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Association Between Advanced Age and Vascular Disease in Different Arterial Territories

A Population Database of Over 3.6 Million Subjects

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Objectives This study sought to determine the relationship between vascular disease in different arterial territories and advanced age.

Background Vascular disease in the peripheral circulation is associated with significant morbidity and mortality. There is little data to assess the prevalence of different phenotypes of vascular disease in the very elderly.

Methods Over 3.6 million self-referred participants from 2003 to 2008 who completed a medical and lifestyle questionnaire in the United States were evaluated by screening ankle brachial indices <0.9 for peripheral artery disease (PAD), and ultrasound imaging for carotid artery stenosis (CAS) >50% and abdominal aortic aneurysm (AAA) >3 cm. Participants were stratified by decade of life. Multivariate logistic regression analysis was used to estimate odds of disease in different age categories.

Results Overall, the prevalence of PAD, CAS, and AAA, was 3.7%, 3.9%, and 0.9%, respectively. Prevalence of any vascular disease increased with age (40 to 50 years: 2%, 51 to 60 years: 3.5%, 61 to 70 years: 7.1%, 71 to 80 years: 13.0%, 81 to 90 years: 22.3%, 91 to 100 years: 32.5%; $p < 0.0001$). Prevalence of disease in each vascular territory increased with age. After adjustment for sex, race/ethnicity, body mass index, family history of cardiovascular disease, smoking, diabetes, hypertension, hypercholesterolemia, and exercise, the odds of PAD (odds ratio [OR]: 2.14; 95% confidence interval [CI]: 2.12 to 2.15), CAS (OR: 1.80; 95% CI: 1.79 to 1.81), and AAA (OR: 2.33; 95% CI: 2.30 to 2.36) increased with every decade of life.

Conclusions There is a dramatic increase in the prevalence of PAD, CAS, and AAA with advanced age. More than 20% and 30% of octogenarians and nonagenarians, respectively, have vascular disease in at least 1 arterial territory.
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Peripheral vascular disease (PVD) is associated with significant morbidity and mortality (1–4). Understanding the relationship between risk factors and disease prevalence may help better guide preventive and risk reduction strategies. Increasing age is a well-known risk factor for atherosclerosis. Increasing age is the strongest determinant of heart disease and stroke risk in multiple risk factor algorithms. However, the precise association of advanced chronological age in vascular disease of different peripheral arterial locations is less well studied. Most data on the epidemiology of peripheral vascular disease are from small screening studies or meta-analyses, which included few older adults, particularly octogenarians and nonagenarians (5–9). Furthermore, most reports were limited such that they combined data from several studies with varying definitions of disease and did not investigate different phenotypes of vascular disease in a single population. To better understand the relationship between advanced age and peripheral vascular disease, we sought to determine the prevalence of peripheral artery disease (PAD), carotid artery stenosis (CAS), and abdominal aortic aneurysms (AAA) stratified by decade of life in a single large population-based study including over 3.6 million subjects.

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Methods

Study population. The study was based on data provided by Life Line Screening Inc. (Independence, Ohio) to the Society for Vascular Surgery for research purposes. The study cohort

consists primarily of self-referred individuals who paid for vascular screening tests out of pocket. Screenings were performed from 2003 to 2008 at more than 20,000 sites nationwide. Before undergoing the screening procedure, individuals completed an extensive questionnaire that included information on demographics, smoking, exercise, cardiovascular risk factors, medical comorbidities, and family history of atherosclerosis and vascular disease.

Ascertainment of PVD. PAD, CAS, and AAA were determined with simple noninvasive procedures that have high sensitivity and specificity: the ankle brachial index (ABI), carotid Duplex ultrasound, and abdominal ultrasound, respectively (10). Systolic blood pressure was measured in both arms (brachial arteries) and both ankles (posterior tibial arteries). If a posterior tibial Doppler signal was inaudible, the dorsalis pedis artery signal was measured. Left and right ABI measurements were obtained by dividing the ankle systolic blood pressure by the highest arm pressure. PAD was defined as an ABI <0.90 in either leg, and subjects with an ABI >1.4 were excluded because these values may be falsely elevated due to calcification of the arterial wall (11). CAS was defined by carotid artery stenosis $\geq$50% in either (or both) internal carotid arteries (internal carotid artery peak systolic velocity $\geq$125 cm/s). The greater of the anteroposterior or transverse ultrasound–based measurements of the infrarenal abdominal aorta was used to identify aortic size. AAA was defined by a diameter of the abdominal aorta $\geq$3 cm.

