FRAMINGHAM HEART STUDY
OFFSPRING/EXAM 8
ECHOCARDIOGRAPHY MANUAL

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Introduction to Performing Echocardiography

Echocardiography is the investigation of choice for the noninvasive assessment of cardiac structure and function. It provides important knowledge of the prevalence, predictors, and prognosis of cardiac disease.

The echocardiography scanning time is approximately 25 minutes. Participant is already in the room, set up with electrodes, placed on his side on the bed, as part of one of five tests being performed in the noninvasive cardiovascular testing station.

Equipment

2 Scanning Rooms each one containing the following:

- Chattanooga Group, Inc. Triton Electric Hi-Lo Treatment Table, Model #200
- Height adjustable sonographer chair
- Philips Medical Systems Agilent Sonos 5500 Ultrasound System, Model # M2424A
- Sonos 5500 Monitor, Model # DR5815
- Transducer – S3 Model #21311A Serial # US 99N05122
- Panasonic SVHS VCR Model # AG-MD835
- Notebook computer for some specific 2-D and PW Doppler flow acquisition; Cardiovascular Engineering, Inc., Norwood, Massachusetts
- Acquisition software provided by Gary Mitchell, MD, Cardiovascular Engineering, Norwood, MA.
- Wall-mounted Monitor KEN 5022 303(Color Display Unit): Samsung Model# 214T S Type # BR21CS
- PAT Notebook computer, EndoPAT 2000 Serial # 200009 ENDO PAT
- Hokanson Blood Pressure Measuring Device Serial # & Model#
- Digital Thermometer Serial # 21497287 Fisher Scientific Thermo- hypo
- Electronic Timer Serial # NO 2 004 378

Echo Storage Server:

- Micron Netframe Server, Model #3550, Serial #ECHK 2200575
- Micron PC 15" Monitor, Model #500Ez, Serial #LTN 28011F00018377
- Micron Standard keyboard, Model #SK-1688, Serial #C0201132105
- 300GB Images Storage

Dicom Gateway Processing System

- Dell Precision 380 Workstation, Serial #870QS71
- Gateway 15" Monitor (FHS surplus)
- Microsoft Optical Scroll Mouse, Model: #M-UVDEL1, Serial #HCA50115948
- Dell USB Keyboard, Model #SK-6115, Serial #CN-0J4628-71616-54O-0MNM

First Digisonics Echo Reading Station

- PC: Dell Model Precision 380 Serial # 8DG1T71
- Monitor: Dell Model #993s MXOX375847605583B4WQ

- Keyboard: Dell Model SK-8115 Serial # CN-0J4628-71616-54P-0H8R
- Mouse: Microsoft Model #M-UVDEL1 Serial #HCA518415QB
- VCR: Make Mitsubishi Model# HS-MD300U Serial# 004049M
- MOD: Sony Model# RMO-5661 Serial# 704888

Second Digisonics Echo Reading Station:

- Micron PC Monitor, Model #910Ex, Serial #SSAM08020200001600
- Micron PC Client Pro Work Station, Model #D850GB-ODY, Serial #3076624-0001
- Micron Standard Keyboard, Model #SK-1688, Serial #C0109226475
- HP Laser Jet 2200d Printer, Model #C7058A, Serial #GRH07192 (shared by all workstations)
- Sony SVHS HiFi Videocassette Recorder, Model #SVO-9500MD, Serial #26312
- Microsoft Optical Scroll Mouse P/N X8022382-001 Serial # 0522
- Sony MODisk Unit, Model #RMO-S551 5.2GB, Serial #751388
- Sony VCR Remote Control Unit, Model #SVRM-100A, Serial #110532
- Sony 15" Monitor, Model #GVM-1311Q
- Digisonics DigiView System Software for Echo measurements, Digisoncis, Inc. Houston, Texas

Third Digisonics Echo Reading Station:

- Micron PC Monitor, Model 910Ex, Serial #SSAM08020200001333
- Micron PC Client Pro Work Station, Model #D845GRG-ODY, Serial #3202705-0001
- Micron Standard Keyboard, Model SK-1688, Serial #C0204060060
- Microsoft Optical Scroll Mouse: P/N X 802382-001 Serial # 0521
- Sony SVHS HiFi Videocassette Recorder, Model #SVO-9500MD, Serial #47912
- Sony VCR Remote Control Unit, Model #SVRM-100A, Serial #110855
- Digisonics DigiView System Software for Echo measurements, Digisoncis, Inc. Houston, Texas

Supplies

- Transducer gel
- ECG electrodes
- S-VHS Video Cassette Tapes
- CD disks, for storing 2-D images and PW Doppler signals
- Sony MOD Magnetic Optical Disks, 5.2 GB, Model #EDM-5200B, for storing 2-D loops and M-mode and Doppler frames of Echo images.

Examination & Data Cleaning Documentation Materials

- Participant and Sonographer Worksheets
- Participant ID tape labels
- Log book
- Log-In sheets

Miscellaneous

- Standard pillow - for participant
- Blanket – for participant
- Towels – for wiping gel off participant
- Latex Free Exam Gloves – for sonographer.

Performing the Echocardiography Test

A succinct **Echocardiography Scanning protocol** is provided in the appendix. Below we will give a brief description of performing the Echocardiography test in a standard fashion at the Framingham Heart Study Clinic.

Initial Test Set Up

In the waiting room the participant reads a set of instructions about the **Echocardiography Test** (see appendix) and signs an informed consent form before arriving at the noninvasive cardiovascular testing station. If not, have the participant read the instructions and sign the consent form before proceeding.

The sonographer fills out the **FHS Echocardiography Sonographer worksheet** (see appendix). The reverse side of this form is used after the test for qualitative and quantitative interpretation of the echocardiography test (see appendix).

Acquisition
Enter the participant initials and ID#, exam #, and sonographer ID # in Gary Mitchell's acquisition computer. Also enter the participant ID# and name and sonographer ID# on the Agilent Sonos 5500 Ultrasound System (in text below referred to as "Sonos 5500").

Labeling storage media & log in sheet
The sonographer should also enter exam date, room #, sonographer ID#, SVHS #, CD #, and miscellaneous information regarding data management, on the **FHS Offspring Exam 8Log Book Sheet For Tonometry, PAT, and Echo tests Log-In Sheet** in the Log Book (see appendix). Put participant ID# and name label on the SVHS cassette tape jacket as well as on 2 CD's.

