The prevalence of peripheral arterial disease in a defined population

MICHAEL H. CRIQUI, M.D., M.P.H., ARNOST FROUNEK, M.D., PH.D., ELIZABETH BARRETT-CONNOR, M.D., MELVILLE R. KLAUBER, PH.D., SAM GABRIEL, B.S., AND DEBORAH GOODMAN, M.P.H.

ABSTRACT Because patients with peripheral arterial disease (PAD) may be asymptomatic or may present with atypical symptoms or findings, the true population prevalence of PAD is essentially unknown. We used four highly reliable, sophisticated noninvasive tests (segmental blood pressure, flow velocity by Doppler ultrasound, postocclusive reactive hyperemia, and pulse reappearance halftime) to assess the prevalence of large-vessel PAD and small-vessel PAD in an older (average age 66 years) defined population of 613 men and women. A total of 11.7% of the population had large-vessel PAD on noninvasive testing, and nearly half of those with large-vessel PAD also had small-vessel PAD (5.2%). An additional 16.0% of the population had isolated small-vessel PAD. Large-vessel PAD increased dramatically with age and was slightly more common in men and in subjects with hyperlipidemia. Isolated small-vessel PAD, by contrast, was essentially unrelated to sex, hyperlipidemia, or age, although it was somewhat less common before age 60. Intermittent claudication rates in this population were 2.2% in men and 1.7% in women, and abnormalities in femoral or posterior tibial pulse were present in 20.3% of men and 22.1% of women compared with the noninvasively assessed large-vessel PAD rate of 11.7%. Thus assessment of large-vessel PAD prevalence by intermittent claudication dramatically underestimated the true large-vessel PAD prevalence and assessment by peripheral pulse examination dramatically overestimated the true prevalence.


THE PREVALENCE of peripheral arterial disease (PAD) in the general population is essentially unknown, primarily because of the lack of data on asymptomatic PAD. Most studies have focused on symptomatic or clinical populations, and previous reports in free-living populations are limited to assessment by symptoms, pulse palpation, or older noninvasive tests.1–13 Recently, highly reliable and valid noninvasive tests for PAD have been developed. These newer methods permit accurate, risk-free evaluation of PAD in subjects unselected for symptoms.14–19

We used such noninvasive tests in a defined, free-living population to determine the true prevalence of PAD and the degree of error resulting from assessment of PAD by the traditional methods, intermittent claudication and pulse palpation.

Methods

All 624 subjects were members of a geographically defined population initially studied under a Lipid Research Clinics (LRC) protocol.20, 21 Subjects were recruited for the study with an introductory letter, followed by a telephone call to schedule an appointment. About half of the subjects (51.7%) were from a random sample of the LRC cohort and the others were selected from the same earlier study for hyperlipidemia, defined as being at or above age- and sex-specific 90th percentiles for cholesterol concentration or 95th percentiles for triglyceride concentration or use of lipid-lowering medications. Subjects were from a predominantly white, upper-middle-class community in southern California, and informed consent was obtained after the procedures had been fully explained.

Eleven subjects (1.8%) were excluded because of missing data or unreliable results of noninvasive testing. Two hundred seventy-five men and 338 women ranging in age from 38 to 82 years (mean 66) remained. One hundred fifty-eight subjects were 38 to 59 years old; 161 were 60 to 69 years old, and 294 were 70 to 82 years old.

Criteria for PAD measurements

Intermittent claudication. Claudication was assessed by the standardized Rose questionnaire developed at the London School of Hygiene and Tropical Medicine. Claudication was defined by the Rose criteria: exercise calf pain not present at rest
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relieved within 10 min by rest. We also defined as "possible" claudication, exercise calf pain not present at rest but otherwise not fully concordant with the Rose criteria. The remaining subjects, including subjects with leg pain at rest and subjects with exercise pain not including the calf, were categorized as not having claudication.

