Lower extremity artery stenosis distribution in an unselected elderly population and its relation to a reduced ankle-brachial index

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Objective: This study evaluated the distribution and degree of symmetry of lower extremity artery stenoses in an unselected elderly population and its relation to a reduced ankle-brachial index (ABI) measurement.

Methods: This was a population-based study set in a university hospital comprising 306 randomly selected 70-year-old individuals participating in the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. Whole-body magnetic resonance angiography (MRA) and bilateral ABI measurements were performed in each participant. The prevalence of stenosis ≥50% was evaluated in nine different arterial segments in both legs: common iliac artery (CIA), external iliac artery (EIA), common femoral artery (CFA), superficial femoral artery (SFA), popliteal artery (PA), tibioperoneal trunk (TPTr), anterior tibial artery (ATA), posterior tibial artery (PTA), and peroneal artery. The relations between the prevalences of stenosis in different arterial segments in the right and left leg were assessed. An evaluation was made of the relation between a ≥50% stenosis and an ABI <0.9 in the different segments.

Results: The prevalence of stenosis was 0% to 21%. In all segments, a stenosis was more commonly found in one of the legs only than in both legs. The prevalence of ≥50% stenosis in the right leg only, left leg only, and both legs was 0.3%, 0.7%, and 0% in the CIA; 0.3%, 1.0%, and 0.7% in the EIA; 0%, 0%, and 0% in the CFA; 2.0%, 1.3%, and 0.7% in the SFA; 0.7%, 0.7%, and 0.3% in the PA; 1.0%, 0.7%, and 0% in the TPTr; 5.6%, 6.3%, and 8.6% in the ATA; 0.7%, 1.7%, and 0% in the peroneal artery; and in 2.0%, 2.7%, and 3.4% in the PTA. When the legs were compared, a significant correlation was found for the presence of a ≥50% stenosis in the EIA, SFA, PA, ATA, and PTA. Seventeen participants showed ABI <0.9. In logistic regression analysis with ABI <0.9 as dependent variable, stenosis in SFA, ATA, and PTA were the major independent variables to explain a low ABI in both of the legs.

Conclusions: The distribution of stenosis differs substantially when legs are compared. Despite this difference, stenosis in SFA, ATA, and PTA was the major determinant of a low ABI in both of the legs. (J Vasc Surg 2009;49:444-51.)

Knowledge about the stenosis distribution and the degree of symmetry between the legs in this regard could be of interest when the pathophysiology of lower extremity atherosclerosis is investigated. Because of constraints related to the use of ionizing radiation, to our knowledge, no x-ray studies have assessed the stenosis frequency in different arterial segments in an unselected population. Neither has it been possible to assess the degree of concordance regarding the stenosis distribution between the right and left leg.

The ankle-brachial index (ABI) is a commonly used screening test for significant leg artery stenoses. In the workup of patients with suspected claudication, an ABI <0.9 is regarded as a sign of hemodynamically significant stenosis in the ipsilateral leg. This is based on old studies that compared ABI with x-ray digital subtraction angiography (DSA) using a small amount of data.1,2 ABI has thus been used as a surrogate marker for atherosclerosis in epidemiologic studies.3,4 It is, however, incompletely known if some arterial segments are more important than others for the development of a reduced ABI measurement.

With the advent of magnetic resonance angiography (MRA), and lately also whole-body MRA (WB-MRA), a bilateral evaluation of large vascular territories is now feasible.6,7 Because WB-MRA is a minimally invasive technique that requires only an intravenous injection of a contrast agent and does not use ionizing radiation, it is possible to use it in larger population studies. The large coverage is an important advantage compared with duplex ultrasound imaging, another noninvasive vascular imaging alternative.

The aim of this study was therefore to use WB-MRA data to compare the distribution of arterial stenoses in the right and left legs in an unselected elderly population and to assess the relation between a low ABI and the presence of high-grade stenoses in the different vascular segments.

MATERIALS AND METHODS

Participants. The study was approved by the Institutional Review Board, and the participants gave written informed consent. A total of 307 individuals (145 women, 162 men) were randomly recruited from the population-based cohort study Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study (www.medsci.uu.se/ pivus) comprising 1016 participants.5 The participants in the...
PIVUS study were chosen from the Population Register of the municipality and were invited in randomized order ≤2 months of their 70th birthday. Of the 2025 individuals invited, 1016 were investigated.

The clinical characteristics of the total PIVUS sample and the WB-MRA subsample were compared, and no significant differences were noted (Table 1). The prevalence of atherosclerotic changes in different vessel territories in this cohort have been reported previously.9 Exclusion criteria for the WB-MRA examination were a pacemaker, valvular prostheses, intracranial clips, and claustrophobia. Of the included participants, 306 could complete the WBMRA examination. A vasovagal attack occurred in the remaining individual before contrast medium administration, and the examination was aborted.