Participant Set-up

- Place 4 electrodes on participant's chest.
  1. White - below right clavicle
  2. Green - right rib cage
  3. Black - below left clavicle
  4. Red - left rib cage
- Ask the participant to lay on his/her left side with left arm on the pillow.
- Start echo test following the scanning protocol (see appendix).

The Ultrasound Scan

The following standard Echocardiography directions should be followed for the standard Echocardiography test. Before proceeding with the scanning, briefly explain to the participant that he will not be able to watch his heart during the test. However, at the end of the test, he will get a printed picture of his heart and also be shown his heart in motion on the monitor.

Apical 5—Chamber [A5C] View

- Cover transducer's matching layer with ultrasound gel and place transducer in 5th intercostal space of participant's chest.
- Angle transducer anteriorly to visualize LVOT, Aortic root and aortic valve in widest excursion. LV endocardium should be clearly visible.
- Place CW Doppler in LVOT and obtain flow with highest velocity and valve clicks. If there is aortic stenosis, interrogate the LVOT and aortic valve accordingly to the description in the Digisonics Reading Protocol (see chapter in this Manual).
- Tape images and flow on Sonos 5500.
- Switch CW to PW. Place PW sample volume in LVOT approx. 0.5 cm from the aortic valve. Record the flow on Sonos 5500 and on G. Mitchell's computer. If the flow velocity is higher than 120 cm/sec switch to high PRF. Do not move baseline (it would make flow analysis difficult).
- Obtain carotid tonometry and save on G. Mitchell's computer.
- **Ask the participant if they are comfortable. If not readjust transducer.**

Parasternal Long Axis [PLA] View

- Move transducer from the apex to the third or fourth intercostal space left from the sternum so that the orientation point is directed toward right shoulder and ultrasound beam is parallel to the imaginary line connecting right shoulder with the left flank.
- Start taping on Sonos 5500 at depth 20 cm optimal long axis of LV, so the anterior septum is not at an angle and all cardiac structures in this view are clearly visible.
- Decrease depth, get the biggest possible image without loosing LV posterior wall and acquire one loop on Sonos 5500. Clear definition of RV, Aortic Root, AV, LA, MV and LV.
- Zoom on LVOT, show clear insertion of AV cusps. Save 5 beats on G. Mitchell's computer and record on Sonos 5500.
- Zoom on Mitral Valve and acquire one loop on Sonos 5500
- Narrow the sector, press color Doppler and tape flow trough MV and AV paying attention to regurgitation.

RV Inflow

- Move transducer left from the sternum as far as possible and tilt inferomedially so a long axis of the RV and RA is obtained. Show anterior and posterior leaflets of TV.
- Tape color flow across TV, paying attention to any regurgitant jet.

Parasternal Short Axis [PSA] View

- Rotate transducer about 90 degrees from PLAX so ultrasound beam is perpendicular to long axis of LV and obtain short axis.

FHS Offspring Exam 8 Echocardiography Scanning Protocol Overview

- Start from the base of the heart showing: Aortic root, 3 aortic valve cusps- right, left and none, LA with clear posterior wall definition (be aware of sidelobing simulating false posterior wall – see figures 1a and 1b).
- Zoom on the Aortic Valve and acquire one loop on Sonos 5500
- Acquire 2 M-Mode frames of Aortic Root, AV and LA. Emphasize box-like opening of aortic valve cusps.
- Tape color Doppler on Sonos 5500 to see AI or TR, if time.
- Tape the sweep from the base of the heart to the apex showing LV wall motion and thickening. On your sweep back from the apex to the base, stop at MV and acquire one M-mode frame of MV.
- Tilt the transducer inferiorly and obtain cross section of the LV at the papillary muscle level. Zoom on the LV and acquire one loop with clear boundaries of endocardium and epicardium.
- Place M-mode cursor across LV and acquire 3 frames with 3 beats each, still in the Zoom mode. (See figures 2a, 2b and 2c.)
- If LV image on PSA is sub-optimal acquire 2-D and M-Mode of LV from subcostal view.

Apical 4-Chamber [A4C] View

- Move the transducer to the apical position and obtain 4-chamber view.
- Start taping at depth 20 cm. Decrease depth to get biggest image possible and acquire one loop on Sonos 5500.
- Tape color Doppler flow across MV, AV, TV. Confirm regurgitation existing in other views.
- Press presets on Sonos 5500 for PV flow. Place PW sample volume in the right pulmonary vein and obtain flow. Digitally save one frame of the flow.
- Switch back to FHS Echo presets. Place PW at MV leaflet tips and obtain highest E and A wave velocities of MV inflow. Save about 20 sec of the flow on G. Mitchell's computer and acquire one frame on Sonos 5500.
- Decrease depth, narrow the sector and obtain long axis of the LV from the apex to the mitral valve annulus. Acquire one loop on Sonos 5500.
- Increase the depth and put M-mode cursor at MV annulus. Acquire one frame on Sonos 5500.
- Press presets on Sonos 5500 for DTI. Place PW sample volume at MV annulus and acquire recordings on G. Mitchell's computer. Acquire one frame on Sonos 5500.

Apical 2-Chamber [A2C] View

- Rotate transducer from apical 4-chamber to apical 2-chamber view (about 90 degrees counterclockwise or until right sided cardiac structures disappear).
- Tape 5 beats showing wall motion and endocardium thickening of LV.
- Tape color Doppler across MV, confirming any regurgitation seen in previous flows.
- Decrease the depth showing anterior and posterior walls of LV from the apex to the MV annulus. Acquire one loop on Sonos 5500.

Apical 3-Chamber [A3C] View (Also called **ALA=Apical Long View)**

- Rotate transducer even more counterclockwise until you see AV and ascending aorta, LA, MV and LV. Acquire one loop on Sonos 5500.
- Increase depth to show LA. Tape color Doppler flow across AV and MV.

- Wipe gel off the participant's chest. Ask him/her to lie supine for the last images from the subcostal region.

Subcostal View

- Begin subcostal examination by placing the transducer in the midline or slightly to the participant's right side. Direct ultrasound beam superiorly and leftward toward left clavicle. Tape subcostal 4-chamber view on Sonos 5500, with special emphasis on RV free wall.
- Tape color Doppler.
- Rotate transducer to subcostal short axis. Tape a few beats showing IVC and short axis of LV from the base to the apex.

Finish the echo test, wiping the gel off the participant. Thank the participant for participation, patience and cooperation. Proceed to the last test, the Peripheral Arterial Tone (PAT) Test.