Symptomatic PAD is defined by aching or pain in the legs that is worse with walking or running, or that is relieved in a few minutes by rest, or a prior lower extremity revascularization. Symptomatic CAS is defined by a history of stroke, transient ischemic attack, or prior intervention on the carotid arteries. Symptomatic AAA is defined by a prior procedure to repair a AAA.

Quality control. All Life Line sites utilize identical protocols and are subject to the quality control program. Included in this program are random monthly audits where ultrasonography images are graded for each team and individual performance is tracked. Physician audits are performed on a quarterly basis. All results are processed by the results center and outliers are all reviewed. Percentage of abnormal findings is tracked per team to identify groups finding abnormally high or low number of disease cases. A clinical leadership team holds monthly review meetings to evaluate performance of teams and individual members. For imaging modalities, annual competencies are performed and all new employees must have demonstrated initial competencies before being allowed to perform testing without supervision.

Other variables of interest. Hypertension was defined as systolic blood pressure of 140 mm Hg or greater in upper extremity, prior physician diagnosis, or medication use. Hypercholesterolemia was defined as physician diagnosis or medication use. Diabetes was defined as self-reported physician diagnosis or the use of diabetes medication. Subjects who had smoked 100 cigarettes during their lifetime and were still currently smoking were considered smokers. Subjects who reported engagement in some kind of vigorous leisure time exercise at least once per week were considered active and all other subjects were considered sedentary. Race and ethnicity were self-reported.

Abbreviations and Acronyms

AAA = abdominal aortic aneurysm
ABI = ankle brachial index
CAS = carotid artery stenosis
CI = confidence interval
OR = odds ratio
PAD = peripheral artery disease
PVD = peripheral vascular disease

Statistical analysis. We calculated the proportion of participants affected with vascular disease across discrete age groups (40 to 50 years, 51 to 60 years, and so on) and examined sex-specific prevalence of vascular disease. We tested for trends with the Cochran-Armitage test (12). The corresponding 95% confidence intervals (CIs) were reported to present uncertainty associated with the estimated prevalence.

Logistic regression models were used to determine the association between risk factors and vascular phenotypes. Age was included as a categorical variable broken down by age deciles (40 to 50 years, 51 to 60 years, 61 to 10 years, 71 to 80 years, 81 to 90 years, 91 to 100 years). Univariate analysis was used to describe the association of age with the 3 types of peripheral vascular diseases and multivariate analysis was used to accommodate other risk factors. The odds of PAD and CAS for subjects in each age decile were determined by comparing to the 40 to 50 years of age group. For AAA, subjects were compared to the 40 to 60 year age group given the very low prevalence among 40- to 50-year-olds. To test for linear trend, age groups were included as a single continuous variable in the logistic regression model.

Regression analysis. To estimate the precise relationship between age and different peripheral vascular disease phenotypes, prevalence values from each disease were plotted against age. Prevalence of AAA, CAS, and PAD was defined as count per 100,000. Prevalence of disease as a function of age was presented using scatter plots. Age was defined on the basis of 55 strata. The first stratum corresponded to subjects aged 40. All subsequent strata were on the basis of 1-year age increments beginning with 41 years of age. Linear regression model was employed to examine trends in AAA, CAS, and PAD prevalence. Because prevalence of PAD and CAS had a right skewed distribution, estimation and inference for PAD and CAS was on the basis of the log scale. Uncertainty associated with the estimated trend was presented using 95% CIs of the regression line.

