5 mmol/L in all patients	46.6% (182/391)
Diabetes	HbA1c <7% in diabetic patients	49.0% (67/137)
Smoking	Complete cessation in all patients	67.3% (263/391) (non-smokers)
BMI	18.5-24.9 kg/m^2 in all patients	27.5% (108/391)

ACE: Angiotensin-converting enzyme; LDL-C: low-density lipoprotein-cholesterol; HbA1c: glycosylated hemoglobin A1c; BMI: body mass index

adequately-controlled (35.5%) or undiagnosed (29.2%) hypertension.

The prevalence of DM was 35% (137/391). Of the affected patients, only 49% (67/137) had properly controlled blood sugar (HbA1c <7%). Furthermore, among patients who were not known to have diabetes, 26.8% (68/254) exhibited an abnormal blood glucose level (FBS >6 mmol/L). Statins were currently prescribed in 61% (238/391) of patients. Despite this, 38.7% of statin-users continued to have LDL >2.5 mmol/L. Among non-statin users, this rate was even higher (76.5%; *P*<.001). Mean LDL level was significantly lower in statin users (2.31 [0.90] mmol/L) than in non-statin users (2.92 [0.96] mmol) (*P*<.01). The majority of patients (72.4%; 283/391) were either overweight (64.3%, 182/283; BMI 25-29.9 kg/m^2) or obese (35.7%, 101/283; BMI >29.9 kg/m^2). Although many patients (67.3%; 263/391) were nonsmokers, 73.4% (193/263) of these individuals were former smokers.

Antiplatelets were prescribed for 78.3% (306/391) of patients, of whom 70.6% (216/306) were taking aspirin, 15.3% (47/306) were taking clopidogrel, 8.8% (27/306) were taking a combination of aspirin and clopidegrol, and 5.2% (16/306) were taking other agents. ACE inhibitors were prescribed for 44.8% (175/391) of patients, of whom 82.3% (144/175) were on ramipril. However, only 36.8% (53/144) of ramipril users were taking the optimal dose of 10 mg/day.[9]

DISCUSSION

Data was collected prospectively on 391 patients who were referred to a vascular surgery outpatient clinic at a tertiary care hospital. Based on the results of our analyses, we have suggested strategies to further increase the use of risk factor managing strategies.

Atherosclerosis is the leading cause of death worldwide.[24] PAD is a marker of advanced atherosclerosis and indicates an elevated risk of cardiovascular mortality and morbidity comparable to patients with coronary artery disease (CAD).[25] Thus, intensive risk reduction therapy is critical in PAD patients. Therapeutic methods include blood pressure control and risk reduction pharmacotherapy (antiplatelets, statins, and ACE inhibitors), which have been proven to reduce the risk of cardiovascular mortality and morbidity of PAD patients in large-scale randomized clinical trials.[9,11,26] Large observational studies have also shown that smoking cessation and blood sugar control help reduce adverse cardiovascular outcomes in patients with atherosclerosis.[6-8] Based on this evidence, several expert cardiovascular panels, including the AHA/ACC and the Canadian Cardiovascular Society, have recommended the use of intensive risk factor control in PAD patients (Table 1).[12-14] We found that many patients were not treated with optimal risk reduction therapy methods, and that, as a result, risk factors were inadequately con-

Table 4. Comparison of compliance with risk factor control recommendations among patients in the current study and previously-published studies.

Study	Number of patients	Setting	Antiplatelet use (%)	Statin use (%)	ACE inhibitor use (%)	BP <140/90 mm Hg (%)	LDL-C <2.5 mmol/L (%)	HbA1c <7% (%)	BMI <25 kg/m^2 (%)	Non-smokers (%)
Anand et al, 1999	195	Canada	38	16	NA	NA	NA	NA	NA	NA
Mukherjee et al, 2002	66	USA	89	57	42	NA	NA	NA	NA	73
Teh et al, 2003	189	Australia	62	35	38	NA	NA	NA	NA	NA
Brown et al, 2004	281	Canada	44	66	62	NA	NA	NA	NA	NA
Sukhija et al, 2005	561	USA	89	79	54	46	54	NA	NA	78
Rehring et al, 2005	1733	USA	NA	31	29	NA	23	40	NA	NA
Hackam et al, 2006	1507	Canada	90	76	58	NA	67	NA	NA	79
Bradley and Kirker, 2006	107	UK	60	47	NA	NA	NA	NA	NA	NA
Kinikini et al, 2006	200	USA	79	61	48	54	36	24	33	73
Current study	391	Canada	78	61	45	35	47	49	27	67

ACE: Angiotensin-converting enzyme; LDL-C: low-density lipoprotein-cholesterol; HbA1c: glycosylated hemoglobin A1c; BMI: body mass index; NA: not available

trolled and risk factor goals were not achieved. For instance, we noted a deficiency in prescription of risk reduction pharmacotherapies.

Our study is not the first to provide data that support a care gap in managing patients with PAD (**Table 4**). The inequities in the use of risk re¬duction therapies between patients with PAD and those with CAD in which the risk reduction should be similar have been well documented in the literature.[27] We hope that these data will be useful in supporting a call-to-action for PAD management and public awareness.[27] There are several possible explanations for our findings. First, the association of PAD and CAD is usually unrecognized by both patients and primary care physicians,[28] and a significant number of patients with PAD may not have symptoms related to their CAD.[15] Second, there may be gaps between what physicians know they should do, and what they actually do, to manage risk factors in patients with PAD.[29-31] Third, there may be a reluctance to apply CAD guidelines to the PAD patient population even though the risks are similar, if not higher.

We admit that this study had some limitations. First, a relatively small number of participants were included in this study. Second, this study reflects the techniques of physicians in one geographic area and therefore may not be generalizable to other locations. However, the validity of these results is strengthened by the prospective nature of our data collection methods.

In conclusion, there is a high prevalence of atherosclerotic risk factors in patients with PAD. However, these individuals are receiving inadequate risk factor management therapies, and/or are not meeting risk factor control goals even when they are receiving treatment. In order to address this care gap, it is vital to develop effective strategies to encourage health professionals to comply with the current guidelines for cardiovascular risk reduction in PAD patients. These may include methods such as self-audit of practice, focused continuing medical education programs, and educational outreach programs.

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