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## Incidence of new cardiovascular events in patients with and without peripheral arterial disease seen in a vascular surgery clinic

### Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

Amit Chhabra<sup>1ABCDEF</sup>, Wilbert S. Aronow<sup>1ACDEF</sup>, Chul Ahn<sup>2CD</sup>, Kurt Duncan<sup>1AB</sup>, Jay D. Patel<sup>1B</sup>, Alexander I. Papolos<sup>1B</sup>, Babu Sateesh<sup>3A</sup>

<sup>1</sup> Department of Medicine, Cardiology Division, New York Medical College, Valhalla, NY, U.S.A.

<sup>2</sup> Department of Clinical Sciences, University of Texas, Southwestern Medical School, Dallas TX, U.S.A.

<sup>3</sup> Department of Surgery, Division of Vascular Surgery, New York Medical College, Valhalla, NY, U.S.A.

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### Summary

#### Background:

To investigate the incidence of death and of new cardiovascular events at long-term follow-up of patients with and without PAD seen in a vascular surgery clinic.

#### Material/Methods:

We investigated the incidence of death, new stroke/transient ischemic attack, new myocardial infarction, new coronary revascularization, new carotid endarterectomy, new peripheral arterial disease (PAD) revascularization, or at least one of the above outcomes at long-term follow-up of patients with and without PAD followed in a vascular surgery clinic.

#### Results:

At least one of the above outcomes occurred in 259 of 414 patients (63%) with PAD at 33-month follow-up and in 21 of 89 patients (24%) without PAD at 48-month follow-up ( $p < 0.0001$ ). Death occurred in 112 of 414 patients (27%) with PAD and in 10 of 89 patients (11%) without PAD ( $p = 0.002$ ). Stepwise Cox regression analysis for the time to at least one of the 6 outcomes showed that significant independent risk factors were men (hazard ratio = 1.394; 95% CI, 1.072–1.813;  $p = 0.013$ ), estimated glomerular filtration rate (hazard ratio = 0.992; 95% CI, 0.987–0.997;  $p = 0.003$ ), and PAD (hazard ratio = 3.520; 95% CI, 2.196–5.641;  $p < 0.0001$ ). Stepwise Cox regression analysis for the time to death showed that significant independent risk factors were age (hazard ratio = 1.024; 95% CI, 1.000–1.049;  $p = 0.048$ ), estimated glomerular filtration rate (hazard ratio = 0.985; 95% CI, 0.974–0.996;  $p = 0.007$ ), and PAD (hazard ratio = 2.157; 95% CI, 1.118–4.160;  $p = 0.022$ ).

#### Conclusions:

Patients with PAD have a significantly higher incidence of cardiovascular outcomes, especially death, new PAD revascularization, and new carotid endarterectomy, than patients without PAD followed in a vascular surgery clinic.

#### key words:

peripheral arterial disease • coronary revascularization • noncoronary revascularization • carotid endarterectomy • myocardial infarction • stroke • glomerular filtration rate

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#### Author's address:

Wilbert S. Aronow, Cardiology Division, New York Medical College, Macy Pavilion, Room 138, Valhalla, NY 10595, U.S.A., e-mail: wsonow@aol.com

## BACKGROUND

Patients with peripheral arterial disease have an increased incidence of all-cause mortality and of mortality from coronary artery disease [1–6]. These studies did not include the incidence of PAD revascularization [1–6]. Patients with PAD also have a high prevalence of moderate or severe chronic kidney disease with an estimated glomerular filtration rate <60 ml/min/1.73 m<sup>2</sup> [7]. The present study investigated the incidence of all-cause mortality, new stroke/transient ischemic attack, new myocardial infarction, new coronary revascularization, new carotid endarterectomy, new PAD revascularization, and of at least one of these 6 outcomes in patients with and without PAD followed in a vascular surgery clinic.

## MATERIAL AND METHODS

We investigated in 503 consecutive patients (414 with PAD and 89 without PAD) followed in an academic peripheral vascular disease outpatient clinic the incidence at long-term follow-up of all-cause mortality, new stroke/transient ischemic attack, new myocardial infarction, new coronary revascularization, new carotid endarterectomy, new PAD revascularization, and of at least one of these 6 outcomes. PAD was diagnosed if the ankle-brachial index was <0.90 or ≥1.40, if the patient had prior PAD revascularization, if the patient had carotid arterial disease, or if the patient had an abdominal aortic aneurysm. All patients with no PAD had a normal bilateral ankle-brachial index and were referred to the vascular disease clinic because of lower extremity symptoms thought to be possible PAD. Coronary artery disease was diagnosed as previously described [8,9].

Student's t-test was used to analyze continuous variables and Fisher's exact test and chi-square analysis for dichotomous variables. Stepwise Cox regression analysis was performed for the time to death or new stroke/transient ischemic attack or new myocardial infarction or new coronary revascularization or new carotid endarterectomy or new PAD revascularization.

This study was approved by the New York Medical College Institutional Review Board and by the Institutional Review Board of Westchester Medical Center.

## RESULTS

Table 1 shows the baseline characteristics in 414 patients with PAD and in 89 patients without PAD and lists levels of statistical significance. Table 2 shows the incidences of all-cause mortality, new stroke/transient ischemic attack, new myocardial infarction, new coronary revascularization, new carotid endarterectomy, new PAD revascularization, and of at least one of these 6 outcomes in patients with and without PAD followed in a vascular surgery clinic. Table 2 also lists levels of statistical significance. Table 3 shows the stepwise Cox regression analysis for the time to at least one of the 6 outcome variables using the baseline variables listed in Table 1, PAD, and carotid arterial disease. Table 4 shows the stepwise Cox regression analysis for the time to death using the baseline variables listed in Table 1, PAD, and carotid arterial disease.