Results

We analyzed data on 3,613,381 subjects age 40 years and older. Overall, the mean age of the overall population was 64.1 $\pm$ 10.2 years of age. The population included 205,593 subjects age 81 to 90 years and 10,129 subjects age 91 to 100 years. Baseline characteristics of the study population are

Table 1 General Characteristics of the 3.6 Million Subjects in Whom PVD Was Assessed

Characteristic	Overall (n = 3,613,381)	40–50 (n = 333,369)	51–60 (n = 1,023,706)	61–70 (n = 1,268,912)	71–80 (n = 771,672)	81–90 (n = 205,593)	91–100 (n = 10,129)
Demographics							
Age	64.1 ± 10.2	46.7 ± 2.8	56.1 ± 2.8	65.3 ± 2.8	74.9 ± 2.8	83.9 ± 2.5	92.8 ± 2.0
Male	35.7	35.9	33.5	37.0	36.7	35.0	32.9
Caucasian	89.1	85.5	88.4	90.2	90.2	87.5	85.0
Black	3.1	4.3	3.6	2.9	2.4	2.3	3.5
Hispanic	2.4	4.4	3.1	2.1	1.4	1.0	0.9
Asian	2.0	3.2	2.5	1.8	1.2	0.8	0.8
Native American	2.9	1.7	1.7	2.4	4.3	7.8	9.1
Other	0.6	1.1	0.7	0.5	0.5	0.7	0.8
BMI	27.7 ± 5.4	28.3 ± 6.0	28.3 ± 5.7	27.9 ± 5.3	26.9 ± 4.7	25.5 ± 4.3	24.4 ± 4.2
Medical history							
Hypertension	47.0	28.0	38.9	50.0	57.5	60.0	56.5
Diabetes	10.9	5.4	8.4	12.0	14.2	13.2	10.7
Current smoker	24.9	27.8	26.2	25.4	22.3	19.8	17.0
Cholesterol	53.4	39.1	50.2	57.4	58.0	50.3	36.5
Exercise	41.9	41.4	41.6	43.8	41.5	33.8	27.2
Family history of CVD	23.0	23.6	23.8	22.4	22.4	22.8	21.3

Values are mean ± SD or %.
BMI = body mass index; CVD = cardiovascular disease; PVD = peripheral vascular disease.

provided for each age decile (Table 1). As expected, risk factors for cardiovascular disease increased with increasing age. However, several risk factors decreased in the octo- and nonagenarians groups. For example, diabetes and hypercholesterolemia increased with advanced age until 80 years of age and declined thereafter.

In the overall population, any type of peripheral vascular disease was present in 7.48% (95% CI: 7.44% to 7.51%). The prevalence of any vascular disease increased significantly with age (Fig. 1) ranging from 2.0% (1 in 50) in the 40 to 50 years age category to 32.0% (~1 in 3) in the 91 to 100 years age category. Among octogenarians and nonagenarians, more than 20% and 30%, respectively, had peripheral vascular disease in at least 1 arterial territory. The association between increasing age and any peripheral vascular disease was similar in women (40 to 50 years: 2.37%, 51 to 60 years: 3.59%, 61 to 70 years: 6.51%, 71 to 80 years old: 11.75%, 81 to 90 years: 20.34%, 91 to 100 years: 31.58%; p for trend <0.001) and men (40 to 50 years: 1.44%, 51 to 60 years: 3.44%, 61 to 70 years: 8.02%, 71 to 80 years: 15.25%, 81 to 90 years: 26.03%, and 91 to 100 years: 34.44%; p for trend <0.001).

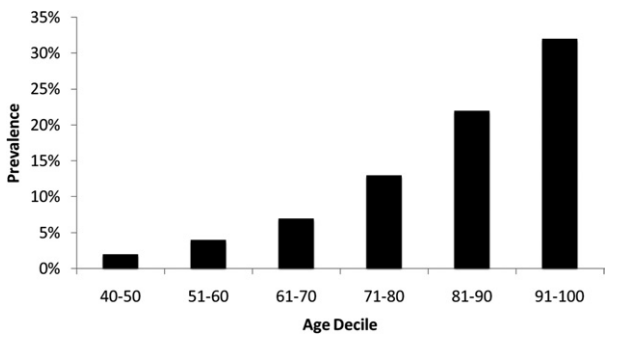

Figure 1 Prevalence of Any Vascular Disease (Peripheral Artery Disease, Abdominal Aortic Aneurysm, or Carotid Artery Stenosis) by Age Decile

Prevalence of any vascular disease increased with age (40 to 50 years: 2%, 51 to 60 years: 3.5%, 61 to 70 years: 7.1%, 71 to 80 years: 13.0%, 81 to 90 years: 22.3%, 91 to 100 years old: 32.5%; p for trend <0.0001).