Pulse palpation. On 508 (82.9%) of the subjects, a single examiner performed a standardized bilateral palpation of the femoral, posterior tibial, and dorsalis pedis arteries, with pulses subjectively graded from 0 to 4, and auscultation of the groin for femoral bruits. Pulses lower than grade 3 or audible bruits were considered abnormal. This examination was done before noninvasive testing, and the examiner was unaware of the subject's responses to the claudication questionnaire.

Noninvasive testing. Four different noninvasive measurements of limb perfusion in the lower extremities were made: segmental blood pressure, flow velocity, postocclusive reactive hyperemia, and pulse reappearance half-time.

Segmental blood pressure. The ratio of arm systolic blood pressure to pressure at five different levels of the lower extremity (upper thigh, above knee, below knee, above ankle, and toe) was recorded by the sphygmomanometric technique and a mercury-in-Silastic gauge attached to the toe.14-16

Flow velocity. The Doppler effect produced by back-scattered ultrasound from red blood cells in motion was used to measure flow velocity in the femoral and posterior tibial arteries.17

Postocclusive reactive hyperemia. This phenomenon was used to mimic exercise blood flow requirements. Arterial flow was halted by inflating a cuff below the knee to a suprasystolic value for 4 min. Upon release of the cuff, the Doppler flow velocity response (reactive hyperemia) was recorded from the femoral artery. The percentage increase above baseline as well as the time for the response to fall to 50% of peak were recorded.18

Pulse reappearance half-time. Simultaneously with the postocclusive reactive hyperemia test, the pulse reappearance half-time, or the time it took after releasing the cuff for the pulse amplitude to reach one-half the baseline value, was recorded.19

Large-vessel PAD. Large-vessel PAD was defined as either an abnormal segment–to–arm blood pressure ratio (LVBP +) or an abnormal large-vessel flow velocity (LVFV +).

LVBP + was defined as either

\[
\begin{align*}
\text{an above ankle or below knee ratio} & \leq 0.8, \\
\text{an above knee ratio} & \leq 0.7, \\
\text{an upper thigh ratio} & \leq 0.8
\end{align*}
\]

LVFV + was defined as either a

\[
\begin{align*}
\text{a femoral peak flow forward of} & \leq 20\text{ cm/sec} \\
\text{a femoral pulse decay of} & \geq 260\text{ msec or} \\
\text{a femoral deceleration of} & \leq 100\text{ cm/sec}^2
\end{align*}
\]

or

\[
\begin{align*}
\text{a posterior tibial peak flow forward of} & \leq 10\text{ cm/sec} \\
\text{a posterior tibial pulse decay of} & \geq 220\text{ msec or} \\
\text{a posterior tibial deceleration of} & \leq 70\text{ cm/sec}^2
\end{align*}
\]

Although these tests measure dynamic aspects of perfusion rather than the degree of anatomic obstruction, they have been demonstrated to have a good correlation with moderate or greater large-vessel-PAD determined angiographically.14-17

Small-vessel PAD. Small-vessel PAD was defined by an isolated toe pressure abnormality or a pulse reappearance half-time abnormality or a combination of abnormalities in pulse reappearance half-time, postocclusive reactive hyperemia, and time for hyperemic response to fall to 50% of peak.

Specifically, the presence of small-vessel PAD was defined as

\[
\begin{align*}
\text{a T ratio} & \leq 0.7 \text{ with the above ankle ratio and the below knee ratio normal} \\
\text{a pulse reappearance half-time} & \geq 20\text{ sec} \\
\text{a pulse reappearance half-time} & \geq 15\text{ sec and a postocclusive reactive hyperemia} \leq 75\% \text{ and} \\
\text{time for hyperemic response} & \text{to fall to 50% of peak} \geq 40\text{ sec}
\end{align*}
\]

The cutoff points chosen represent extreme values from previous studies of normal control subjects.18,19 Since small-vessel PAD cannot be reliably assessed angiographically, anatomic correlation of these tests is impractical.

Surgery for PAD. Subjects were asked whether they had ever had surgery for poor circulation to the extremities, other than for varicose veins, and the nature and location of the surgery. Subjects with documented surgery for PAD underwent the noninvasive testing along with other subjects. For this analysis, subjects who had had surgery were arbitrarily considered to be LVBP + and LVFV +.