## DISCUSSION

Patients with peripheral arterial disease have an increased incidence of all-cause mortality and of mortality from coronary

**Table 1.** Baseline characteristics in patients with and without peripheral arterial disease.

Variable	PAD (n=414)	No PAD (n=89)	P value
Age (years)	72±10	66±11	<0.0001
Men	270 (65%)	57 (64%)	NS
Women	144 (35%)	32 (36%)	NS
GFR			0.010
GFR ≥60 ml/min	152 (37%)	48 (53%)	
GFR 30–59 ml/min	202 (49%)	33 (37%)	
GFR <30 ml/min	60 (14%)	8 (9%)	
Hypertension	343 (83%)	65 (73%)	0.032
Diabetes mellitus	197 (48%)	37 (42%)	0.302
Dyslipidemia	292 (71%)	63 (71%)	0.962
Current smoking	79 (19%)	14 (16%)	0.460
Body mass index ≥30 kg/m <sup>2</sup>	123/404 (30%)	39/85 (46%)	0.006
Coronary artery disease	259 (63%)	52 (58%)	0.467
Stroke/TIA	64 (15%)	7 (8%)	0.062
Abdominal aortic aneurysm	67 (16%)	0 (0%)	<0.0001
Follow-up (months)	33±5	48±17	<0.0001

PAD – peripheral arterial disease; GFR – estimated glomerular filtration rate; TIA – transient ischemic attack.

**Table 2.** Incidences of death, new stroke/transient ischemic attack, new myocardial infarction, new coronary revascularization, new carotid endarterectomy, new peripheral artery disease revascularization, or at least one of these 6 outcomes in patients with and without peripheral arterial disease.

Outcome	PAD (n=414)	No PAD (n=89)	P value
Death	112 (27%)	10 (11%)	0.002
New stroke/TIA	20 (5%)	1 (1%)	0.147
New myocardial infarction	17 (4%)	1 (1%)	0.221
New coronary revascularization	52 (13%)	11 (12%)	0.959
New carotid endarterectomy	35 (8%)	0 (0%)	0.005
New PAD revascularization	139 (34%)	1 (1%)	<0.0001
One of above 6 outcomes	259 (63%)	21 (24%)	<0.0001

TIA – transient ischemic attack; PAD – peripheral arterial disease.

**Table 3.** Stepwise Cox regression analysis for the time to at least one of the 6 outcomes of death, new stroke/transient ischemic attack, new myocardial infarction, new coronary revascularization, new carotid endarterectomy, or new peripheral artery disease revascularization.

Parameter	Parameter estimate	Standard error	P-Value	Hazard ratio	95% CI
Men	0.332	0.134	0.013	1.394	1.072, 1.813
GFR	-0.008	0.003	0.003	0.992	0.987, 0.997
PAD	1.258	0.241	<0.0001	3.520	2.196, 5.641

CI – hazard ratio confidence limits; GFR – estimated glomerular filtration rate; PAD – peripheral arterial disease.

**Table 4.** Stepwise Cox regression analysis for the time to death.

Parameter	Parameter estimate	Standard error	P-Value	Hazard ratio	95% CI
Age	0.024	0.012	0.048	1.024	1.000, 1.049
GFR	-0.015	0.006	0.007	0.985	0.974, 0.996
PAD	0.769	0.335	0.022	2.157	1.118, 4.160

CI – hazard ratio confidence limits; GFR – estimated glomerular filtration rate; PAD – peripheral arterial disease.

artery disease [1–6]. These studies did not include the incidence of PAD revascularization or carotid endarterectomy [1–6]. Patients with PAD also have a high prevalence of moderate or severe chronic kidney disease with an estimated glomerular filtration rate <60 ml/min/1.73 m<sup>2</sup> [7].

The present study performed in 503 patients followed in a vascular surgery clinic showed that the patients with PAD were older and had a significantly higher prevalence of hypertension, of an abdominal aortic aneurysm, and of a low estimated glomerular filtration rate and a significantly lower incidence of obesity than the patients without PAD. The follow-up was significantly higher in patients with no PAD (48 months) than in patients with PAD (33 months).

At follow-up, compared to patients with no PAD, patients with PAD had a significant increase in all-cause mortality (27% vs. 11%, p=0.002), an insignificant increase in new stroke/transient ischemic attack (5% vs. 1%), no significant

difference in new myocardial infarction or new coronary revascularization, a significant increase in new PAD revascularization (34% vs. 1%, p<0.0001), a significant increase in new carotid endarterectomy (8% vs. 0%, p=0.005), and a significant increase in at least one of these 6 outcomes (63% vs. 24%, p<0.0001).

## CONCLUSIONS

Our study also showed that men were 39% significantly more likely to develop at least one of these 6 outcomes. Patients with a lower estimated glomerular filtration rate were significantly more likely to develop at least one of these 6 outcomes. Patients with PAD were 3.5 times significantly more likely to develop at least one of these 6 outcomes. In addition, our study also showed that patients who were older and who had a lower estimated glomerular filtration rate were significantly more likely to die. Patients with PAD were 2.2 times significantly more likely to die. These data support that

patients with PAD must be treated with risk factor modification to try to reduce these unfavorable outcomes.

#### Conflict of interest

None of the authors have any conflicts of interest pertaining to this article.

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