Among all individuals, prevalence of PAD, CAS, AAA was present in 3.68% (95% CI: 3.66% to 3.70%), 3.86% (95% CI: 3.84% to 3.88%), and 0.88% (95% CI: 0.87% to 0.89%) of subjects, respectively. In each vascular territory, prevalence of disease increased substantially with advanced age (Fig. 2), ranging from 1.2% to 24.1% for PAD, 0.9% to 11.3% for CAS, and 0.05% to 3.5% for AAA between the lowest (40 to 50 years) and highest (91 to 100 years) age categories. Association between age and vascular disease was significant for both symptomatic and asymptomatic subjects (Online Table 1). Prevalence data by age was plotted to determine trends in the prevalence of PAD, CAS, and AAA. Regression analysis calculated a formula for a subject's prevalence of a particular disease with respect to age (Fig. 3). The coefficient of determination (r^2) for the PAD, CAS, and AAA regression models are 0.98, 0.96, and 0.90, respectively. The prevalence of PAD and CAS follow an exponential curve, increasing dramatically with advanced age, while the prevalence of AAA increases linearly with advanced age. Prior to age 55 years, CAS and PAD show a similar prevalence. From age 55 years to approximately age 78 years, the prevalence of CAS is greater than PAD, while after age 78 years, the prevalence of PAD increases substantially and its prevalence far outweighs that of CAS. AAA has a lower prevalence that CAS or PAD for

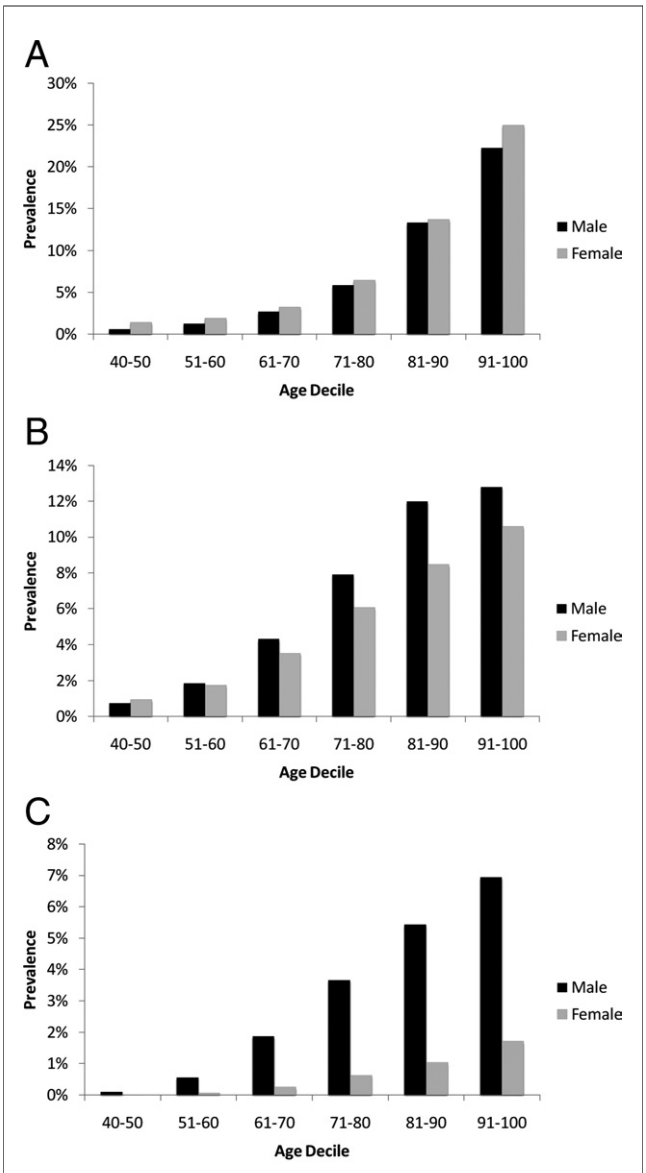

Figure 2 **Sex-Specific Prevalence of PAD, CAS, and AAA by Age Decile**

Prevalence of **(A)** peripheral artery disease (PAD), **(B)** carotid artery stenosis (CAS), and **(C)** abdominal aortic aneurysm (AAA) increased with age in both women and men, respectively (p for trend <0.0001 for each comparison).

every age group. Actual prevalence values for all disease phenotypes deviate from the predicted curve after 90 years of age.

