CHAPTER 14

PERIPHERAL ATERIAL DISEASE (PAD) AND

ANKLE BRACHIAL INDEX (ABI) MEASUREMENT

Study Documents for ABI Measurement:

Ankle Brachial Index

San Diego Claudication Questionnaire

CHAPTER 14

PERIPHERAL ATERIAL DISEASE (PAD) AND

ANKLE BRACHIAL INDEX (ABI) MEASUREMENT

14.1. BACKGROUND

Lower extremity peripheral arterial disease (PAD) affects eight million men and women in the United States (1), and is particularly prevalent among older men and women. Among community dwelling participants in the Cardiovascular Health Study (CHS), 12% of men and women age 65 and older had a low ankle brachial index (ABI), consistent with PAD (2). Prevalences of PAD are > 20% among men and women age 80 and older (2).

Men and women with PAD have greater functional impairment and faster rates of functional decline, compared to those without PAD (3-6). For example, at four-year follow-up, men and women with PAD have a 1.6-fold increased rate of mobility loss, compared to those without PAD (5). Because the LIFE study population is older and because LIFE participants will have some baseline functional impairment (i.e. short physical performance battery (SPPB) score <10), we anticipate that approximately 20% of LIFE participants will have PAD.

Despite the high prevalence of functional impairment and the high risk for functional decline and mobility loss associated with PAD, few therapies have been demonstrated to improve functional performance in men and women with PAD. The large number of PAD participants anticipated in LIFE provides a unique opportunity to study important questions regarding the ability of a physical activity intervention to prevent mobility loss in men and women with PAD.

Although intermittent claudication is the most classic manifestation of PAD, most men and women with PAD do not have classic intermittent claudication symptoms (7, 8). Many people with PAD are asymptomatic and others have exertional leg symptoms other than intermittent claudication. PAD patients who are asymptomatic have significant functional impairment and experience substantial declines in functional performance, even though they do not experience exertional leg symptoms (4,9). Similarly, PAD patients with atypical leg symptoms other than intermittent claudication have greater functional impairment and faster functional decline than individuals without PAD (3,4).

Supervised treadmill exercise training, performed three times weekly, improves treadmill walking performance and six-minute walk distance among men and women with PAD, both with and without intermittent claudication (10). However, most insurance companies (including Medicare) do not pay for supervised exercise training for patients with PAD. Few alternative effective therapies are available for improving walking performance in patients with PAD. Currently data are mixed regarding whether exercise programs other than supervised treadmill exercise performed three times weekly can improve walking performance in men and women with PAD. New studies are needed to identify exercise regimens, not requiring frequent supervised treadmill training, to improve walking performance in patients with PAD.

In addition, most previous exercise trials in men and women with PAD have employed exercise interventions of six months or shorter duration. To our knowledge, no prior studies have tested the ability of exercise interventions >18 months to improve walking performance in PAD participants. Since prior work demonstrates that gains in walking performance related to

supervised treadmill exercise are not maintained after cessation of supervised exercise, it is important to determine whether exercise interventions of prolonged duration (i.e. > 6 months) can successfully prevent mobility loss in participants with PAD. It is also unknown whether exercise training programs increase physical activity levels during daily life in participants with PAD, since prior randomized controlled trials have demonstrated mixed results (10,11).

We anticipate that approximately 20% of LIFE participants (or 320 participants) will have a low ABI, consistent with PAD. This prevalence of PAD may be conservative, since the LIFE inclusion criterion of a sedentary lifestyle and an SPPB score < 10 is expected to increase the prevalence of PAD. It is also important to point out that most men and women with PAD are unaware of the presence of PAD. Thus, the ABI is likely to detect PAD in a substantial number of LIFE participants who were previously unaware that they had PAD.

The LIFE study provides a unique opportunity to address important specific aims in participants with PAD. Specific aims regarding PAD are as follows:

14.2 SPECIFIC AIMS

14.2.1 Primary Specific Aim

1. Among the subset of LIFE participants with PAD at baseline, we will determine whether the physical activity intervention prevents disability at a mean follow-up of 2.7 years. Disability is defined as becoming unable to complete the 400-meter walk test at follow-up. PAD at baseline will be defined as a baseline ABI < 0.90 or history of lower extremity revascularization at baseline.

