

Exam 7 Walk test Protocol.

A. Eligibility criteria

Subjects undergoing this test will be free of (a) any known CHD and (b) any disability preventing a six minute walk on the treadmill. All walk tests will be overseen by a cardiologist or cardiologist in training with prior training in the conduct of treadmill exercise testing. All subjects will sign a usual study informed consent prior to participation in this test.

B. Study Materials and Equipment.

Refer to Marquette Electronics manual for walk test machine.

C. Test Procedure

See Appendix 1 for a Test Procedure Checklist.

1. Pre-Exam Notification and Informed Consent

Each participant in Offspring Cycle 7 will receive a mailed packet indicating the date and time of the scheduled visit. In this packet, they will be asked to wear loose fitting clothing and comfortable shoes for the walk test. Upon intake at the start of the examination, each participant will be asked to sign an informed consent in which consent is given to perform the six-minute walk test.

2. Pre-Test Screening Questionnaire

The objective of the pre-test screening questionnaire (Appendix 2) is to identify persons who are ineligible for this test. In general, participants with a known diagnosis of coronary heart disease, severe congestive heart failure or inability to walk on a treadmill will be excluded from this test. Each Offspring participant in Cycle 7 will undergo screening according to the questionnaire.

The exercise technologist will first pre-screen the participant chart for a known CHD diagnosis. When an exclusionary diagnosis is present, it will be noted on the screening questionnaire and the participant excluded from the test. If no diagnosis is present, the questionnaire will be administered to the participant upon his/her arrival in the test room. If a definite exclusionary diagnosis is present, it will be noted on the screening questionnaire and the participant excluded from the test. If there is uncertainty regarding the presence of an exclusionary diagnosis (e.g., participant was admitted to the hospital “for my heart” with no further information available), the walk test will not be performed until *after* participant has been examined by a physician in clinic and the physician examiner deems that there is no evidence of prior clinical coronary heart disease.

Walk tests will be conducted after the fasting blood test (and, in subjects undergoing oral glucose tolerance testing, after the two-hour glucose challenge is completed) to avoid interference of low-level exercise with blood test results.

3. Start-up of Marquette CardioSys machine

These procedures are outlined in detail in the Marquette operations manual (Appendix 6).

4. Participant Preparation

The participant's chest will be exposed and prepared as follows: The exact site for placement of the V-leads will be marked from the supine position according to the "Heart Square" protocol (see Appendix 4). If the participant has received the standard examination 12 lead ECG earlier during the clinic examination, the markers used for the standard ECG will be utilized. The participant will then be asked to stand up for placement of the electrodes. In order to maximize electrical conduction from the participant into each ECG electrode, the chest wall skin will be prepared by wiping with alcohol or a mildly abrasive pumice/soap solution and then abraded with gauze padding at the planned site of electrode placement. The leads will then be placed systematically from right to left as per the usual ECG protocol in the Framingham clinic (Heart Square protocol, Appendix 4) and the electrode apparatus attached to the abdomen with an elastic belt. After completion of electrode placement, the participant's chest and abdomen will be appropriately covered to preserve modesty.

The test technologist will check the CardioSys connection screen for evidence of lead misplacement and she will examine leads V2, V5, etc for visual evidence of baseline artifact.

The participant will then be placed in the supine position (with one pillow under head, for participant comfort) and the test technologist will again check the CardioSys connection screen for evidence of lead misplacement and she will examine leads V2, V5, etc for visual evidence of baseline artifact. While the participant is supine, the appropriate sized blood pressure cuff will be placed on the participant's left arm and if necessary affixed with paper tape.

5. Stage I: 4 Minute Rest Supine

In the supine position and resting state, a 4 minute resting supine ECG measurement will be obtained as follows:

Continuous ECG strip (minutes 0-4). From this point on, continuous ECG data will be collected until the test is terminated (average estimated time of continuous ECG data acquisition, 20 minutes).

Supine left arm blood pressure (minute 2), using the usual Framingham Heart Study blood pressure procedure modified for a supine subject (Appendix 5). The blood pressure reading will be entered onto the walk test blood pressure form (Appendix 3).

12 lead supine ECG (minute 3) will be obtained (with the blood pressure reading printed out as well).

Completion of Stage 1 (minute 4): participant will rise slowly to a standing position.