Settings for Echo PW and Tissue Doppler

The following settings for Echo PW and tissue Doppler should be used during the standard Echocardiography test:

Pulmonary vein PW

Filter:	300 Hz
Gain:	65%
Focus:	Down
Sweep:	50

Mitral Valve PW

Filter:	300 HZ up to 400 HZ
Gain:	60%
Scale:	80 cm/sec
Sweep:	50

LVOT PW

Filter	300 HZ – 400 HZ
Gain:	65% Avoid high PRF
Scale:	120 cm/sec (marked 120 cm/sec but actually shows up to 180 cm/sec)
Sweep:	50

Tissue Doppler

Filter	50 HZ
Gain:	55%
Scale	20 cm/sec
Sweep:	50

Policy regarding how "hard to press" to obtain measurable ultrasound images

Our policy on 'pressing hard' with the ultrasound transducer on the participant's chest, particularly the obese, states that we will tolerate worse images and will not press to the point of discomfort, if a participant complains during the test.

Policy regarding the length of time of the scan

Since we are limited by a time constraint in the Clinic, we have also made it a policy not to spend more than 25-30 minutes of scanning time on each participant, even if it is difficult to perform the echocardiography test on the participant, due to obesity, heavy smoking history, COPD, prior chest surgery, etc.

In the event that a participant has an abnormal echocardiogram [e.g. aortic or mitral stenosis], that requires more scanning time, the sonographer should inquire with the clinic staff if they may take an extra 5 and maximum of 10 additional minutes. If the clinic staff is concerned about work flow, and requests that the test not be extended, the sonographer may add additional images at the end of clinic, if the participant is willing to wait.

Echo Reading & Interpretation Protocol

- The ECG shouldn't overlie M-mode septal images.
- Make sure that the posterior wall of structures is contained on the frame so that back wall can be measured.
- The septum in the PLA view should be parallel with the top of the screen [a number of the septums are angled, which when rotated into the PSSA will make for an oblong/eggy LV short axis.
- Please make the LV short axis as round as possible.
- Please be mindful not to snub the apex in the apical 4 chamber focused view. This would spoil the LV length and LV fractional shortening measurements.

Reading Protocol Steps

- Click on ERS32 icon, DigiView Cardiovascular Image Management and Reporting
- Click on open study icon in left upper corner of the screen
- Recall study; Sort by name, ID, or study date
- Select original study
- Open study
- Create new study from existing study by clicking on file and select "New Read from current study" Ensure "New Study From Existing Patient" is selected.
- Check ID
- Change interpretation date
- Enter Interpreter ID#
- Enter Sonographer ID#
- Click on patient information and verify date of study
- Hit OK
- Read icon [yellow circle]
- Click on images, fhs-digiserv Y-drive or optical disk e-drive
- Click on images folder
- Select the first folder which should be named for the date that study was initially acquired (= virgin study), if more than one folder [should be study date & interp date folders].
- Highlight all .dcm files, then press open, which will read the clips into local hard drive (hold shift key, highlight first and last .dcm).

Measurement tips for analogue tape

- Perform **qualitative reading** off the analogue tape.
- Note abnormalities in left margin as one reads.
- Make quick rough hand-held caliper measurements of LA, AV, LV wall thickness & internal dimensions.
- These measurements are for guidance only.
- LVWT you can measure in PLAX or PSAX. LVID in PSAX only.
- **Verify that M-Modes are appropriate by carefully observing the 2-D images:**
  - LV is not too eggy and/or not too apical.
  - LA is contained inside the frame.
  - MV is not too eggy, etc.
  - As soon as digital images have been loaded, look at the digital images before looking at the study on the tape, in order to notice some details on the tape, e.g. Pericardial Effusion or where to measure posterior wall of LA on M-mode

- After the entire analogue tape has been reviewed, code qualitative abnormalities;
  - Put the symbol of a square, □, on left margin for sections to be coded after measurements are made
  - **Don't forget to check LV wall motion in each view**
  - Don't forget to code right heart abnormalities
  - Code technical quality of 2D study, CW AV, Color Doppler
- Don't make on-line 2D measurements except for:
  - RVH, RVE, MV thickness, if necessary or
  - if M-Mode of a structure is unmeasurable and you need guidance for coding sheet

Digisonics "Tricks" to think about before measuring

1. **How many beats?**
   - Measure at least 3 beats if they are technically adequate, and the inter-beat differences are due to biologic (e.g. respiratory) variation.
   - If third beat is technically inferior and the given frame is the best available one (see below), measure only two beats. It is better to have two good accurate measurements than to have the results skewed by a third unreliable estimate.
   - All 3 beats should be from the same frame
   - If rhythm is atrial fibrillation/flutter, measure at least 4 complexes; you may need to measure more than one frame; try to measure adjacent complexes
2. **Extra-systoles?**
   - Look at the cardiac rhythm on screen. Avoid measuring premature beats or beat immediately following a premature beat.
3. **Which frame?**
   - Choose the frame that best defines the leading edges of the structure being measured
   - Scan the M-mode frames prior to reading 2-D study, focusing specifically on clarity of leading edges. Make a note on the possible frames you would select for measurement. Make a mental note of presence of multiple linear structures that could represent the leading edge.
   - Clarity of leading edges for LV diastolic measurements is a more important consideration compared to clarity of the systolic phase of the cardiac cycle.
   - Try to measure aortic root and aortic cusp separation on the same frame
   - If two frames are identical in terms of quality, select the first frame as a convention
4. **Measuring, general**
   - Which order are cardiac structures measured in? Begin with Ao Root, Ao cusp separation, LA in systole, LA in diastole, E-point to septal separation (EPSS), and lastly LV dimensions.
   - Which order of beats: Of three beats on the chosen frame, measure the best looking one first. If all three beats look alike, start measurements of beats from left to right
   - "leading edge to leading edge" for LA/Ao Root & LV
   - inner to inner for E-point septal separation (EPSS) and aortic cusp separation.
   - Make sure that each **M-mode measurement reflects reality**. Is it close to your 2-D impression of the cardiac structure (based on either eye balling or on online measurement of the screen with an external caliper?
   - Think about reproducibility...If you are guessing don't measure.
   - Remember to calibrate before measuring structures on frames captured from the tape every time the depth is changed, e.g. MV leaflet displacement; Highlight "measure," highlight "2-D," highlight "scale." Then touch two points on screen 6cm apart. After first measurements click RMB. Repeat for next two measurements.
   - Score from overall wall motion. If overall wall motion is abnormal and you paint the

walls yellow for hypo or brown for akinetic, you need to paint the rest of the walls to get the correct score.