14.2.2 Secondary Specific Aims.

1. Among the subset of LIFE participants with PAD at baseline, we will determine whether the physical activity intervention improves physical activity levels during daily life at a mean follow-up of 2.7 years. Physical activity levels during daily life will be measured using accelerometry. PAD will be defined as specified in our Primary Specific Aim.

2. Among the subset of LIFE participants with PAD at baseline who are asymptomatic, we will determine whether the physical activity intervention prevents disability at a mean follow-up of 2.7 years. Disability is defined as becoming unable to complete the 400-meter walk test at follow-up. PAD will be defined as specified in our Primary Specific Aim. Asymptomatic will be defined as absence of exertional leg symptoms at baseline.

3. Previous study demonstrates that PAD participants with an ABI 0.90 to 0.99 have significantly increased rates of mobility loss at five-year follow-up, compared to PAD participants with an ABI of 1.00-1.30 (6). Therefore, among LIFE participants with a baseline ABI < 1.00, we will determine whether the physical activity intervention prevents disability at a mean follow-up of 2.7 years. Disability is defined as becoming unable to complete the 400-meter walk test at follow-up.

14.2.3 Exploratory Specific Aims.

1. Among LIFE participants with a normal ABI at baseline (i.e. ABI 0.90 to 1.30), we will determine whether the physical activity intervention is associated with a lower incidence of PAD at follow-up. Incident PAD at follow-up will be defined as new onset of an ABI < 0.90 at follow-up or hospitalization for lower extremity revascularization during follow-up.
2. Among LIFE participants with PAD at baseline, we will determine whether participants randomized to the physical activity intervention have lower declines in their ABI at 30-month follow-up, compared to those in the Healthy Aging condition.

3. We will determine whether the presence of PAD modifies the effect of the physical activity intervention on mobility loss at 30-month follow-up. We hypothesize that PAD participants will achieve greater benefit from the physical activity intervention than participants without PAD.
4. We will determine whether PAD participants have poorer adherence rates to the physical activity intervention compared to participants without PAD.
5. Among participants with PAD, we will determine whether lower ABI values modify the effect of the physical activity intervention on mobility loss at a mean follow-up of 30 months. We hypothesize that among participants with PAD, lower ABI values will be associated with more favorable responsiveness to the physical activity intervention at 30-month follow-up.

14.3. LIFE PAD Measurements

14.3.1. PAD Symptoms.

The most classic symptom of PAD is intermittent claudication (12). However, most men and women with PAD do not have classic symptoms of intermittent claudication (7,8). Many people with PAD are asymptomatic and others have exertional leg symptoms that are atypical (i.e. not consistent with intermittent claudication). In the Women's Health and Aging Study (WHAS), fully 2/3 of participants with PAD did not have classic intermittent claudication symptoms (9).

In LIFE, we will use the San Diego claudication questionnaire to measure PAD symptoms. The San Diego claudication questionnaire is based on the original Rose claudication questionnaire and the Edinburgh claudication questionnaire (12). However, the San Diego claudication questionnaire allows one to assess leg symptoms in the left and right legs separately. Using the San Diego claudication questionnaire, previous studies have identified specific leg symptom categories that are associated with more adverse lower extremity outcomes, including adverse muscle characteristics, greater functional impairment, and more rapid functional decline (4,8,13).

In addition to the San Diego claudication questionnaire, we will also inquire about prior history of lower extremity revascularization, since some LIFE participants with a normal baseline ABI may have a history of prior lower extremity revascularization and thus should be classified with PAD at baseline. Participants will be asked at baseline whether they have a prior history of PAD.

Completing the San Diego Claudication Questionnaire

The first question of the San Diego Claudication Questionnaire (question #5 on forms 52 and 53) is, "Do you get pain in either leg or buttock when walking?" If the participant responds "no" to this question, then the remainder of the San Diego Claudication Questionnaire form should be skipped.

If the participant responds "yes" to the question, "Do you get pain in either leg or buttock when walking?", (question #5 on the form) the participant is asked about which leg they get the symptoms in. If the participant indicates that they get the pain in only one of their legs, the remainder of the questionnaire items (i.e. items 6 through 15) need only address the leg with the symptoms. The items for the leg without symptoms should remain blank. Specifically, if the participant responds (question #5) that they get pain in their **right leg or buttock only**, then the remaining questions (i.e. items 6 through 15) should address the right leg symptoms only and items 6 through 15 with regard to the left leg should remain blank.