Statistical analysis. Tests for association in 2 × 2 tables were performed with Pearson’s chi square with Yates’ correction. The Mantel-Haenszel chi-square procedure corrected for continuity was used to test for association in ordered contingency tables.23 The independent associations of age, sex, and selection reason (random sample or hyperlipidemia) with PAD were assessed by multiple logistic regression.24

Results

Table 1 shows the prevalence of PAD in this population as assessed by the traditional methods of intermittent claudication by history and pulse palpation by examination. For this and subsequent tables, numbers of subjects vary slightly because of missing or incomplete data. The proportion reporting Rose claudication was somewhat higher for men than women (2.2% vs 1.7%), and this difference was magnified when Rose and possible claudication were combined. For both Rose and Rose-plus-possible claudication, the prevalence increased steadily with age, reaching 2.7% for Rose and 7.7% for Rose-plus-possible claudication in the 70 years and older group. None of the trends noted above were statistically significant, perhaps in part because of the small number of subjects with claudication. However, the associations with age were suggestive (p < .09).

The prevalence of abnormal pulses was grouped into femoral (including femoral bruit), posterior tibial, dorsalis pedis, and an "any pulse abnormality" group defined as an abnormal femoral or posterior tibial pulse or a femoral bruit. The dorsalis pedis pulse was excluded from the "any pulse abnormality" category because it is unilaterally or bilaterally congenitally absent in 4% to 12% of subjects.25,26 The prevalence of an abnormal femoral pulse or bruit was more common
TABLE 1
Prevalence of PAD by traditional assessment: intermittent claudication and pulse palpation

<table>
<thead>
<tr>
<th></th>
<th>% Claudication</th>
<th>% Pulse abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Rose Rose + possible</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>275</td>
<td>2.2 7.2</td>
</tr>
<tr>
<td>Women</td>
<td>338</td>
<td>1.7 4.9</td>
</tr>
<tr>
<td>Age (yr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>158</td>
<td>0.0 3.1</td>
</tr>
<tr>
<td>60–69</td>
<td>161</td>
<td>2.4 5.4</td>
</tr>
<tr>
<td>70+</td>
<td>294</td>
<td>2.7 7.7</td>
</tr>
</tbody>
</table>

^Excludes dorsalis pedis.

in men than women (11.5% vs 6.8%; p = .052), whereas an abnormal posterior tibial pulse was slightly more common in women (17.7% vs 13.2%; p = NS). For the "any pulse abnormality" category, the prevalence was quite similar in men and women, 20.3% and 22.1%, respectively. Dorsalis pedis abnormalities were highly prevalent, reflecting to some extent congenital absence, but the prevalence also increased with age, reflecting true occlusion with age.

For the other pulse categories, the prevalence of abnormalities rose sharply with age, with the prevalence in the "any pulse abnormality" group increasing from 5.6% at ages under 60 years to 15.9% at ages 60 to 69 and 33.8% at ages 70 and older (p < .001).

Figure 1 shows the overall prevalence results from noninvasive testing. A total of 27.7% of the population had large-vessel PAD or small-vessel PAD; 11.7% had large-vessel PAD as manifested by LVbp+ or LVfv+. Proportions of subjects with various combinations of LVbp+, LVfv+, and previous surgery for PAD are shown. About 10% of the subjects with large-vessel PAD were so categorized because of previous surgery, half of whom still had large-vessel PAD on noninvasive testing.
Sixteen percent of subjects had isolated small-vessel PAD (small-vessel PAD only). However, of the 11.7% of subjects with large-vessel PAD, about half (5.2%) also had small-vessel PAD for an overall small-vessel PAD prevalence of 21.2%.

Figure 2 shows the prevalence of large-vessel PAD by age and sex. The prevalence of large-vessel PAD rose sharply with age, from less than 3% at under 60 years to over 20% at age 75 and older. At most ages large-vessel PAD was slightly more common in men.