The unadjusted odds ratios (ORs) associated with age deciles of 40 to 50 (reference group), 51 to 60, 61 to 70, 71 to 80, 81 to 90, and 91 to 100 years of age were 1, 1.51, 2.72, 5.76, 13.52, and 27.26 (p for trend <0.001) for PAD; 1, 2.04, 4.49, 8.14, 12.10, and 14.34 (p for trend <0.001) for CAS; and 1, 1, 4.78, 9.95, 14.81, and 19.8 (p for trend <0.001) for AAA, respectively. A similar relationship between age and vascular disease was demonstrated in women and men, respectively (Table 2).

Following adjustment for sex, race/ethnicity, body mass index, smoking, hypertension, physical activity, hypercholesterolemia, diabetes, and family history of cardiovascular disease, the ORs associated with age decile were 1, 1.37, 2.27, 4.84, 12.03, and 26.70 (p for trend <0.001) for PAD; 1, 1.77, 3.39, 5.83, 8.88, and 11.57 (p for trend <0.001) for CAS; and 1, 1, 3.97, 8.34, 13.58, and 21.37 (p for trend <0.001) for AAA, respectively. The association between age and disease was more apparent for men in PAD and CAS and more apparent for women in AAA (Table 3).

Compared to subjects in the youngest age category, octogenarians were approximately 12-fold likely to have PAD (OR: 12.03; 95% CI: 11.54 to 12.54), nearly 9-fold likely to have CAS (OR: 8.88; 95% CI: 8.48 to 9.30) and nearly 14-fold likely to have an AAA (OR: 13.58; 95% CI: 12.82 to 14.39). Nonagenarians were nearly 27-fold likely to have PAD (OR: 26.70; 95% CI: 24.78 to 28.75), 12-fold likely to have CAS (OR: 11.57; 95% CI: 10.56 to 12.66), and over 21-fold likely to have an AAA (OR: 21.37; 95% CI: 18.42 to 24.68).

Following multivariable adjustment, the ORs for the association of peripheral vascular disease with increasing age (per 10-year increments) were significant for PAD (OR: 2.14; 95% CI: 2.12 to 2.15), CAS (OR: 1.80; 95% CI: 1.79 to 1.81), and AAA (OR: 2.33; 95% CI: 2.30 to 2.36) (Fig. 4).

Polyvascular disease increased with increasing age as well; vascular disease in more than 1 location was 0.04% in the 40

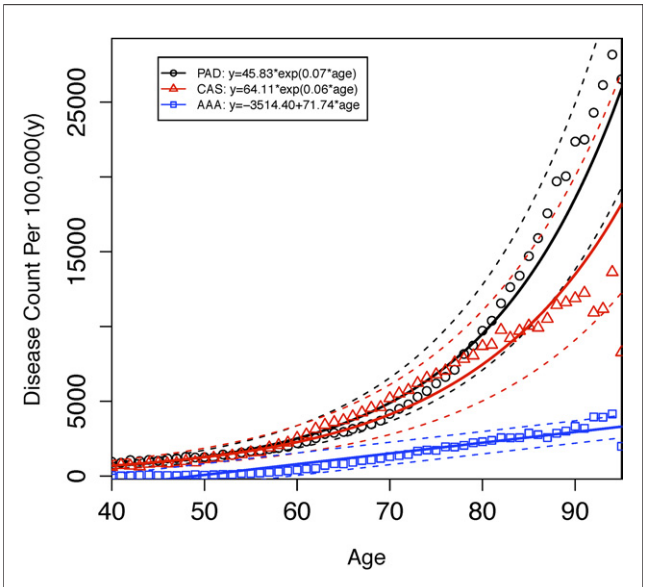

Figure 3 **Prevalence of PAD, CAS, and AAA by Age**

Prevalence of each disease phenotype was defined as count per 100,000 and presented using scatter plots. Regression analysis calculated a formula for a subject's prevalence of a particular disease with respect to age. The coefficient of determination (r^2) for the PAD, CAS, and AAA regression models are 0.98, 0.96, and 0.90, respectively. **Solid black line** = PAD; **dashed black line** = 95% confidence interval of PAD; **solid red line** = CAS; **dashed red line** = 95% confidence interval of CAS; **solid blue line** = AAA; **dashed blue line** = 95% confidence interval of AAA. Abbreviations as in Figure 2.