14.3.2. Ankle Brachial Index

The ankle-brachial index (ABI) is a sensitive and specific measure of lower extremity peripheral arterial disease. The ABI measurement also gauges the degree of obstruction due to

atherosclerosis in the lower extremities. A recent critical analysis of the ABI demonstrated a sensitivity of 79% and a specificity of 96% for angiographically significant peripheral arterial disease (14). Since arterial pressures normally increase with greater distance from the heart, due to increasing amplitude of systolic pressure with increasing distance from the heart, a truly normal ABI is greater than 1.00 (15,16).

14.3.3. PAD Definition: In LIFE, a participant will be presumed to have lower extremity arterial disease when the ABI is < 0.90 or if they have an ABI $\underline{\geq}$ 0.90 but have history of lower extremity revascularization. However, since a truly normal ABI is > 1.00, our Secondary Specific Aim #3 will determine whether LIFE participants with a baseline ABI < 1.00 randomized to the Physical Activity Intervention have lower rates of mobility loss compared to LIFE participants with a baseline ABI < 1.00 who are randomized to the Healthy Aging condition.

14.3.4. Equipment

1. Nicolet Vascular Pocket-Dop II™ Doppler
2. Ultrasound gel
3. A standard aneuroid sphygmomanometer
4. Blood pressure cuffs in four sizes: adult, large, thigh, and pediatric
5. Tissues to remove conducting gel
6. Supply of AA batteries
7. Ex am table.

14.3.5. Universal Precautions: If the participant has open ulcers of the lower extremity, the data collector must wear protective gloves during the measurement. A clean, protective wrap (Tegaderm) must be placed over the open wounds of the lower extremity before the blood pressure cuff is secured.

14.3.6. ABI Procedure

When the 400 M walk test is performed at the same visit as ABI, the ABI should be performed at least 30 minutes after completion of the 400 m walk test. The reason is that walking exercise, such as the 400 m walk, can temporarily reduce the ABI in patients who have mild lower extremity atherosclerosis. The objective in the LIFE Study is to obtain a resting ABI.

The Ankle-Brachial Index measurement is performed after the participant has lain supine for at least five minutes. During these five minutes, the participant should refrain from talking, in order to ensure maximal relaxation. Additionally, during the ABI measure, the participant is advised not to talk, to ensure that the participant remains relaxed throughout the testing.

Lower extremity atherosclerosis commonly affects the systolic pressure in the posterior tibial artery and the dorsalis pedis artery in the affected extremity. An ABI can be calculated for the posterior tibial and the dorsalis pedis arteries in each leg. ABI values for the posterior tibial and dorsalis pedis arteries in a given leg are highly correlated (17). Previous study demonstrates that measuring the ABI using the posterior tibial artery alone is a highly sensitive and specific method for identifying PAD (18). Therefore, to ensure a time- efficient but accurate ABI measurement, the LIFE ABI will measure arterial pressures in the brachial and the posterior tibial arteries in both lower extremities.

14.3.7. Procedure

1. Ask participant to remove shoes and stockings so that the ankles are bare to mid-calf. Nylon stockings must be removed.
2. Place a fresh sheet on the bed and covering the pillow. Participant then lies supine on the

bed. The participant should lie as flat as is comfortable, preferably on one pillow with the bed flat. The head should not be propped up.
3. Long sleeves should be rolled up several inches above the elbows, or if this is impossible, have the participant remove the shirt and wear a hospital gown during testing.
4. Keep participant supine for at least five minutes before starting ABI measurements.
5. Advise the participant that we will not talk during the ABI measurement because talking can affect the pressure readings.
6. In general, the probe should be positioned at a 45 degree angle and should be angled toward oncoming flow. In this position, the pulse should be most readily audible.

14.3.8. Systolic Pressure Readings

Whenever possible, place all blood pressure cuffs in the participant before starting to take measurements.