5. **Cursor placement?**
   - What if the leading edge is thickened? (e.g.. calcified aortic root), the measurement cursor is "buried" into the leading edge
   - While reading the 2-D study, keep in mind the importance of assessing which of the possible linear structures most likely represents the leading edge of the structure that will be measured on M-Mode. This judgment is based on excluding the possibility of ventricular trabeculae, chordae tendinae, "side-lobe artifacts," posterior effusions, and other miscellaneous structures that could obscure/mimic the leading edge.
   - Look carefully at the M-mode for incomplete or partial **dropout** in lines that may well represent the true leading edge.
   - It is permissible to **extrapolate** and drop the measurement cursor to an imaginary leading edge which corresponds in position to an adjacent beat if no leading edge is discernible in a particular beat @ the appropriate time of placement and the beat is otherwise technically adequate for measurement (e.g. isolated dropout in the leading edge of LVPW in one beat alone)
   - Remember to **bracket** your cursor placement - place the cursor above, below then exactly where you want to place it.
6. **Measuring the LV**
   - Check for the presence of an "egg" appearance in the 2-D short axis-view of the ventricle (from which the M-mode is derived). If the ratio of length/ breadth of the ventricle is >1.3, do not make LVID measurements. You can still code the left ID & WT as normal or abnormal depending on the 2-D impression.
   - Start measuring from the second beat (Onset of QRS is more readily visible at this point)
   - Write down diastolic and systolic frame numbers to identify the frames to be used when tracing epicardium and endocardium on PSA protocol
   - Check that the cursor placement is at the tips of the papillary muscles, i.e. that the cursor is not too apical & that the RV is still present as more than a sliver.
   - Check that you are not measuring RV moderator band, papillary muscle or pericardial effusion.
   - If you skip measurements make sure the Digisonics hasn't borrowed numbers from elsewhere.
7. **Measuring the LA, EPSS, aorta**
   - Beware of side lobes creating false posterior **LA** walls
   - If **Ao** heavily calcified bury leading LA edge
   - **EPSS** Place cursor on the same side of the E-point of the mitral tracing as the peak downward excursion of the septum; an "inner edge to inner edge" technique is used. We extrapolate to point of maximum downward excursion of the septum. Do not measure M-mode of EPSS if participant has moderate AI that might restrict opening of anterior MV leaflet.
   - Measure the **aortic root cusp** separation in early systole using an "inner edge to inner edge" technique (i.e. trailing edge to leading edge)
8. **Qualitative Coding**
   - Try to confirm presence of mild or borderline findings in more than one view
   - e.g. MAC, aortic calcification or trivial regurgitation in more than one view
   - If you aren't sure about MAC, aortic calcification, MV thickening, etc. code it as probably normal
   - If you really don't know if something is normal or not, code it as unknown

- Look @ specific definitions on posted coding sheet.

9. **Coding Quality**
   - For CW AV, code it as fair if only imaging CW used, &/or only from one view; code good quality if non-imaging CW probe and > 1 view are recorded of adequate quality
   - **Good** means highly accurate (reflects reality) & excellent reproducibility
   - **Fair** means basic questions are answered correctly, reproducibility reasonable
   - **Poor** means reproducibility poor, some ability to comment on questions
   - **Inadequate** means accuracy and reproducibility unacceptable

- **Click on "Measure" to start measuring Digisonics Dicom images and follow protocol using the Dicom Images Table.**

Dicom Images Table

Measure	Units of Measure	Mandatory	Elective	Comment
Score – Wall Motion		Every subject		If all normal click Overall Wall Motion • Overall wall motion is normal • If global pattern click overall wall motion & appropriate category. • If Regional wall motion abnormality • Click on appropriate statement and then click on appropriate segment **Don't forget to click on Score from Overall Wall Motion!!! Ventricle should be colored.**
MM: Ao/LA Protocol • Aortic Root diameter • Aortic cusp separation • LA_{es} • LA_{ed}	**(cm)**	3	Total 6 + average	• All measurements are leading edge to leading edge except **aortic cusp separation**, which is inner edge to inner edge. • LAd anterior point should be in same place as AoR posterior point
MM: MVEPSS mitral valve • **NOT** Mitral Valve Protocol • Click: Mitral Valve EPSS	(cm)	3	Total 3 + average	• EPSS – inner edge to inner edge – extrapolate to most posterior point of septum and most anterior point of MV • 2 points do NOT have to be perpendicular • Do not measure EPSS when measurement appears to be incorrect due to "eggy" LV etc Do not measure M-mode of EPSS if participant has moderate AI that might restrict opening of anterior MV leaflet.
MM: Mitral Valve Annular Descent • Click on M-Mode, then Mitral Valve, then MV Annular Descent		3		• Measure 3 times • Systole is the smallest internal diameter
MM: LV/RV Protocol • IVS_{ed} • $LVID_{ed}$ • $LVPW_{ed}$ • IVS_{es} • $LVID_{es}$ • $LVPW_{es}$	**(cm)**	3 • If <3 measure anyhow	Total 6 + average	• Take time to select best frame • Note frame on sheet • Don't forget to touch R wave between cycles • Fractional Shortening should be greater than 28%.
2D PSA Ice Pick Protocol • IVS_{ed} • $LVID_{ed}$ • $LVPW_{ed}$ • $LVID_{es}$ • Computer calculates mean LVWT & LVFS	**(cm)**	2	2	• Called **PLA** on Report. • Measure twice in the **PSSA** • Start measuring diastole from the second beat and record frame number • Systole is the smallest internal diameter • DON'T FORGET! DO **NOT** measure RV septal wall and posterior LV epicardium • Skip LA in diastole and click on Next. • Skip LA in systole and click on Next.

Measure	Units of Measure	Mandatory	Elective	Comment
2D SAX Protocol • Trace epicardium$_{ed}$ • Trace endocardium$_{ed}$ • Trace epicardium$_{es}$ • Trace endocardium$_{es}$ • Leave arrow on 2-D image & right-click for diastole • Computer calculates…..	**(cm/cm^2)**	2	2	• Measure twice in PSSA, PSSA is called parasternal short axis in the report. • Diastole @ onset QRS on second beat • Systole is the smallest internal diameter • Measure clockwise • Start where endocardium/epicardium is clearest.
2D LV Longitudinal FS** • Click on 2-D, then LV Protocol, then LV diastolic dimensions • LV length$_{ed,}$ measure twice	**(cm)**	2	2	**Measure in A4C in narrower cut [cone down view] unless open image superior** • Watch in "real time" for apical endocardium • Diastole @ onset QRS • Proximal point at MV annulus level, distal point at apical endocardium; right mouse button, repeat X 2 • Before measuring "LV End Diastolic Dimension" check which view is preferable Apical-4 or decreased depth of LV in Apical-4.
2 Chamber View • Click on 2-D Then left ventricle Then CH Protocol • Trace endocardium$_{ed}$ • Touch the top of the pap. muscle on lateral wall. • Trace endocardium$_{es}$ • Touch lateral and medial border of Mv annulus. • Measure 2 beats			Total 4 + average	• Measure in magnified view of LV in Apical 4, or in full Apical 4 view. • Choose view that has best echocardial definition.

