The Prevalence and Predictors of an Abnormal Ankle-Brachial Index in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial

Premanjan P. Singh, MD1
J. Dawn Abbott, MD2
Manuel S. Lombardo, MS3
Kim Sutton-Tyrrell, DRPH4
Gail Woodhead, RN7
Lakshmi Venkitachalam, PhD3
Nicholas P. Tsapatsaris, MD4
Thomas C. Piemonte, MD4
Rodrigo M. Lago, MD3
Martin K. Rutter, MD5
Richard W. Nesto, MD4
BARI 2D Study Group*

OBJECTIVE—To examine ankle-brachial index (ABI) abnormalities in patients with type 2 diabetes and coronary artery disease (CAD).

RESEARCH DESIGN AND METHODS—An ABI was obtained in 2,240 patients in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial. ABIs were classified as: normal, 0.91–1.3; low, ≤0.9; high, >1.3, or noncompressible artery (NC). Baseline characteristics were examined according to ABI and by multivariate analysis.

RESULTS—ABI was normal in 66%, low in 19%, and high in 8% of patients, and 6% of patients had NC. Of the low ABI patients, 68% were asymptomatic. Using normal ABI as referent, low ABI was independently associated with smoking, female sex, black race, hypertension, age, C-reactive protein, diabetes duration, and lower BMI. High ABI was associated with male sex, nonblack race, and higher BMI; and NC artery was associated with diabetes duration, higher BMI, and hypertension.

CONCLUSIONS—ABI abnormalities are common and often asymptomatic in patients with type 2 diabetes and CAD.

From the 1Ocala and Munroe Regional Medical Center, Ocala, Florida; 2Rhode Island Hospital, Providence, Rhode Island; the 3Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania; 4Lahey Clinic Medical Center, Burlington, Massachusetts; and the 5Cardiovascular Research Group, School of Biomedicine, University of Manchester, Manchester, U.K., and the Manchester Diabetes Centre, Manchester Academic Health Science Centre, Manchester NIHR Biomedical Research Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, U.K. Corresponding author: J. Dawn Abbott, jdabott@lifespan.org
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*A complete list of the BARI 2D Study Group is available as Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc10-1734/-/DC1.
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Statistical analysis
We compared clinical characteristics between ABI groups using the normal ABI group as referent. We used \( \chi^2 \) tests for categorical variables and Student \( t \) tests for continuous variables. Associations between clinical variables and presence of low ABI, high ABI, or NC artery were assessed with logistic regression using predictor variables that had biological plausibility for being causally related to the outcome variable. We present odds ratios (ORs) (95% CIs) for this model. A value of \( P \approx 0.05 \) was considered statistically significant. SAS version 9 for Windows was used for all analyses (version 9.2; SAS Institute).

RESULTS
Baseline characteristics according to ABI
The distribution of ABI was approximately symmetrical, with a mean value of 1.05. A normal ABI was found in 66% (\( n = 1,489 \)), low ABI in 19% (\( n = 430 \)), high ABI in 8% (\( n = 182 \)), and NC artery in 6% (\( n = 139 \)) of patients. The baseline
| Variables hypothesized to be causally related to ABI | Normal ABI (ref. n = 1,489) | Low ABI (n = 182) | High ABI (n = 139) | Adjusted OR (95% CI) |
|-----------------------------------------------|----------------------------|------------------|------------------|---------------------|
| Age (years)                                   | 61.9 (8.8)                 | 63.4 (8.9)*      | 61.9 (8.5)       | 1.29 (1.13–1.48)    |
| Sex (% female)                                | 28.3                       | 38.8†            | 17.6*            | 1.41 (1.10–1.79)    |
| Black race vs. all others (%)                 | 15.2                       | 27.4†            | 4.9†             | 0.30 (0.15–0.60)    |
| Diabetes duration (years)                     | 9.7 (8.1)                  | 11.4 (9.0)       | 10.2 (9.1)       | 1.18 (1.03–1.34)    |
| Insulin treatment (%)                         | 25.9                       | 32.3*            | 25.3             | 2.40 (1.76–3.26)    |
| HbA1c (%)                                     | 7.6 (1.6)                  | 7.8 (1.6)        | 7.6 (1.8)        | 0.87 (0.79–0.97)    |
| Hypertension (%)                              | 87.8                       | 92.3*            | 87.4             | 1.56 (1.04–2.33)    |
| Hypercholesterolemia (%)                      | 81.6                       | 82.1             | 76.9             | 0.67 (0.44–1.02)    |
| Current cigarette smoker (%)                 | 11.6                       | 20.7†            | 3.8*             | 0.30 (0.14–0.66)    |
| Chronic renal dysfunction (%)                | 2.5                        | 4.4*             | 2.7†             | 2.70 (1.95–3.40)    |
| CRP log (mg/ml)                               | 0.85 (1.25)                | 1.06 (1.22)*     | 0.83 (1.19)      | 1.12 (1.01–1.23)    |
| White race vs. all others (%)                 | 65.1                       | 58.1*            | 83†              | 0.56 (0.42–0.74)    |
| Hispanic vs. all others (%)                   | 13.9                       | 10.5             | 8.2*             | 0.81 (0.61–1.08)    |
| Other (vs. white/black/Hispanic) (%)          | 5.8                        | 4.3†             | 3.8              | 0.83 (0.66–1.04)    |
| Cardiac disease (%)                           | 6.3                        | 14.9†            | 3.3†             | 0.30 (0.14–0.66)    |
| Number of disease regions (%)                 | 0                          | 3                | 2                | 1                  | 0