14.3.9 Right Arm Systolic Pressure Measurement

1. Sit or stand next to the participant's right arm.
2. Place a blood pressure cuff of appropriate size above the right elbow, directly on the skin, with the midpoint of the bladder over the right brachial artery.
3. Locate the brachial artery by palpation.
4. Apply ultrasound gel over the brachial artery.
5. Locate the brachial artery using the Doppler probe, and position the probe so that the pulse is as loud as possible. Position the probe at a 45 degree angle toward oncoming arterial flow.
6. Measure the systolic blood pressure using the Doppler probe.
   a. Quickly inflate cuff to <u>at least</u> 20 mmHg above pressure at which you last hear a pulse.
   b. Deflate at 2 mmHg/second until you hear a sustained systolic pulse.
   c. Ensure there is at least 20 mm Hg of silence prior to the onset of a sustained systolic pulse.
   d. Quickly deflate cuff completely.
7. Record right brachial systolic blood pressure.

14.3.10. Right Ankle Systolic Pressure Measurement: Posterior Tibial Artery

1. Locate the posterior tibial artery by palpation if possible.
2. Apply ultrasound gel over the posterior tibial artery.
3. Locate the pulse using the Doppler probe, and position the probe so that the pulse is as loud as possible. Position the probe at a 45 degree angle toward oncoming arterial flow.
4. Measure the systolic blood pressure using the Doppler probe.
   a. Quickly inflate cuff to at least 20 mmHg above pressure at which you last hear a pulse.
   b. Deflate at 2 mmHg/second until you hear a sustained systolic pulse.
   c. Ensure there is at least 20 mm Hg of silence prior to the onset of a sustained systolic pulse.
   d. Quickly deflate cuff completely.
5. Record right posterior tibial systolic blood pressure.

14.3.11. Left Ankle Systolic Pressure Measurement: Posterior Tibial Artery

1. Locate posterior tibial artery by palpation if possible.
2. Apply ultrasound gel over posterior tibial artery.

3. Locate the pulse using the Doppler probe, and position the probe so that the pulse is as loud as possible. Position the probe at a 45 degree angle toward oncoming arterial flow.
4. Measure the systolic blood pressure using the Doppler probe.
   a. Quickly inflate cuff to at least 20 mmHg above pressure at which you last hear a pulse.
   b. Deflate at 2 mmHg/second until you hear a sustained systolic pulse.
   c. Ensure there is at least 20 mm Hg of silence prior to the onset of a sustained systolic pulse.
   d. Quickly deflate cuff completely.
5. Record left posterior tibial systolic blood pressure.

14.3.12. Left Arm Systolic BP Measurement

1. Sit or stand next to the participant's left arm.
2. Place blood pressure cuff of appropriate size over the left brachial artery.
3. Locate the brachial artery by palpation.
4. Apply ultrasound gel over the brachial artery.
5. Locate the pulse using the Doppler probe, and position the probe so that the pulse is as loud as possible.
6. Measure the systolic blood pressure using the Doppler probe.
   a. Quickly inflate cuff to at least 20 mmHg above pressure at which you last hear a pulse.
   b. Deflate at 2 mmHg/second until you hear a sustained systolic pulse.
   c. Ensure there is at least 20 mm Hg of silence prior to the onset of a sustained systolic pulse.
   d. Quickly deflate cuff completely.
7. Record left brachial systolic blood pressure.

14.3.13. Repeat of ABI Measurements

Repeat the sequence of measures in the opposite order: left arm, left ankle, right ankle, right arm. Remove ultrasound gel with tissues. Remove blood pressure cuffs.

Comments and Tips.

The following points will greatly improve the speed and accuracy of measurements.

1. Hold the Doppler probe absolutely still while inflating and deflating the cuff by resting part of the hand holding the probe against the skin. Moving a few millimeters will lose the pulse.
2. Always use plenty of gel to assure good transmittal of the flow signal.
3. Record the pressure at which the first sustained systolic pulse is audible. If you hear two beats and then a silence, do not record the pressure prior to the silence or pause. Instead, record the pressure that is followed by at least two consecutive additional beats.
4. The pulse of the posterior tibial artery may be barely audible or inaudible. In this case, record "0" for the systolic pressure for that artery.

A demonstration of how perform this measure can viewed at the following link: http://content.nejm.org/cgi/content/short/361/19/e40.

14.4. CALCULATING THE ABI

The ABI will be calculated by the data entry software. This should minimize ABI calculation errors. The program will use the following procedure:

To derive the brachial systolic pressure for calculation of the ABI, compare the first set of right and left brachial readings to each other and the second set of right and left readings to each

other. If one arm has higher readings than the other in both sets of readings, *and* one of the differences between right and left is 10 mmHg or more, average the readings from the higher arm. Otherwise, average all four readings. The resultant average is used as the denominator for calculating the ABI.