Optional Dicom Image Measurements			
Doppler AS Aortic Valve area by continuity (cm^2)	Optional suspect AS	3	• **AV area by continuity equation** • Calculation method [TVI vs.diam]: **Both** • Select area method: **diameters** • Enter orifice area: **Measure** off PLA digital image, about 5 frames into systole; place 2 points for $LVOT_{ed}$, then measure another $LVOT_{ed}$ hit average • RMB to continue • Trace LVOT TVI – make sure to calibrate • **Scale** – for Doppler. Touch 2 points 100 cm/sec apart & touch 1 sec. **Note that scale is often different than on old HP.** • Trace LVOT TVI, **then RMB** • Trace another, then RMB • Trace another, then RMB • Hit **Average** • Enter Doppler angle – 0 • Trace AV TVI, then click RMB • **Scale = Doppler scale** Touch 2 points 100 cm/sec apart & touch 1 sec. • **Trace AV TVI, RMB** • **Another AV TVI, RMB** • **Another AV TVI, RMB** • **Average, then RMB** • **Review report**
Doppler MS (m/sec)	Optional suspect MS	3	• Only if MS is suspected or Doppler project* • Need to figure out about ½ placement • Need to make 2 D MV area
2D MV Area (Cm^2)	Optional suspect MS	3	• Measure 4 off the video tape • Be sure to CALIBRATE
2D MV Leaflet Thickness (cm)	Optional suspect MVP	3	Measure under major dimension
2D MV Superior Displacement		3	• Measure under minor dimension • Measure in PLA dicom image (no calibration needed) • Measure at maximum MV Leaflets displacement into LA • Draw an imaginary line connecting hinge points of MV leaflets insertion. • Put first dot on imaginary line and second dot on the leading edge of MV leaflet at the point of maximum MV leaflet displacement.

* LV Dimensions - Normal Range: $LVID_{ed}$: 3.5-5.8cm; $LVID_{es}$: 2.2-4.0cm; Frac. Short.: 25%-43%

** Apical 4-Chamber View - Normal Range: Major $LVID_{ed}$: 6.9-10.3cm;

While measuring, **click on report after each measurement package is completed** and review measurements as follows:

➔ Consistency, are they within 10% of each other

- ➔ Number of measurements correct? If 2D LVM is > or < 40gm different than the M-Mode please reevaluate your measurements.
- ➔ Range, are they within reasonable range? If 2D LVFS is > or < 10% different than the M-Mode please reevaluate your measurements.
- ➔ Logic, do they make sense with your 2D impression? If LVFS is <28% is the LVEF coded abnormal/deceased?

To delete measurements

- Go to Data Entry menu, click on Edit Measurement Grid. By and large it is easier and safer to delete the entire measurement.
- If you want to delete just one out of three measurements, it can be done. After deleting the measurement in the Edit Measurement Grid, you want to make a new measurement. Go back to the Protocol you were in. Then click on one of the measurements that you have already made in the Protocol Measurement Tree. This will allow you to start measuring again.

Quick Measurements are not saved – to make quick measurements

- On digital images, right click on image; select 2D; make measurements.
- On the SVHS tape images right click on the screen, select scale, then select 2-D vs. MM vs. Doppler to calibrate, and then measure the image. You have to recalibrate each time.
- You can convert analogue SVHS images into a DICOM image. Details to follow.

Miscellaneous tips

- "Start over" command is equivalent to getting rid of all prior measurements;

Change measurement name

- Click on Configure: click on 'trees'; right click on item; rename item.

How to change personal information, i.e. name and ID on a study

- Open up an image from "Images Folder" from the erroneous study to check that time on image coincides with the right time that the study was done in Clinic.
- Open ERS32 program.
- Look for erroneous study (i.e. no ID#, no name) by time and date.
- Go to "Data Entry" menu and select "Study Information".
- Enter Pt. ID# and name in appropriate field.
- Click OK.
- Close ERS32 program.
- In "Images Folder", erroneous study folder will be renamed with new ID# and new name.

Backing up daily virgin studies to MOD (Magnetic Optical Disk)

- Back up Echo studies daily from Digisonics on 2 virgin copies.
- Label MOD virgin copies as follows:
  - Save on the appropriate disk, according to the month and year of acquisition, e.g. 7-2006
  - Put MOD in Sony E:drive – Side 1 up (A), arrow pointing in.
  - Open a new MOD, label it correctly: Echo, Offspring Exam 8, and then sequential numbers (see above).
  - Begin by formatting MOD:
  - Double click on My Computer Icon on blue screen.
  - Message dialogue box will say: "This disk is not formatted. Do you want to format it?
  - Press Yes.
  - On screen, leave as is:

- Capacity: 2.40 GB
- File system: FAT
- Allocation Unit Size: Default allocation size
- Volume label: Leave blank
- Format options: Check Quick Format
- Click OK
- Message dialogue box will issue warning and ask you to format the disk.
- Click OK.
- Now you can start backing up daily Echo studies:
- Look at list of studies in Images Folder on Y:drive.
- Click on "Created" to get dates in order.
- Highlight each study performed that day by looking at Echo log book sheets from both rooms 106 & 108.
- Double click to open each study.
- Check that images have been successfully transferred by opening each folder from that day.
- Double click on random image, i.e. a Jpg file or a Video clip.
- When done checking each study, highlight all studies from that day by left-clicking on the studies. Each study will be about 30 MB.
- Left-click on box with highlighted studies and drag them to the E:drive (which should be open and on the screen).
- Copying will start. Copying takes about 8 minutes for 7-8 studies.
- When done, immediately copy on virgin Copy 2 as well. (This is the copy which will be stored off-site.)
- Check off in special MOD Back-up Echo studies in white binder by entering MOD number. Person who is storing MODs should also initial it.
- Check on E:drive that studies were copied.