**Blood pressure measurements.** Systolic blood pressure was measured in the supine position in the posterior tibial artery with the highest systolic pressure obtained in the brachial arteries.

**MRA.** The WB-MRA examination was performed with a quadrature body coil in a 1.5 Tesla (T) Gyroscan Intera scanner (gradients: amplitude 30 mT/m, rise time 200 μs, slew rate 150 mT/m/ms), using standard MobiTrak software (Philips Medical System, Best, The Netherlands). The individual was placed supine with feet-first on the table, to which an extension of the tabletop was attached, allowing for larger coverage. The arms were positioned over the patient’s head to avoid foldover. A 2-mL test bolus of gadodiamide (Omniscan, GE Healthcare, Oslo, Norway) was used with a coronal dynamic acquisition. From these images, the time taken from injection of the contrast agent into the antecubital vein to its arrival in the proximal descending aorta could be measured.

The WB-MRA examination was divided into four stations. The first station included the supra-aortic arteries and the thoracic aorta. The second station contained the abdominal aorta, including the renal arteries, and the third started at the external iliac arteries and continued to the popliteal arteries. The fourth station continued for a varying distance below the ankle. An overlap of 3 cm between each station gave a maximum total length of coverage of 171 cm. Breath-holding was performed only for the second station.

A 3-dimensional RF-spoiled T1-weighted gradient echo acquisition was done at these four stations, beginning with the fourth station, before the injection. The scan time for each station was 17 seconds. The tabletop was moved automatically with the table in the cranial direction. The scan time for the noncontrast-enhanced images was 87 seconds, including instructions for breathholding and table movement, which took 4 seconds each for the three movements. Thereafter, 40 mL of gadodiamide was injected intravenously with an automated injector (MR Spectris, Medrad, Pittsburgh, Pa) at a rate of 0.6 mL/s in 67 seconds, followed by 20 mL of saline solution. The scan was set to start after the defined time following the test bolus examination. The stations were scanned in reversed order during the contrast administration, with the first station first, during another 87-second period.

The sequence parameters were repetition time, 2.5 ms; echo time, 0.94 ms; flip angle, 30°; bandwidth, 781.3 Hz/pixel; matrix size 256 × 256; field of view, 450 mm; 60 slices × 4-mm thickness; 80% scan percentage. The measured voxel size was 1.76 × 1.76 × 4.0 mm, and this was reconstructed by zero-filling to 0.88 × 0.88 × 2.0 mm, which gives a 1.54 mm³ volume of reconstructed voxel. Linear K-space sampling was used for the first station. For the other stations, randomly segmented centric view order (Centra, Philips Medical System, Best, the Netherlands) was used. The mean interval between ABI recording and WB-MRA was 16 months (range, 3-24 months).

**Evaluation.** The pelvic and leg arteries were divided into nine segments on each side. The pelvic and thigh arterial segments comprised the common iliac (CIA), ex-
Table II. Relation between presence of ≥50% stenoses in the right and left legs

<table>
<thead>
<tr>
<th>Vessel segment</th>
<th>Right leg</th>
<th>Left leg</th>
<th>Both legs</th>
<th>Total</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common iliac artery</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>306</td>
<td>.93</td>
</tr>
<tr>
<td>External iliac artery</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>306</td>
<td>.0002</td>
</tr>
<tr>
<td>Common femoral artery</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>306</td>
<td></td>
</tr>
<tr>
<td>Superficial femoral artery</td>
<td>6</td>
<td>0</td>
<td>2</td>
<td>305</td>
<td>.0058</td>
</tr>
<tr>
<td>Popliteal artery</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>300</td>
<td>.016</td>
</tr>
<tr>
<td>Tibioperoneal trunk</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>305</td>
<td>.88</td>
</tr>
<tr>
<td>Anterior tibial artery</td>
<td>17</td>
<td>19</td>
<td>26</td>
<td>302</td>
<td>.0001</td>
</tr>
<tr>
<td>Peroneal artery</td>
<td>2</td>
<td>5</td>
<td>0</td>
<td>297</td>
<td>.85</td>
</tr>
<tr>
<td>Posterior tibial artery</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>295</td>
<td>.0001</td>
</tr>
</tbody>
</table>

*The P value refers to the assessment of the relation between the prevalence of ≥50% stenosis in different arterial segments in the right and left leg.

The prevalence of ≥50% stenosis varied from 0% in the CFA to 21% in the ATA among the segments.