Data are means (SD) unless otherwise indicated. ACR, urine albumin-to-creatinine ratio; MJI, myocardial jeopardy index. *P value for comparison with normal ABI > 0.05, †P value for comparison with normal ABI > 0.001.

Table I — Baseline characteristics and clinical predictors of an abnormal ABI.
characteristics according to ABI are presented (Table 1).

**ABI and lower extremity symptoms**

With respect to symptoms status, 68% of patients with a low ABI did not have claudication. Compared with low-ABI patients with claudication, symptomatic subjects had higher mean ABI values (0.75 vs. 0.66, P < 0.0001), were less likely to have peripheral neuropathy (28 vs. 55%, P < 0.0001), carotid artery disease (8 vs. 29%, P < 0.0001), and chronic renal dysfunction (3 vs. 8%, P = 0.047), and were less likely to be current smokers (16 vs. 31%, P = 0.0003), suggesting that the severity of atherosclerotic disease may play a role.

**Abnormal ABI risk factors**

After adjustment, with normal ABI as referent, low ABI was independently associated with older age, female sex, black race, diabetes duration, lower mean BMI, hypertension, current smoking, and higher C-reactive protein (CRP). Using similar methodology, a high ABI was associated with male sex, nonblack race, nonsmoking status, and higher mean BMI; an NC artery was associated with diabetes duration, higher mean BMI, and hypertension (Table 1).

**CONCLUSIONS**—In this large study of patients with type 2 diabetes and CAD, we found a high prevalence of obstructive PAD and arterial stiffness and identified risk factors for an abnormal ABI. A longer duration of type 2 diabetes and hypertension were independently associated with a low ABI and NC artery. Certain factors, however, were associated only with a low ABI, such as older age, female sex, black race, current smoking, and higher CRP level. A higher prevalence of PAD among women and blacks has been observed and does not appear to be due to known atherosclerosis risk factors (3,4).

Our study extends these findings to patients with type 2 diabetes and CAD. The higher prevalence of PAD in women and blacks may be due to biologic or social differences, as well as slightly lower normal ABI values in these populations (5). Older age, smoking, and CRP, similar to our study, are associated with the presence or progression of PAD in patients with diabetes (6,7).

Similar to a low ABI, a high ABI or NC artery is associated with an increased risk of mortality, cardiovascular events, and amputation (8–10). We observed a high prevalence of arterial stiffness, similar to that seen in older individuals, American Indians, and dialysis patients (9,10). As observed in our study, diabetes duration has been identified as a risk factor for obstructive PAD and arterial stiffness (11,12). Unlike PAD outcomes, which are not known to improve with glycemic control, intensive treatment of diabetes can reduce peripheral arterial calcification and therefore may prevent development of NC arteries (13). The association between higher mean BMI and a high ABI or NC artery in our population may be related directly to adiposity or differences in physical activity levels.

This is a large study of well-characterized patients that includes a large number of women and minority ethnic groups. Limitations include the cross-sectional study design, which limits any conclusions about causality, the fact that ABI measurement may not detect all obstructive PAD, and the fact that an NC artery can mask obstructive PAD.

In summary, we have shown that both an abnormally low or high ABI are common in patients with established type 2 diabetes and CAD and that associated factors can be identified and deserve further study of causality. Prior studies have shown that PAD is frequently overlooked in high-risk patients and that the absence of symptoms does not modify the risk of cardiovascular events (14). The high prevalence of asymptomatic patients in our study supports the recommendations for a more aggressive approach to PAD detection. Whether early identification of PAD and implementation of aggressive medical measures can influence the progression of lower-extremity vascular disease or associated cardiovascular mortality in type 2 diabetes is unknown.

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