Appendix Item 1

FHS Vascular Function Tests – Handout for Participant

The Framingham Study's Noninvasive Cardiovascular Testing Station

In the cardiovascular testing station you will receive four tests that noninvasively examine your heart and blood vessels' structure and function. None of the tests involve radiation. You will receive the following tests:

1. Blood pressure

- The sonographers will carefully measure your blood pressure while listening with headphones.

2. Arterial tonometry

- The sonographer will hold a flat pressure-sensing device (the tonometer) against the superficial pulses in your arm, leg and neck for approximately a minute at each of these four sites. This approach allows us to assess blood vessel stiffness. At the very end of all 4 tests, the sonographers will measure the distances between the 4 sites where the recordings were taken. **Details of the test are provided on the reverse side.**

3. Echocardiogram

- The sonographer will hold an ultrasound transducer at several points over your left chest. The echocardiogram uses sound waves to take a picture of your heart. The test measures the heart's size and function.

4. Peripheral Arterial Tone Test/ Fingertip Pulse Test

- The fingertip pulse test measures the health of the blood vessels at the ends of your fingers by measuring changes in volume pressure when exposed to increased blood flow. The examiner will place a blood pressure cuff on your lower arm and two arterial sensing devices on the index finger of both hands to measure the blood vessel waveforms at baseline, and during and after blood pressure cuff inflation. The finger devices will measure the pulse in your fingers at rest for two minutes, while a blood pressure cuff is inflated on your lower arm for 5 minutes, and after the cuff is released for an additional 3 minutes. The PAT measures the health of the blood vessels by testing the increase in pulse volume when exposed to increased blood flow. The test may cause temporary numbness and tingling. Rarely subjects develop painless red spots, which disappear in a few days. .
- **Details of the test are provided on the reverse side.**

5. Carotid Artery Ultrasound Test

- We will be evaluating the arteries in your neck with an ultrasound device. This device takes images of your neck arteries, showing their structure and how blood is flowing to your brain. The test is completely safe and does not involve any radiation.

- **If you have a <u>very abnormal</u> echocardiogram test the results will be sent to your physician.** Since the test is performed in a research context, and read without any knowledge of your symptoms or history, the results would need to be interpreted by your doctor in the context of your clinical history.

- The Arterial Tonometry Test and the Peripheral Arterial Tone Test are solely used for research purposes. They are not used in clinical practice or to guide medical decisions. For this reason we will not be sending the results to your physician.

If at any point during the testing you are uncomfortable and would like to terminate the tests, please tell the technicians.

Thank you for your support of the research at The Framingham Study.

<u>The Arterial Pressure Waveform Test (tonometry)</u>

The Framingham Study's Noninvasive Cardiovascular Testing Station

How is the test performed?

- Measurements are made by gently pressing the tip of flat pressure sensing device (the tonometer) against the superficial pulses in the arm, leg and neck for approximately a minute at each of four sites. This device records the pressure waveform that is associated with each pulse or heartbeat.
- Next, the distance from the base of the neck to each of the pulse sites is measured.
- You will be asked to lie quietly during this phase of the testing. There should be no discomfort. This test has been performed safely in thousands of patients.
- At a later date, using a computerized analysis, we will examine the shape of the pressure waveforms and calculate the speed at which pressure waves travel through the large arteries.

Why are we doing this test?

- The arterial pressure waveform test is a noninvasive method to evaluate the stiffness of the large arteries.
- This test will allow us to evaluate the relationship between cardiac risk factors, arterial stiffening and the development of cardiovascular disease.

The Peripheral Arterial Tone Test/ Fingertip Pulse Test

For this test you will be asked to do the following:

- Have finger probes placed on a fingertip of each hand.
- Have a blood pressure cuff inflated on your lower right arm for 5 minutes.
  When the cuff is inflated your arm may feel like it is going to sleep or numb.
- After the cuff is released we continue to monitor your pulse volume for 3 more minutes.
  When the cuff is released your arm may feel pins & needles, warm or cold.
- At a later date we will make computer measurements of the amount that the pulse volume increases after the cuff is released. The changes are very small, so we cannot tell you the results while we are doing the study.
- ***To get the best information it is very important that you not move when we are monitoring the pulse volume in your fingertips.***
- This noninvasive test has been performed in thousands of research participants safely.
- After the test, approximately 0.5% of participants develop painless red spots on the arm, which resolve on their own within a few days. This is harmless, but if it occurs please call the sonographer (508-935-3445 or 508-935-3406) so we can track the frequency & the time to resolution.

Why are we doing this test?

- This test is designed to look at the function of the blood vessel lining.
- We are doing the test to understand if the results relate to risk factors for heart disease and to understand if the results will help predict the development of heart disease and stroke and to understand the predictors of healthy aging.

If you have further questions about the noninvasive tests please contact Dr. Emelia Benjamin by leaving a message at 508-935-3406 or 617-638-8968 or Dr. Ramachandran S. Vasan at 508-935-3450.

Appendix Item 2

FHS Echocardiography Ultrasonographer Worksheet

OMB NO=0925-0216 12/31/2007

1st Keyer: Block:1, Worksheet Repeat#:1, Page:1
2nd Keyer: Click on "Interpretations.1"

FHS ECHOCARDIOGRAPHY ULTRASONOGRAPHER WORKSHEET

Study Date___/___/___ **Study type** 0 1 2 (0=exam, 1=repeat study, 2=other) **EXAM** __ __

Data entry date___/___/___ ; ___/___/___ **Data entry ID** _____1st _____2nd

ECHO done? ☐ Yes=1 ☐ No=0 **Room #** 106 108

Tech ID __ __ **Height (inches)** ___ ___ **Sex** M F

SVHS #_____ if no SVHS#, code 0 **SVHS location**_____

Images available for measuring: ☐ **Video images ONLY** ☐ **Digital images ONLY**
(If neither box is checked, then both video and digital images were available for measuring)

STUDY QUALITY

Quantitative	Good	Fair	Poor	Inadequate
M-mode Ao/LA	☐ =1	☐ =2	☐ =3	☐ =4
M-mode LV	☐ =1	☐ =2	☐ =3	☐ =4
2-D LV	☐ =1	☐ =2	☐ =3	☐ =4
PW mitral inflow	☐ =1	☐ =2	☐ =3	☐ =4
Qualitative				
2-D study	☐ =1	☐ =2	☐ =3	☐ =4
CW AV	☐ =1	☐ =2	☐ =3	☐ =4
Color Doppler	☐ =1	☐ =2	☐ =3	☐ =4
Overall study quality	☐ =1	☐ =2	☐ =3	☐ =4