Relationships between the prevalences of stenosis in different arterial segment in the right and left leg. The prevalence of ≥50% stenosis in the different segments is given in Table II. The prevalence in the right leg only, left leg only, and both legs was 0.3%, 0.7%, and 0% in the CIA; 0.3%, 1.0%, and 0.7% in the EIA; 0%, 0%, and 0% in the CFA; 2.0%, 1.3%, and 0.7% in the SFA; 0.7%, 0.7%, and 0.3% in the PA; 1.0%, 0.7%, and 0% in the TPTr; 5.6%, 6.3%, and 8.6% in the ATA; 0.7%, 1.7%, and 0% in the peroneal artery; and in 2.0%, 2.7%, and 3.4% in the PTA. It was thus more common to only have a stenosis in one of the legs than in both legs for all separate arterial segments evaluated. Despite this, there were significant associations between the prevalences of stenosis in the left and the right leg for CIA, SFA, PA, ATA, and PTA. No significant associations between the prevalences of stenosis in the left and the right leg were seen for CIA, TPTr, and peroneal. The CFA could not be evaluated due to lack of stenosis in this segment.

Relationship between ABI in the right and left leg. The ABIs in the right and left leg were significantly correlated (r = 0.70, P < .0001; Fig). However, when only those with ABI < 0.9 were evaluated, six were found with ABI < 0.9 in the right leg only, five with a reduced ABI in the left leg only, and six were found with ABI < 0.9 in both legs (P < .0001 when comparing the left and the right leg with Fisher’s exact test).

Relationships between stenosis in different vascular segments and the ABI. In the 306 individuals, all vessel segments were assessable with WB-MRA on the right side in 268 and on the left side in 265. At least one ≥50% stenosis was found in 19% (51 of 268) on the right side and in 23% (61 of 265) on the left side, and the respective corresponding prevalences for ABI < 0.9 were 4.5% (12 of 268) and 4.2% (11 of 265). This resulted in a sensitivity, specificity, and positive and negative predictive value of ABI < 0.9 for the identification of a ≥50% stenosis of 20%, 99%,...
Table III. Segments in legs with a significant relation between ≥50% stenoses and ankle-brachial index <0.9

<table>
<thead>
<tr>
<th>Arterial segment</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right leg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superficial femoral</td>
<td>18.4</td>
<td>2.45-138</td>
<td>.0046</td>
</tr>
<tr>
<td>Anterior tibial</td>
<td>8.76</td>
<td>2.13-36.0</td>
<td>.0026</td>
</tr>
<tr>
<td>Posterior tibial</td>
<td>20.6</td>
<td>4.38-97.0</td>
<td>.0001</td>
</tr>
<tr>
<td>Left leg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superficial femoral</td>
<td>64.5</td>
<td>3.02-1380</td>
<td>.0077</td>
</tr>
<tr>
<td>Anterior tibial</td>
<td>46.5</td>
<td>9.00-240</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Posterior tibial</td>
<td>5.18</td>
<td>0.96-27.9</td>
<td>.056*</td>
</tr>
</tbody>
</table>

CI, Confidence interval; OR, odds ratio.
*aMarginal significance for posterior tibial artery.

83%, and 84% on the right side and of 15%, 99%, 82%, and 80% on the left side.

When ABI <0.9 (as a binary variable) was used as a dependent variable and stenosis in the nine different vascular segments was used as an independent variable in stepwise multiple logistic regression models for the right and left leg separately, stenosis in the SFA, ATA and PTA in the right leg were significantly related to a low ABI in the right leg. The same vascular segments were independently related to a low ABI in the left leg, although PTA in this case only reached borderline significance (P = .0556; Table III).

When instead of ABI <0.9 (as a binary variable) as the dependent variable in logistic regression analysis we used ABI (as a continuous variable) as the dependent variable, the significant relation in the right leg was maintained. On the contrary, ABI variations in the normal range could only be explained by the amount of stenosis in the SFA, ATA, and PTA in the right leg. The non-significant relation between ABI <0.9 and 50% stenosis in the left leg is probably due to the high prevalence of 50% stenosis in the left leg, which makes it difficult to detect a significant relation.

A significant relation was found between ≥50% stenoses and an ABI <0.9 in the SFA, ATA, and PTA in both legs, although only at borderline level for the left PTA. No significant relation between ≥50% stenoses and an ABI <0.9 was found for the other segments. We used separate analysis for the legs, because we by this approach could replicate our own findings, and the same relationship generally was seen in both legs, regardless of whether we used ABI <0.9 as a binary variable or ABI as a continuous variable, further supporting our results. No stenoses were detected in the CFA and hence no evaluation made of the relation between stenosis and ABI. A possible explanation, at least partly, for the absence of a significant relation between ≥50% stenoses and an ABI <0.9 in the CIA and EIA could be the proximity of these segments, since it has been shown that flow curve restitution that takes place with increasing distance from a vessel constriction.