To derive the ankle systolic pressure for calculation of the ABI, average the two posterior tibial pressure readings for each leg. This results in an ankle systolic pressure for each leg. To calculate the ABI, divide the ankle pressure for each leg by the brachial pressure, using the definitions above for the ankle and brachial pressures. Calculate an ABI for each leg. If the software is not available, an excel spreadsheet should be used for calculating the ABI.

14.5. TIME TABLE FOR PAD MEASUREMENTS

The table shows the proposed measurements and time-table for PAD outcomes.

Table 14.1. Proposed PAD measurement plan.

Baseline		One-year follow-up	30-month follow-up	Closeout[2]
ABI	X X			X
Claudication questionnaire	X X			X
Lower extremity revascularization	X[1] X		X	X
Known history of PAD?	X			

[1] At baseline we will determine whether the participant has a prior history of lower extremity revascularization. When the participant has had more than one lower extremity revascularization, only the most recent lower extremity revascularization will be recorded.
[2] Measures to be obtained at closeout only if the measures were missed at 30-month follow-up or if the 30-month follow-up visit occurred more than one year prior to the closeout visit.

14.6. NOTIFYING PATIENTS OF RESULTS

All participants will be notified of their results. Patients with PAD have significantly increased rates of cardiovascular events (19,20). Furthermore, certain therapies, such as statins and anti-platelet agents, have been demonstrated to lower cardiovascular event rates in PAD (21). Our result letter will advised participants with PAD to follow-up with their physician.

ALERTS:

1. Systolic blood pressure elevation:

If the final reading of either brachial artery systolic pressure (i.e. left or right) is 170 mmHg or higher, check the blood pressure by a standard method. If the systolic pressure is still $\geq$ 170 mmHg, follow the procedures for reporting elevated blood pressure in Chapter 21 – Safety Management.

2. Absent Doppler signal in the leg:

If a participant has no audible blood flow in the posterior tibial artery of either leg, a qualified

clinical staff person should inquire about symptoms of claudication or rest pain, inspect the leg for ischemia and check for a dorsalis pedis signal. The clinical staff person should also check for the posterior tibial pressure. If significant ischemia is noted, the staff person should discuss further with the study physician and an appropriate referral made.

3. Low ABI (< 0.90). PAD is associated with significantly increased rates of cardiovascular events (19,20). Furthermore, certain therapies, such as statins and anti-platelet agents, have been demonstrated to lower cardiovascular event rates in PAD (21). Therefore, LIFE participants will be notified of their ABI results, if their ABI is < 0.90.

See attached example result letter for participants with an ABI < 0.90 in either leg at their baseline or follow-up visits than can be incorporated with other clinical information provided to the participant. (Appendix A).

14.7. ABI TRAINING.

Assessors without any specialized training can learn to properly perform the ABI. However, appropriate training and certification is required and experience with research protocol blood pressure measurement is recommended. The procedures are as follows.

1. Research assistants will observe an ABI measurement.

2. Research assistants will perform at least three ABI measurements.

3. Research assistants will be certified in ABI measurement, by performing the ABI in the presence of a trained certifier. A checklist will be used by the examiner to ensure that the trainee meets all criteria for proper technique during certification (See MOP Chapter 24- Quality Control). A minimum of 2 measures per month are required to maintain certification, otherwise recertification is required. Retraining and recertification will be required annually. Recertification will consist of re-reading the ABI MOP, re-taking the ABI quiz, watching the ABI video, and observation of the ABI by an individual certified in the LIFE ABI procedure. The certifier will ensure that each element of the ABI recertification checklist is completed during the ABI measurement.

14.8 ABI Quality Control

Several measures are in place to ensure optimal quality of ABI data collection.

1. Test re-test reliability measurements. Beginning in early 2011, each site will have a second assessor perform the ABI on 10 LIFE participants. The second assessor will perform the ABI measurement immediately after the main (first) ABI measurement. For efficiency sake, it is not necessary for the second assessor to remove and replace each blood pressure cuffs. The second assessor will repeat the ABI measurement using the same procedures as outlined above. Each pressure will be measured twice as outlined above. Each site will collect the 10 test re-test reliability ABI measures over a 2 to 3 month period. Although 10 consecutive measures should be attempted, this may not be practical given staffing issues. Thus, collecting the additional 10 additional measures over 2-3 months is acceptable. This information will be used to calculate test re-test reliability measures for each site and overall for the LIFE study. This information will be reviewed and discuss by the MEA committee.