Figure 3 shows the results for isolated small-vessel PAD (small-vessel PAD accompanying large-vessel PAD excluded). Isolated small-vessel PAD, in contrast to the results in figure 2, showed little difference in prevalence between the sexes and little change in prevalence with age after age 60. The prevalence appeared lower before age 60, but the result was of borderline statistical significance (p = .076).

To evaluate the independent associations of age, sex, and subject selection criteria (random sample vs hyperlipidemia) with large-vessel PAD and isolated small-vessel PAD, we estimated relative risks using multiple logistic regression, a technique that allows us to evaluate the contribution of a given factor while simultaneously adjusting for other factors considered. Table 2 shows the results. Age was strongly and significantly related to large-vessel PAD, with the risk increasing stepwise. With subjects less than 60 years of age as the reference value, subjects 75 years of age or older had about an eightfold greater risk. There was also 27% more large-vessel PAD in men than women and a 29% excess in patients with hyperlipidemia, but neither increment was statistically significant with our sample size. However, in the small group of subjects with large-vessel PAD with both LVBP and LVFV (figure 1), the RR for men compared with women was 2.66 (p = .04).

Isolated small-vessel PAD was unrelated to sex or hyperlipidemia. The overall association with age was also nonsignificant, although there was a 60% to 90% excess for each older age group compared with the group less than 60 years old.

**Discussion**

Our claudication rates of 2.2% in men and 1.7% in women in a population with an average age of 66 years tend to be lower than earlier results in men but comparable with those in women. Earlier studies have generally evaluated younger populations and most have used the Rose questionnaire. In men 50 to 59 years old the percent prevalence of claudication in six earlier studies was 0.8%, 1.1%, 1.2%, 2.3%, 2.8%, and 3.1%. 8-10

**TABLE 2**

Independent relative risks* of age, sex, and selection reason for large-vessel PAD and isolated small-vessel PAD

<table>
<thead>
<tr>
<th></th>
<th>LV-PAD</th>
<th></th>
<th>Isolated</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>p value</td>
<td>RR</td>
<td>p value</td>
</tr>
<tr>
<td>Age (yr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>1.00b</td>
<td></td>
<td>1.00b</td>
<td></td>
</tr>
<tr>
<td>60-64</td>
<td>1.30</td>
<td></td>
<td>1.85</td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>4.78</td>
<td>&lt;.001</td>
<td>1.92</td>
<td>.27</td>
</tr>
<tr>
<td>70-74</td>
<td>6.02</td>
<td></td>
<td>1.60</td>
<td></td>
</tr>
<tr>
<td>75+</td>
<td>7.94</td>
<td></td>
<td>1.59</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>1.00b</td>
<td></td>
<td>1.00b</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>1.27</td>
<td>.34</td>
<td>0.97</td>
<td>.87</td>
</tr>
<tr>
<td>Selection criteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random sample</td>
<td>1.00b</td>
<td></td>
<td>1.00b</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemic</td>
<td>1.29</td>
<td>.34</td>
<td>1.04</td>
<td>.82</td>
</tr>
</tbody>
</table>

LV-PAD = large-vessel peripheral arterial disease; SV-PAD = small-vessel peripheral arterial disease.

*From multiple logistic regression model.

bFixed reference value.
A recent Finnish study also evaluating subjects 50 to 59 years old found high claudication rates in both men (4.6%) and women (2.8%).

Previous reports concerning men 60 years old and older have indicated claudication rates of 1.3% and 2.7%. A Danish study found Rose claudication prevalence rates of 5.8% in men and 1.3% in women at age 60. A study in England found a 2.2% prevalence in men aged 45 to 69 and 1.2% in women aged 50 to 69. However, criteria in that study included ankle blood pressure measurements, and the prevalence of claudication alone may have been closer to 3% in men and 2% in women.

The claudication excess in men in our study was thus less pronounced than that in earlier studies, but the sex ratio in our study did increase when possible claudication was included. The stepwise increase in prevalence with age is concordant with earlier studies and is concordant with reports of increasing incidence with age in the Framingham cohort.