Comments:_____

☐ Priority MD overread:
- ☐ Severe AS
- ☐ Severe MS
- ☐ Mod-severe _____regurgitation
- ☐ Thrombus
- ☐ Vegetation
- ☐ Mass
- ☐ Large pericardial effusion
- ☐ Significant LV dysfunction≤30 % LVEF
  will call MD if Pt. not known to have cardiomyopathy or prior MI
- ☐ Other_____
- ☐ Ventricular wall thickness≥15 mm

Called Dr._____ Date/time:_____

☐ MD overread, other:
- ☐ > Mild LAE
- ☐ > Mild AoR dil.
- ☐ RA/RV abnormality
- ☐ Any LVH
- ☐ Any LVE
- ☐ LV WMA
- ☐ LVEF
- ☐ MS
- ☐ > Mild MAC
- ☐ Any MVP
- ☐ AS
- ☐ Bicuspid AV
- ☐ Valve prosthesis
- ☐ > Mild _____regurgitation
- ☐ Other_____

☐ Requested by:

☐_____ ☐ For Dr._____ Date: _____

Reader____ **OverReader**____ **Reading 1 2** **Date interpreted**___/___/___ (mo/day/yr)

OMB NO=0925-0216 12/31/2007

LA enlargement	☐ **0=no**	☐ **1=borderln.**	☐ **2=mild**	☐ **3=moderate**	☐ **4=severe**	☐ **9=unknown**
Other LA comment						
Mitral Valve	☐ **0=normal**	☐ **1=prob nl**	☐ **2=abnormal**		☐ **4=prosth.**	☐ **9=unknown**
MV thickening	☐ 0=no	☐ 1=minimal	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
MS	☐ 0=normal	☐ 1=possible	☐ 2=likely			☐ 9=unknown
MAC	☐ 0=no	☐ 1=minimal	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
MVP	☐ 0=no	☐ 1=min.sup.disp	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
Other MV comment						
Aortic Valve	☐ **0=normal**	☐ **1=prob nl**	☐ **2=abnormal**		☐ **4=prosth.**	☐ **9=unknown**
AV thickening	☐ 0=no	☐ 1=minimal	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
AV cusp excursion	☐ 0=normal	☐ 1=minimal	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
Bicuspid AoV	☐ 0=no	☐ 1=yes	☐ 2=maybe			☐ 9=unknown
Aortic Root	☐ **0=normal**	☐ **1=prob nl**	☐ **2=abnormal**			☐ **9=unknown**
Aortic root dilation	☐ 0=no		☐ 2=present			☐ 9=unknown
Aortic root calcium	☐ 0=no	☐ 1=minimal	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
Other AV/AR comment						
LV Structure	☐ **0=normal**	☐ **1=prob nl**	☐ **2=abnormal**			☐ **9=unknown**
LV enlargement	☐ 0=no	☐ 1=borderline	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
LVWT, concentric	☐ 0=no	☐ 1=borderline	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
LVWT, other	☐ 0=no	☐ 1=DUSK	☐ 2=ASH	☐ 3=ISH	☐ 4=oth_____	☐ 9=unknown
LV Regional WMA	☐ **0=normal**	☐ **1=prob nl**	☐ **2=abnormal**			☐ **9=unknown**
Septum	☐ 0=normal	☐ 1=paradoxic	☐ 2=hypokinetic	☐ 3=akinetic	☐ 4=dyskinetic	☐ 9=unknown
Anterior	☐ 0=normal		☐ 2=hypokinetic	☐ 3=akinetic	☐ 4=dyskinetic	☐ 9=unknown
Anterior/Anterolateral	☐ 0=normal		☐ 2=hypokinetic	☐ 3=akinetic	☐ 4=dyskinetic	☐ 9=unknown
Posterior	☐ 0=normal		☐ 2=hypokinetic	☐ 3=akinetic	☐ 4=dyskinetic	☐ 9=unknown
Inferior	☐ 0=normal		☐ 2=hypokinetic	☐ 3=akinetic	☐ 4=dyskinetic	☐ 9=unknown
Apex	☐ 0=normal		☐ 2=hypokinetic	☐ 3=akinetic	☐ 4=dyskinetic	☐ 9=unknown
LV Systolic Function	☐ **0=normal**	☐ **1=prob nl**	☐ **2=regional**		☐ **4=global**	☐ **9=unknown**
LV ejection fraction	☐ 0=normal	☐1=borderline	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
						LVEF ___%
Other LV comment						
Right Heart/Pericardium	☐ **0=normal**	☐ **1= prob nl**	☐ **2=abnormal**			☐ **9=unknown**
RA enlargement	☐ 0=no	☐ 1=borderline	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
RV enlargement	☐ 0=no	☐ 1=borderline	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
RV hypertrophy	☐ 0=no	☐ 1=borderline	☐ 2=mild	☐ 3=moderate	☐ 4=severe	☐ 9=unknown
Pericardial fluid	☐ 0=no/syst.		☐ 2=small	☐ 3=medium	☐ 4=large	☐ 9=unknown
Other right ☐/pericardium						
Valve Regurgitation	☐ **0=none**		☐ **2=present**			☐ **9=unknown**
Mitral	☐ 0=none	☐ 1=trace	☐ 2=mild	☐ 3=moderate	☐ 4=m-s ☐5=sev	☐ 9=unknown
Aortic	☐ 0=none	☐ 1=trace	☐ 2=mild	☐ 3=moderate	☐ 4=m-s ☐5=sev	☐ 9=unknown
Tricuspid	☐ 0=none	☐ 1=trace	☐ 2=mild	☐ 3=moderate	☐ 4=m-s ☐5=sev	☐ 9=unknown
Mitral Stenosis	☐ **0=none**	☐ **1=trivial**	☐ **2=mild**	☐ **3=moderate**	☐ **4=severe**	☐ **9=unknown**
Aortic Stenosis	☐ **0=none**	☐ **1=trivial**	☐ **2=mild**	☐ **3=moderate**	☐ **4=severe**	☐ **9=unknown**
Other Doppler comment						

Comments:_____

Clinical correlation is suggested	☐ **0=not applicable**	☐ **1=yes**
Technically limited study	☐ **0=no**	☐ **1=yes**

Appendix Item 3

Offspring Exam 8 Log Book Sheet for Tonometry, Echo & PAT Tests

OFFSPRING EXAM 8 LOG BOOK SHEET FOR TONOMETRY, PAT AND ECHO TESTS

OMB NO=0925-0216 12/31/2007

Date of Clinic Visit ____ - ____ - _____ (Mo Day Yr) **Room #** **106** **108**

TONOMETRY

Test done?	**yes** (test was done, even if all 4 pulses could not be acquired and recorded)	**no** (test was not attempted or done)	**If no , why: Circle all that apply**
30 49 88 740 750 54 _____	**Sonographer ID#**		1. Subject refusal 2. Subject discomfort 3. Time constraint 4. Equipment problem, specify _____ 7. Other, specify _____
|__|__|__|-|__|__|__|	**Video CD#**		
___/___/____	**TONOMETRY test date** if different from Clinic Date above.		