ABI Retest Data Collection

ABI retest data for 10 participants will be collected using the Ankle Brachial Index (ABI) Retest

Measurement Form found on the LIFE website. This form will be completed by a second assessor during the retest of the ABI.

As with all LIFE forms, you will need to provide the standardized header information (PID, Acrostic, Examiner ID, Visit Code and Date of Visit) on the retest form. The participant's ID label with PID and acrostic can be used to provide this information. This header information is critical to the retest analysis. Please make certain the visit code and date of visit are the same on the original ABI Measurement Form and the ABI Retest Measurement Form.

To complete the ABI Retest Measurement Form, repeat all ABI pressure measurements as outlined in this MOP chapter and record the measurements. Measurement #1 will be entered in questions 1-4 in the respective spaces provided. Measurement #2 will be entered in questions 5-8 in the respective spaces provided.

DO NOT change any measurements on the original form as a result of the retest. This is for QC purposes only. The original form will still be used as the participant's official study data.

ABI Retest Data Entry Instructions

To data enter the ABI Retest Measurement Form go to the main menu on the LIFE website and click on "Tools > Quality Control > ABI Retest". Enter the PID and click "Submit". When the data entry screen comes up, enter the data from the retest form. When finished, click on "Save". If there are any questions regarding the data (i.e. missing data, out of range) a warning message will appear at the top of the screen in orange text indicating the issue. Please double check that the data entry matches the CRF and if so, click on "Save with warnings".

Following data entry the ABI Retest Measurement forms should be filed in the participant's chart and should be clearly distinguishable from the original study measurement.

2. Monthly Review of ABI data. Drs. McDermott and Newman will review reports of ABI measurement values by site. These reports, generated by the DMAQC, include mean and median values for each pressure measurement, mean and median ABI measurement, the prevalence of ABI < 0.90 at each site, the prevalence of an ABI > 1.30, and the correlation between the 400 meter walk test and the ABI. Data are provided by site and overall for the entire cohort. Data will be discussed periodically on the MEA telephone conference call.

3. Site visits. The ABI will be observed at each site visit. Where possible, an expert in the measurement of ABI will attend site visits to observe the ABI. A local ABI expert will be identified by the site visitor. The local ABI expert will be a staff member who is observed to be particularly adept at the ABI measurement. This local expert will observe other assessors performing the ABI on a periodic basis and provide feedback on their technique.

APPENDIX A

Sample ABI Result Letter for Patients

[Date]

Dear [patient name]

Peripheral arterial disease is a blockage of the arteries in the legs that can show up as a reduced systolic blood pressure in the legs. During your study visit today, the systolic blood pressure of the arms and ankles were measured. The ratio between your ankle systolic blood pressure and your arm systolic blood pressure on both sides are shown in the table below. A normal ankle brachial index (ABI) is greater than 1.00 and less than 1.30. A borderline ABI is greater than 0.90 but less than 1.00. An abnormal ABI is less than 0.90 or greater than 1.30. An ABI value less than 0.90 is consistent with presence of significant blockages in the lower extremity arteries.

Your results were:

Lower Extremity Blood Flow Measurement Results

	ABI Value	Normal ABI	Borderline ABI	High ABI	Low ABI
Left					
Right					

A blockage in the legs, manifest as a low ABI, is usually due to atherosclerosis. Presence of a low ABI frequently means there could be atherosclerosis in other parts of the body, including the heart and brain. People with such problems should be evaluated carefully by their physician. The significance of a high ABI is unclear, but typically indicates calcification of lower extremity arteries and may be associated with increased rates of heart disease events. We encourage you to share this result letter with your physician.

If you have any questions regarding your results, you may contact the project coordinator, .