6. Stage II: 2+ Minute Rest Stand

Once the participant is standing for approximately one minute, a blood pressure and ECG will be obtained:

Phase II, Minute 1, a standing left arm blood pressure will be obtained using the usual Framingham Heart Study blood pressure procedure modified for a standing subject (Appendix 4). The blood pressure reading will be entered into the CardioSys screen X.

Phase II, Minute 1.5, a 12 lead standing ECG will be obtained (with the blood pressure reading printed out as well).

Participant is then asked to step on the treadmill.

7. Stage IV: Warm up on treadmill

Skip stage III (Hyperventilation) and proceed to Stage IV ("Warm up").

The treadmill is then turned on to XX MPH at a 0° Grade. Once the participant is accommodated to walking on the treadmill (10-60 seconds of warm-up), Phase I of the walk test is begun. During Stage IV, the responsible physician is called into the room.

8. Phases I and II: 6 Minute Walk

Participants will be asked to use the horizontal bar at the front of the treadmill for balance but not to grasp the bar if possible. Also, participants will be asked to look forward at the wall in front and not down at the feet. Once the participant is accommodated, the 6 minute walk test will begin. This test consists of the first two stages of the Standard Bruce Protocol. Phase I (ie, stage 1 Bruce protocol) consists of XX M.P.H. at X degrees incline and Phase II (ie, stage 2 Bruce protocol) consists of XX M.P.H. at X degrees incline.

Phase I, Minute 2, a walking left arm blood pressure will be obtained using the usual Framingham Heart Study blood pressure procedure modified for a walking subject (Appendix 4). The blood pressure reading will be entered into the CardioSys screen X.

Phase I, Minute 3, a 12 lead walking ECG will be obtained (with the blood pressure reading printed out as well) and the participant will be questioned about the presence of any symptoms of chest discomfort, dyspnea or other discomfort.

Phase II, Minute 5, a walking left arm blood pressure will be obtained using the usual Framingham Heart Study blood pressure procedure modified for a walking subject (Appendix 4). The blood pressure reading will be entered into the CardioSys screen X.

Phase II, Minute 6, a 12 lead walking ECG will be obtained (with the blood pressure reading printed out as well) and the participant will be questioned about the presence of any symptoms of chest discomfort, dyspnea or other discomfort.

Phase II, Minute 6, treadmill stops automatically.

7. Recovery: 6+ Minute Supine Recovery

Recovery, Minute 0, an immediate recovery standing blood pressure will be obtained while the participant is standing on the treadmill using the usual Framingham Heart Study blood pressure procedure modified for a standing subject (Appendix 4). The participant will then be assisted off the treadmill and placed in a supine position as per the pre-test supine examination, and the participant will be questioned about the presence of any symptoms of chest discomfort, dyspnea or other discomfort.

Recovery, Minute 1-6, recovery supine blood pressures will be obtained at minutes 3 and 5, using the usual Framingham Heart Study blood pressure procedure modified for a supine subject

(Appendix 4). A 12 lead supine ECG will be obtained at minutes 3 and 6 (with the blood pressure readings printed out as well).

At the end of the test, the participant will be questioned about the presence of any symptoms of chest discomfort, dyspnea or other discomfort.

8. Completion of Test

The responsible physician will review all printed ECGs and blood pressure data and will follow up on any symptoms reported during the walk test or in recovery. Once the final report is printed, the responsible physician will sign the report to document his or her presence during key portions of the test.

D. Safety Algorithms

At the beginning of each day of testing, the technologist will check that the responsible physician is present in the building.

Appendix 1. Test Procedure Checklist

At beginning of day, check that responsible physician is in the building.