Table 2 Unadjusted Odds Ratio of Age and Sex for PAD, CAS, and AAA

	PAD			CAS			AAA		
	Overall	Female	Male	Overall	Female	Male	Overall	Female	Male
40–50 yrs	1.00	1.00	1.00	1.00	1.00	1.00	1.00*	1.00*	1.00*
51–60 yrs	1.51 (1.45–1.57)	1.36 (1.30–1.43)	2.02 (1.86–2.21)	2.04 (1.96–2.13)	1.85 (1.75–1.95)	2.48 (2.30–2.69)	1.00*	1.00*	1.00*
61–70 yrs	2.72 (2.62–2.83)	2.32 (2.22–2.42)	4.34 (3.99–4.71)	4.49 (4.31–4.69)	3.82 (3.63–4.02)	5.96 (5.54–6.43)	4.78 (4.55–5.02)	5.49 (4.87–6.21)	4.31 (4.09–4.56)
71–80 yrs	5.76 (5.55–5.98)	4.78 (4.58–4.99)	9.67 (8.91–10.51)	8.14 (7.81–8.49)	6.69 (6.36–7.04)	11.31 (10.51–12.20)	9.95 (9.48–10.45)	14.2 (12.66–16.01)	8.56 (8.11–9.03)
81–90 yrs	13.52 (13.00–14.07)	10.93 (10.45–11.43)	23.77 (21.86–25.90)	12.10 (11.58–12.66)	9.57 (9.07–10.11)	17.94 (16.62–19.41)	14.81 (14.02–15.65)	23.17 (20.43–26.36)	12.94 (12.16–13.76)
91–100 yrs	27.26 (25.40–29.25)	22.86 (21.01–24.85)	44.20 (38.62–50.57)	14.34 (13.14–15.64)	12.26 (10.98–13.66)	19.32 (16.67–22.33)	19.80 (17.19–22.69)	38.83 (29.98–49.66)	16.79 (14.11–19.84)

Values are odds ratio (95% confidence interval). *40 to 60 used as a reference.
AAA = abdominal aortic aneurysm; CAS = carotid artery stenosis; PAD = peripheral artery disease.

Table 3 Adjusted Odds Ratio of Age and Sex for PAD, CAS, and AAA

	PAD			CAS			AAA		
	Overall	Female	Male	Overall	Female	Male	Overall	Female	Male
40–50 yrs	1.00	1.00	1.00	1.00	1.00	1.00	1.00*	1.00*	1.00*
51–60 yrs	1.37 (1.32–1.43)	1.28 (1.22–1.34)	1.69 (1.54–1.84)	1.77 (1.69–1.85)	1.61 (1.52–1.70)	2.12 (1.96–2.30)	1.00*	1.00*	1.00*
61–70 yrs	2.27 (2.19–2.37)	2.02 (1.94–2.12)	3.13 (2.88–3.40)	3.39 (3.25–3.54)	2.91 (2.76–3.06)	4.45 (4.12–4.80)	3.97 (3.78–4.18)	4.85 (4.29–5.50)	3.8 (3.60–4.02)
71–80 yrs	4.84 (4.65–5.03)	4.27 (4.09–4.47)	6.58 (6.05–7.16)	5.83 (5.59–6.09)	4.84 (4.60–5.11)	7.93 (7.35–8.56)	8.34 (7.94–8.78)	12.65 (11.22–14.32)	7.55 (7.15–7.99)
81–90 yrs	12.03 (11.54–12.54)	10.58 (10.09–11.1)	16.09 (14.76–17.58)	8.88 (8.48–9.30)	7.11 (6.72–7.52)	12.61 (11.65–13.68)	13.58 (12.82–14.39)	22.2 (19.45–25.41)	11.98 (11.23–12.78)
91–100 yrs	26.70 (24.78–28.75)	24.33 (22.26–26.58)	33.33 (28.94–38.36)	11.57 (10.56–12.66)	9.83 (8.76–11.00)	15.15 (13.01–17.59)	21.37 (18.42–24.68)	40.85 (31.12–52.9)	17.37 (14.51–20.63)

Values are odds ratio (95% confidence interval). *40 to 60 used as a reference.
Abbreviations as in Table 2.