The presence of a well-established collateral network could also explain a normal ABI despite ≥50% stenosis. This could be true for the segments in the knee region (PA, tibioperoneal trunk) where a collateral network is present also normally. The peroneal artery does not consistently communicate with the PTA, where the pressure measurement was made, so lesions in this segment would not be expected to affect the ankle pressure. The significant relation between stenoses in the ATA and a reduced ABI is more difficult to explain. Possibly, a high-grade ATA stenosis leads to a decreased resistance in the pedal arch vessels and hence a lower PTA ankle pressure in these cases. It should, however, also be pointed out that there were rather low numbers with ≥50% stenoses in some of the segments. The absence of a significant relation between ≥50% stenoses and an ABI <0.9 in some segments could thus also be an effect of a low statistical power.

A limitation with the present study is the sometimes quite long interval between WB-MRA and the ABI measurements. Unfortunately, we have no information about any clinical deterioration in the participants during this time, to our knowledge, been able to establish the distribution of lower extremity artery stenoses in an unselected elderly population. A substantial variation was found between the stenosis pattern in the right and left legs. The effect of a stenosis on the ABI differed between the segments but was similar in both legs.

Although there were significant associations between the legs regarding the stenosis prevalences in the EIA, SFA, PA, ATA, and PTA segments, unilateral stenoses were more common than bilateral in all evaluated segments. This finding suggests that the atherosclerotic process is to a large degree a random event. In a previous study that investigated 100 candidates for vascular surgery, a marked symmetry was found in stenosis location, with a perfect agreement between the legs in 53% to 76% of contralateral vessels. This study is difficult to compare with ours because it was performed on the clinical results of claudicant patients, where the stenosis prevalence can be expected to be higher, rather than in an unselected population. The method of evaluating the degree of symmetry in the stenosis pattern was also completely different.

The significant and high overall correlation in ABI between the legs can be explained by a high degree of correlation between the right and left ABI values in the normal range (Fig). There were variations in this range between participants, but the ABI values tended to be similar when the legs were compared. ABI variations in the normal range can be explained mainly by differences in brachial pressure. The poorer correlation between the legs in a finding of an ABI <0.9 suggests however, in line with the factor analysis, that the pathophysiologic events leading to a hemodynamically significant lesion are stochastic to a high degree.
period. The possible consequence of this delay between ABI measurement and WB-MRA is that of a falsely high ABI. This could result in a somewhat reduced sensitivity of an ABI <0.9 for the detection of ≥50% stenosis. It is, however, unlikely that the atherosclerosis should progress at such a pace for this to substantially affect our results.

Another limitation is the spatial resolution of the WB-MRA technique, which is lower than can be achieved with phased-array surface coils. A somewhat lower resolution could, conversely, result in both under-estimation and over-estimation of stenoses and is not likely to have affected the conclusions of the study. The WB-MRA technique was also used in a previous study where conventional DSA was available in a subset of patients and segments. A high degree of concordance was found between the two techniques for the identification of ≥50% stenoses, with identical results obtained with the two techniques in 72 of 79 compared segments. In the seven discordant segments, WB-MRA over-graded the stenosis compared with DSA in three and under-graded the stenosis compared with DSA in four. The interobserver, and intraobserver reproducibility of the WB-MRA assessment has also been reported in a previous PIVUS WB-MRA article. This showed high intraobserver reproducibility (κ = 0.73) and excellent interobserver reproducibility (κ = 0.83).

We used a measurement in the PTA for the calculation of the ABI; however, there are other possible ways of doing this. Some have used the lower of the ATA and PTA, and some have used the mean of the two pressures. Our rationale for the use of only the PTA was a practical one: The use of two measurements would have increased the examination time. In addition, we considered measurements in the ATA to be more difficult to obtain in a reproducible way. Compared with use of the lower of the ATA and PTA, our method can have resulted in some overestimation of the ABI.

CONCLUSIONS

In a previous PIVUS report, we presented the whole-body distribution of arterial stenoses in an unselected elderly population. In the present study we extended the evaluation of this material and compared the distribution of arterial stenoses in the two legs. We have also assessed the influence of a ≥50% stenosis in different segments on the ABI. There was considerable variation in the lower extremity stenosis pattern when the legs were compared, although significant relations were found between the left and right sides for some vascular segments. Our interpretation of this finding is that of a substantial random influence on the atherosclerotic process. We further found the relation between high-grade stenoses and a reduced ABI to depend on the stenosis location, with only SFA, ATA, and PTA stenoses having a significant relation to an ABI <0.9. This finding should be borne in mind when ABI measurements are interpreted in both clinical and epidemiologic studies.

AUTHOR CONTRIBUTIONS

Conception and design: LL
Analysis and interpretation: JW, LL, LJ
Data collection: JW, TH, HA, LL
Writing the article: JW
Critical revision of the article: LL, TH, HA, LJ
Final approval of the article: JW, TH, HA, LJ, LL
Statistical analysis: LL
Obtained funding: LL, HA, LJ
Overall responsibility: LL

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Submitted Oct 16, 2008; accepted Mar 10, 2009.