1. **Informed Consent Signed by clinic staff**
2. **Administer Pre-Test Screening Questionnaire (participant chart will be checked on prior day)**
 - If excluded or refused, do not perform test.
 - If “gray zone” condition, ask responsible physician or send for clinic exam first.
3. **Start-up of Marquette CardioSys machine**
 - “Heart Square” protocol
 - Electrode placement, check for proper connections
 - Cover participant’s chest
 - Place BP cuff
4. **Participant Preparation**
 - Patient demographics screen
 - XXX screen
5. **Stage I: 4 Minute Rest Supine**
 - Begin continuous ECG strip monitoring
 - Minute 2, supine left arm BP, enter reading onto CardioSys
 - Minute 3, 12 lead ECG (with BP reading printed out as well)
 - Minute 4, supine to standing position
6. **Stage II: 2+ Minute Rest Stand**
 - Allow participant to equilibrate
 - Approximately minute 1, standing BP
 - Approx minute 1.5, 12 lead ECG (with BP reading printed out as well)
 - Call responsible physician into room
7. **Phases I and II: 6 Minute Walk**
 - Participant stand on treadmill
 - Instruct participant about handrest and where to look and to clearly say “stop the test” if there is any reason to stop
 - Start machine at XX MPH (Stage IV on Cardiosys), check that participant is accommodated
 - Start 6 Minute Walk Test (Bruce Protocol 1 and 2)
 - Phase I, Minute 2, left arm BP
 - Phase I, Minute 3, 12 lead ECG
 - Ask participant about symptoms of chest pain, SOB or other symptoms.
 - Phase II, Minute 5, a left arm BP
 - Phase II, Minute 6, 12 lead ECG
 - Ask participant about symptoms of chest pain, SOB or other symptoms
 - Minute 6, automatic stop of treadmill
8. **Recovery: 6+ Minute Supine Recovery**
 - Minute 0, immediate recovery standing BP
 - Lie participant down on table
 - Minute 3, recovery supine BP and 12 lead ECG
 - Minute 3, ask participant about symptoms of chest pain, SOB or other symptoms
 - Minute 5, recovery supine BP and 12 lead ECG
 - Minute 6, recovery supine BP and 12 lead ECG
 - Minute 6, ask participant about symptoms of chest pain, SOB or other symptoms
 - End continuous ECG strip monitoring
9. **Completion of Test**
 - Review of printed ECGs and clinical/blood pressure data by responsible physician

Preliminary signature by responsible physician that it is safe for participant to leave

Appendix . Criteria for Notification of Participant's Personal Physician

Framingham Heart Study Offspring Cycle 7, Walk Test

Proposed criteria for a “positive” test requiring that a report be sent to a physician:

1. Occurrence of sustained (ie, one minute or greater) chest pain during exercise.
2. Occurrence of hypotension defined as a drop of at least 20 mmHg systolic blood pressure during exercise.
3. Occurrence of ST segment depression or elevation during the exercise component or in recovery:
 - In the absence of baseline (standing) ST or T wave abnormality, the presence of at least 2.0 mm horizontal or downsloping ST segment depressions in two or more contiguous* leads
 - In the presence of baseline (standing) ST or T wave abnormality, the presence of at least 2.0 mm horizontal or downsloping ST segment depressions from the baseline in two or more contiguous* leads
 - In the absence of Qwaves, the presence of horizontal ST segment elevations 2.0 mm or greater from the baseline
 - In recovery, the sustained occurrence of significant T wave inversion in two or more leads with or without significant ST segment depression in two or more contiguous* leads
4. Occurrence of any of the following asymptomatic arrhythmias including:
 - Ventricular tachycardia of greater than 4 beats
 - Supraventricular tachycardia for greater than 4 seconds
 - Bradycardia with pauses exceeding 2 seconds
 - In addition, any arrhythmia associated with significant symptoms should be reported
5. Other abnormalities as per the examining MD's judgement.

*Examples of contiguous leads: inferior leads (II, III, avF); precordial-anteroapical leads (V1-V6); lateral leads (I, avL). However, could also consider the following to be contiguous leads: apicolateral (eg, V6 *and* I or avL), or inferolateral (eg, II, III or avF and I or avL), or inferoapical (eg, II, III or avF and V6).

QUALITY ASSURANCE AND QUALITY CONTROL (QC) PROCEDURES AT THE WALK STATION AT THE FRAMINGHAM HEART STUDY

Quality assurance (QA) at the Walk Station at the Framingham Heart Study include those activities that are designed to assure data quality and took place prior to data collection. Quality control (QC) includes measures to monitor quality of the data and takes place at identified points during data collection and processing.

Five distinct sources of differences, or variability can be identified in our Walk Test studies, namely i) true 'subject to subject' and 'within' subject variations, ii) differences generated by different technicians performing the test, iii) differences among different interpreters, and iv) measurement errors within and between technicians and readers, v) temporal drifts in test performance and test interpretation. The QA and the QC procedures are designed to minimize these variabilities.