Previous reports of the population prevalence of specific abnormal pulses have varied considerably. In subjects 60 years old and older, the dorsalis pedis pulses was reported to be absent in 22.7% of men but only 9.8% of women in a British study and 31.6% of men and 19.5% of women in a Michigan study as compared with diminished pulses in 30% of both men and women in our study. The posterior tibial pulse was absent in 12.8% of men and 20.6% of women in the British study and 23.7% of men and 37.5% of women in the Michigan study compared with diminished pulses in 13.2% of men and 17.7% of women in our study. Our results are not directly comparable because we included diminished as well as absent pulses, but the studies do agree that a posterior tibial abnormality may be more common in women despite their lesser claudication prevalence. The Danish study that found a high claudication rate in 60-year-old men of 5.8% reported the prevalence of either an absent dorsalis pedis or posterior tibial pulse to be only 11.9% in men and 8.8% in women.

Our data suggest a steep rise in abnormal femoral or posterior tibial pulses with age, from 5.6% at less than age 60 to 33.8% at age 70 and greater, but no marked sex differential. In addition, the dorsalis pedis pulse was so frequently absent at younger ages in our study that its clinical significance appears limited. The prevalence of "any pulse abnormality" was approximately 10 times the Rose claudication prevalence and about three times the Rose-plus-possible claudication prevalence in men and four times that in women.

The true population prevalence of PAD in our study, as assessed by noninvasive testing, indicated 11.7% of subjects had large-vessel PAD, half of whom also had small-vessel PAD, and an additional 16.0% prevalence of isolated small-vessel PAD. The category of isolated small-vessel PAD was defined because of the possibility that some of the small-vessel PAD accompanying large-vessel PAD might reflect reduced small-vessel flow primarily as a result of proximal stenoses in larger vessels. There was a clear association of large-vessel PAD with age and somewhat more large-vessel PAD in men. In contrast, isolated small-vessel PAD, while less prevalent before age 60, was unrelated to age after age 60 and did not show an excess in men. The multivariable logistic analysis confirmed these associations, although the excess in men for large-vessel PAD was not statistically significant. The logistic analysis also suggested some association with hyperlipidemia, albeit not statistically significant, for large-vessel PAD but not for isolated small-vessel PAD. This suggests our prevalence estimates are only slightly biased as a result of our population sample. PAD has been previously reported to be much more closely associated with cigarette smoking and diabetes than with hyperlipidemia. An analysis of the association of PAD with cardiovascular risk factors in our population will be reported separately.

The sharp difference in the association of age, sex, and hyperlipidemia with large-vessel PAD as compared with isolated small-vessel PAD further suggests that isolated small-vessel PAD is a distinct entity rather than early or subcritical large-vessel PAD.

Our objective in this report was to define the true amount of occlusive disease in our population, regardless of signs or symptoms. Only four previous studies have had a comparable aim. Three studies were done in unselected populations but used a limited noninvasive assessment. Eight percent of men 60 to 64 years old in Basel, Switzerland, had a peripheral arterial occlusion, with pulse oscillography used as a major screening tool. Two studies in The Netherlands found a 3% and 4% prevalence of an above-ankle ratio of ≤ 0.9. A study in Denmark also used a criterion of an above-ankle ratio ≥ 0.9 and found a 14.3% prevalence in 666 men and women aged 60. The fourth study used extensive noninvasive testing in 458 diabetics with an average age of 52.6 years and found an expectedly very high PAD prevalence of 36.0%. Thus our study is the first to use extensive noninvasive testing in a defined population unselected for disease status and the first to report results separately for large-vessel PAD and small-vessel PAD. We are unaware of other studies of isolated small-vessel PAD prevalence.

In conclusion, the prevalence of intermittent claudic-
cation was only about one-fifth the true prevalence of large-vessel PAD in our population, whereas the prevalence by pulse abnormalities was nearly twice the true rate. Thus population estimates of large-vessel PAD determined only by symptoms or pulse evaluation result in a distorted view of the extent of occlusive disease.

Also of interest is the degree of association between PAD assessed by traditional methods and large-vessel PAD and isolated small-vessel PAD defined by non-invasive testing. This is the subject of the companion report.29

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