Sincerely,

Professor of Medicine
Department of Medicine
Department of Preventive Medicine

REFERENCES

1. Lloyd-Jones D, Adams R, Carnethon M, DeSimone G, Ferguson TB, Flegal K, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics committee and Stroke Statistics Subcommittee. Circulation 2009; 119(3):480-6.
2. Newman AB, Siscovick DS, Manolia TA, Polak J, Fried LP, Borhani NO, et al. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. Cardiovascular Heart Study (CHS) Collaborative Research Group. Circulation 1993;88(3):837-45.
3. McDermott MM, Greenland P, Liu K, Guralnik JM, Celic L, Criqui MH, et al. The Ankle Brachial Index is associated with Leg Function and Physical Activity: The Walking and Leg Circulation Study. Ann Intern Med 2002;136(12):873-83.
4. McDermott MM, Liu K, Greenland JM, Criqui MH, Chan C, Pearce WH, et al. Functional decline in peripheral arterial disease: Associations with the ankle brachial index and leg symptoms. JAMA 2004;292(4):453-61.
5. McDermott MM, Guralnik JM, Tian L, Ferrucci L, Liu K, Liao Y, et al. Baseline functional performance predicts the rate of mobility loss in persons with peripheral arterial disease. J Am Coll Cardiol 2007;50(10):974-82.
6. McDermott MM, Guralnik JM, Tian L, Liu K, Ferrucci L, Liao Y, et al. Associations of borderline and low normal ankle-brachial index values with functional decline at 5-year follow-up: the WALCS (Walking and Leg Circulation Study). J Am Coll Cardiol 2009;53(12):1056-62.
7. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 2001;286(11):1317-24.
8. McDermott MM, Greenland P, Liu K, Guralnik JM, Criqui MH, Dolan NC, et al. Leg symptoms in peripheral arterial disease: associated clinical characteristics and functional impairment. JAMA 2001;286(13):1599-606.
9. McDermott MM, Fried L, Simonsick E, Ling S, Guralnik JM. Asymptomatic peripheral arterial disease is independently associated with impaired lower extremity functioning: the women's health and aging study. Circulation 2000;101(9):1007-12.
10. McDermott MM, Ades P, Guralnik JM, Dyer A, Ferrucci L, Nelson M, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial. JAMA 2009;301(2):165-74.
11. Gardner AW, Katzel LI, Sorkin JD, Goldberg AP. Effects of long-term exercise rehabilitation on claudication distances in patients with peripheral arterial disease: a randomized controlled trial. J Cardiopulm Rehabil 2002;22(3):192-8.
12. Rose GA. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. Bull World Health Organ 1962;27:645-58.
13. McDermott MM, Guralnik JM, Ferrucci L, Tian L, Liu K, Liao Y, et al. Asymptomatic peripheral arterial disease is associated with more adverse lower extremity characteristics than intermittent claudication. Circulation 2008;117(19):2484-91.
14. Lijmer JG, Hunink MG, van den Dungen JJ, Loonstra J, Smit AJ. ROC analysis of noninvasive tests for peripheral arterial disease. Ultrasound Med Biol 1996;22(4):391-8.
15. Winsor T. Influence of Arterial Disease on the Systolic Blood Pressure Gradients of the Extremity. *Am J Med Sci* 1950;220:117-26.
16. Yao ST. Haemodynamic Studies in Peripheral Arterial Disease. *Br J Surg* 1970;57:761-6.
17. McDermott MM, Criqui MH, Liu K, Guralnik JM, Greenland P, Martin GJ, et al. Lower ankle/brachial index, as calculated by averaging the dorsalis pedis and posterior tibial arterial pressures, and association with leg functioning in peripheral arterial disease. J Vasc Surg 2000;32(6):1164-71.
18. Feigelson HS, Criqui MH, Fronek A, Langer RD, Molgaard CA. Screening for Peripheral

Arterial Disease: The Sensitivity, Specificity, and Predictive Value of Noninvasive Tests in a Defined Population. 1994;140(6):526-34.
19. Heald CL, Fowkes FG, Murray GD, Price JF; Ankle Brachial Index Collaboration. Risk of mortality and cardiovascular disease associated with the ankle-brachial index: Systematic review. Atherosclerosis 2006;189(1):61-9.
20. Ankle Brachial Index Collaboration, Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA 2008;300(2):197-208.
21. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA et al; American Association for Vascular Surgery/ Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines. ACC/AHA guidelines for the Management of Patients with Peripheral Arterial Disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Associations for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (writing committee to develop guidelines for the management of patients with peripheral arterial disease)—summary of recommendations. J Vasc Interv Radiol 2006;17(9):1383-97.