QUALITY ASSURANCE

Test Protocol Development

- 1) Development of new 2 page coding sheets to focus interpretations of the Walk Test to key variables of research interest (Appendix 1)
- 2) Development of following protocols & written manuals including:

Reproducibility Procedures

1) Laboratory meetings

Weekly or fortnightly meetings of Walk Station personnel will take place to review:

- Status of readings (reviewing Walk Test log book)
- Data Storage and back up
- Results of reproducibility studies
- Interpretation issues
- Review abnormal studies together to prevent readers from drifting apart

2) Data entry

To minimize errors, we will ensure that data keying is performed by one individual. The individual is instructed to return to the interpreter any Walk Test interpretation forms that are incompletely filled out.

3) Data cleaning

Data cleaning will occur on an ongoing basis, to give timely feedback to readers. Logic and consistency checks will be conducted to make sure interpretations are correct.

3) Reproducibility

We have a requirement that technicians performing the test meet acceptable reproducibility standards for test performance before they are certified to perform the test. This would include BP measurement certification and ECG acquisition certification.

QUALITY CONTROL MEASURES

QC of Equipment

A) Sphygmomanometer:

Daily: Monitor daily for

- bouncing,
- erratic oscillations,
- beading outside column.

If identified, replace instrument. Check that mercury is at zero with no pressure.

Monthly: Check that the cap of the manometer column fits properly.

B) Blood pressure Cuffs

Daily: Check that appropriate cuffs are available. Check for leaks in the cuff and tubing.

C) Marquette Exercise Station

Daily: Maintenance of machine, ECG cables at the end of the tests.

Weekly: Clean the instrument with a moist cloth (avoid phenol/peroxide compounds); Clean cables with moist cloth.

Annual technical inspection by Marquette personnel.

QC of Walk Test Performance

A) Electrode placement:

Monthly verification of appropriate placement of electrodes by technicians

B) ECG tracings

Monthly assessment of quality of a random sample of 20 tracings

- Assessing noise
- ST segment drifts,
- Calibration
- Accuracy of computerized tracings to identify arrhythmias

Blood Pressure Measurements

- Quarterly assessment of digit preference
- Quarterly comparison of adjusted means for technicians (comparison with adjusted means for previous quarter for each technician; comparison with adjusted means for the other technician during the same quarter)

Walk Station Exclusions:

Monthly assessment of consistency of exclusion criteria and to examine possibilities of 'over' exclusion of participants from the test. Interobserver variability in exclusions will be examined (number of exclusions per month, criteria for exclusions).

We will also review charts where the tests were terminated prematurely to ensure consistency in reasons for termination of the test.

QC of Walk Test Interpretation

A) Technician reproducibility

Calibration set of 20 EKGs (10 with ST segment abnormalities and 10 without ST segment abnormalities randomly arranged):

Inter- and intra-technician variability assessed by repeating coding of these EKGs every *quarter*.

B) Physician reproducibility

The two physicians in the Walk Station will also code the ECGs in the calibration set to assess interobserver variability in interpretation of ST segment responses.

Data Cleaning Procedures

Monthly check for outlier values of blood pressure, heart rate, and codes.

We will run data cleaning programs on an ongoing basis to get prompt feedback to interpreters & data entry personnel about problems. The data cleaning program will be divided into 2 parts.

Initially the demographic data is cleaned. The demographic cleaning ensures that the appropriate subject was interpreted by checking that the ID matches the exam date, etc. Subsequently the measurement data is cleaned against the qualitative interpretations. This helps detect calibration, coding or keying errors. Essentially the measurements are checked that they are in range and that the qualitative and quantitative data are consistent.

Quality Control- Statistical Aspects: Intraobserver & interobserver variability tests

The following statistical tests will be used to assess coding and Blood pressure measurement reproducibility:

- a. Correlation coefficients, agreement between observers
- b. Systematic differences between readers and within readers will be assessed by bias & % bias
- c. Random bias will be assessed by precision & % precision
- d. Mean across subjects
- e. Estimated variance for a single reading chosen at random
- f. Estimated standard deviation for true subject-to-subject variation