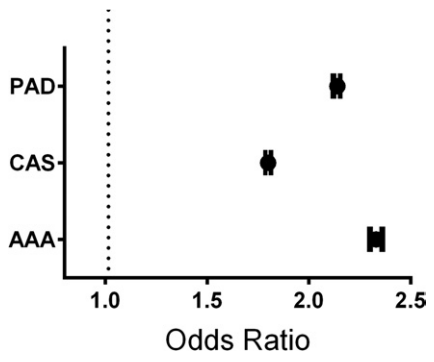

Figure 4 **Adjusted Odds Ratio for Vascular Disease by Each Decade of Life**

Adjusted odds ratio with 95% confidence intervals for PAD, AAA, and CAS after adjustment for age (every 10 years), sex, race/ethnicity, body mass index, smoking, hypertension, physical activity, hypercholesterolemia, diabetes, and family history of cardiovascular disease. Odds ratio >1.0 indicates that the prevalence of vascular disease increases with increased age.

to 50 years old age group, 0.19% in the 51 to 60 years age group, 0.66% in the 61 to 70 years age group, 1.7% in the 71 to 80 years age group, 3.58% in the 81 to 90 years age group, and 6.56% in the 91 to 100 years age group (p for trend <0.001). Overlap of vascular disease by decade is illustrated in the Online Figure 1.

Discussion

This study demonstrates the striking association between increasing age and prevalence of peripheral vascular disease in different vascular territories. Using data from a population-based screening study of more than 3.6 million people in the United States, we were able to include data from more than 200,000 individuals older than age 80 years making this by far the largest study of age and peripheral vascular disease. There are several important findings in this paper. First, the prevalence of any peripheral vascular disease increased from 1 in 50 in the 40 to 50 years old age group to nearly 1 in 3 in the 91 to 100 years old age group. Second, the prevalence of each type of PVD (PAD, CAS, and AAA) increased considerably with advanced age overall and for women and men, respectively. Third, the association between age and PVD remained even after adjustment for baseline demographics and clinical risk factors. For every 10-year increase in age, the odds of PAD (2.14), CAS (1.80), and AAA (2.33) increased significantly. Finally, while the prevalence of PAD, CAS, and AAA increased with advanced age, each disease type acted differently across the spectrum of age.

There is a well-established relationship between age and coronary artery disease. The Framingham and other cardiovascular risk scores place a significant emphasis on the subjects' age in determining the individuals' risk for a coronary event (13,14). While it is well known that a subjects' risk of atherosclerotic disease increases with age, the precise relationship between age and peripheral vascular disease in different vascular territories is less well known.

Most prior studies of age and peripheral vascular disease examined the prevalence of PAD. As expected, several studies demonstrated the prevalence of PAD increases with age (5,6,15–22), ranging from 0% among 60- to 69-year-olds (22) to over 50% among subjects over 85 years of age (6). The most likely explanations for the reported variability in prevalence are the different populations evaluated (e.g., hyperlipidemia [5] and nursing home population [6]), different diagnostic criteria for PAD (5), or imprecision due to the limited small sample size (18,19). For example, the study by Criqui et al. included subjects with hyperlipidemia and reported a 33.8% prevalence of PAD in subjects age 70 to 82 years; however, PAD was defined by either ABI ≤0.8 or abnormal flow velocities (5). In a more representative population, the Cardiovascular Health Study (18) and National Health and Nutritional Examination Survey (19) studies demonstrated an increase in PAD with advanced age. However, the Cardiovascular Health Study and National Health and Nutritional Examination Survey studies included only 184 and 779 individuals over the age of 85 years, respectively, thus limiting the generalizability to the octogenarian and nonagenarian populations.

Fewer reports have investigated the relationship between age and carotid artery disease and abdominal aortic aneurysms. While CAS studies have noted an association between disease and age (23–25), ranging from 1.2% among 60- to 69-year-olds (23) to over 11% among subjects 85 years old or older (25), no study included subjects 90 years old and older and the reported studies utilized varied definitions of clinical CAS ranging from 35% (24) to 60% (23) stenosis.

An association between advanced age and AAA has been noted as well (9,26–28), ranging from 1% among 60- to 64-year-olds (9) to 15% among subjects over 75 years of age (26). Unfortunately, significant representation among older adults is lacking among these studies as well, with only 1 study including subjects over 80 years of age (28). With more than 3 million subjects (of whom 200,000 are greater than 80 years of age), we provide important prevalence data on older adults lacking from previous PAD, CAS, and AAA reports.

In all 3 arterial territories, prevalence was highest among the oldest age groups. Atherosclerosis is considered the main contributor to vascular disease and is known to increase with age (29). Increased prevalence and severity of atherosclerosis risk factors are thought to explain this progression (30). Yet, in older adults, certain risk factors declined in our study. For example, the prevalence of diabetes and hyperlipidemia increased until 80 years of age and then declined suggesting a survival bias in our population. Nonetheless, the prevalence of vascular disease increased until approximately 95 years of age (Fig. 3). Physical activity is considered antiatherogenic (31), and declined in our population after age 70 years, which may contribute to

the increased prevalence of vascular disease in older adults. Moreover, vascular dysfunction has been shown to increase with age because of decreased compliance (32), angiogenesis (33–35), endothelial antithrombotic properties (36,37), and increased inflammation (32), possibly due to vascular endothelial cell senescence (38), which also increases with age.

Interestingly, all 3 vascular diseases show different patterns of progression with advanced age (Fig. 2). Both CAS and PAD result from systemic atherosclerosis, yet PAD was far more prevalent among older subjects. It is possible that the differences in progression of disease are simply due to the diagnostic criteria used to determine disease prevalence; an ABI <0.9 may only represent mild stenosis in the lower extremity peripheral vasculature, whereas the CAS cutoff that we utilized (>50% stenosis) represents comparatively more advanced disease. Alternatively, the ABI may be falsely lower in the very elderly due to aortic disease, thus overestimating the burden of PAD in the very elderly. Finally we cannot exclude a survivor effect whereby those patients with significant atherosclerosis developed fatal stroke or myocardial infarction and thus the prevalence of CAS is not as high in the oldest old age groups. AAAs are less prevalent than CAS or PAD among all age groups, possibly due to a mechanism independent of atherosclerosis (39).

Limitations and strengths. This observational and cross-sectional study provides no longitudinal data including long-term follow-up to evaluate outcomes and determine whether identifying PVD changed the course of the disease. Furthermore, a single measure of vascular disease was utilized, thus not identifying individuals with disease who require additional techniques for diagnosis. Although the regression analysis in Figure 3 could be useful in assessing the likelihood of someone having a particular vascular disease, there is uncertainty in the oldest ages. Finally, this study included a self-selected population of subjects willing to pay for the diagnostic tests out of pocket and thus may not be generalized to other populations. While the prevalence of disease may be altered by the symptom status of subjects included, the association between age and prevalence of disease should not differ. In fact, the association between age and vascular disease was present for both symptomatic and asymptomatic vascular disease (Online Table 1). It is worthwhile to point out that the prevalence of different cardiovascular risk factors in this database were similar to those of the general population (Online Table 2).

The main strengths of this study include its large population size, wide age representation, availability of lifestyle and medical data, and evaluation of 3 vascular diseases all in the same population. Furthermore, the individual age prevalence values and equations with high r^2 values in Figure 3 provide a unique tool for clinicians to assess the likelihood of any of the 3 vascular diseases being present in the patient.

Conclusions

In a large database of more than 3.6 million self-referred individuals, we conclude that peripheral vascular disease is common and strongly associated with increased chronological age. In all vascular territories examined, prevalence increased significantly with age, but a trend of progression varied among different vascular disease phenotypes. The high prevalence of PVD illustrates the need to further research potential benefits of screening and treatment in appropriately aged populations.

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Key Words: abdominal aortic aneurysm ■ age ■ carotid artery stenosis ■ peripheral artery disease ■ vascular disease.

APPENDIX

For supplemental tables and figures, please see the online version of this article.