ECHO

Test done?	**yes** (test was done, even if recorded on video only)	**yes, partial** (i.e. only apical OR only parasternal images were acquired)	**no** (test was not attempted or done)	**If no or partial, why: Circle all that apply**
30 49 88 740 750	**Sonographer ID#**			1. Subject refusal 2. Subject discomfort 3. Time constraint 4. Equipment problem, specify _____ 7. Other, specify _____
|__|__|__|-|__|__|__|	**SVHS#**			
___/___/____	**ECHO test date** if different from Clinic Date above.			
MD overread required: (determined at the time of image acquisition)	☐ **yes**	☐ **no**		

PAT

Test done?	**yes** (test was done) attempted	**yes, partial** (yes, partial test was done but suspect data problems)	**no** (test was not or done)	**If no or partial, why: Circle all that apply**
30 49 88 740 750 54 _____	**Sonographer ID#**			1. Subject refusal 2. Subject discomfort 3. Time constraint 4. Equipment problem, specify _____ 5. test contraindication 7. Other, specify_____ 8. Latex allergy
|__|__|__|-|__|__|__|	**Video CD#**			
___/___/____	**PAT test date** if different from Clinic Date above.			

Appendix Item 4

FHS Echo Protocol

FHS ECHO PROTOCOL – Offspring 8				
Set up	*Connect ECG, tall R wave; Enter Subject ID, last name, first name; Sonographer ID; On sheet code tape # & location start +MOD#*			
VIEW	**DATA SOUGHT**	**Loop/Disk**	**Priority**	**EMPHASIS**
A5C	2-D LV Wall motion, CW AoV		Medium	
	PW LVOT	**GM save**	**High**	Cursor in LVOT ~ .5 cm from AV
Tonometry	**Carotid**	**GM save**	**High**	
PLA	2-D – start 20 cm - ↓ depth		Med	Chamber size & fxn, valve & AoR
	2-D LVOT - magnify	**GM save**	**High**	LVOT diameter
	2-D LV, RV, LA & Ao; MV & AV	**2D 1 loop**	**High**	LV wall motion & thickness; MV/AV
	2-D zoomed MV	**1 loop**		
	Color flow: AV/MV		Med	
*RV inflow**	*2-D & Color flow TV*		*Low*	*If short on time – abandon*
PSA	2-D of AV, LA		**High**	AV opening & # leaflets
	2-D zoomed AOV	**2D 1 loop**		
	M-mode full screen of AV&LA- narrow sector, ↓ depth	**MM 2 frames**	**HIGH**	Clear boundaries
	2-D sweep: LV (pap → apex → pap) narrow sector, ↓ depth		**High**	LV wall motion
	2-D of MV			
	M-mode full screen of MV	**MM 1 frame**	Med	Clear boundaries Epicardial +
	2-D LV PSA below MV tips magnify narrow sector, ↓ depth	**2D 1 loop**	**HIGH**	Endocardial definition
	M-mode LV same level – magnify	**MM 3 frames**	**HIGH**	Ensure Clear boundaries.
Apical 4	**2-D all 4 chambers – start 20 cm - ↓ depth**	**2D 1 loop**	**High**	Chamber size & function: RV & LV
	Color flow: MV, TV & AV		Med	Regurgitant flows
	#PW Pulmonary veins – speed @ 50	**GM save & PW 1 frame**	Med	Diastolic function – spend only 30 sec
	PW MV tips inflow: speed @ 50	**GM save & PW 1 frame**	**High**	Cursor @ leaflet tips (max velocity)
	2-D LV & MV annulus - narrow sector, ↓ depth	**2D 1 loop**	Med	Endocardial definition
	M-mode MV annulus @ 50	**MM 1 frame**	Med	Diastolic function
	#Tissue Doppler PW of the MV annulus - speed @ 50	**GM save PW1 frame**	Med	Diastolic function
Apical 2	**2-D LA&LV - narrow sector ↓ depth**	**2D 1 loop**	**High**	LV wall motion, endocardial definition
	Color flow: MV		Med	Regurgitant flow
Apical long	Color flow: MV & AV		Med	Regurgitant flows
	2-D LA/ LV /Ao narrow sector ↓ depth	**2D 1 loop**	Med	LV wall motion, endocardial definition
*Subcostal**	*2-D (valves/chambers (RV):see wall thickness*		*Low*	*Focus if study TLS; RVWT*
Check that desired images are saved in loops; 6 loops+10 frames=16 pages File, Save; -Paper work *Delete if short on time #preset				

Appendix Item 5

Framingham Heart Study Vascular Function Participant Worksheet

Vascular Testing

Exam 8
Framingham Study Vascular Function Participant Worksheet

	Keyer 1: _____ **Keyer 2:** _____
0 1 9 If yes, ☞ discontinue PAT	**Do you have a latex allergy?** (0=No, 1=Yes, 9=Unknown)
0 1 9 If yes, ☞ discontinue brachial	**Do you have active Raynaud's disease, as manifested by daily attacks of Raynaud's currently blue fingers or ischemic finger ulcers?** (0=No, 1=Yes, 9=Unknown)
0 1 2 3 8 9 If 1(right), ☞ discontinue brachial If 2(left), ☞ BP on right	**Women Only: Have you had a radical mastectomy on right side?** A radical mastectomy is the removal of the breast, associated lymph nodes, and underlying musculature. Does NOT include lumpectomy or simple mastectomy. (0=No, 1=Yes, right, 2=Yes, left, 3=Yes, both, 8=Male, 9=Unknown)
0 1 9 if yes fill ☞	**Have you had any caffeinated drinks in the last 6 hours?** (0=No, 1=Yes, 9=Unknown) |__|__| How many cups? (99=Unkown)
0 1 9	**Have you eaten anything else including a fat free cereal bar this morning?** (0=No, 1=Yes, 9=Unknown)
0 1 9 if yes fill ☞	**Have you smoked cigarettes in the last 6 hours?** (0=No, 1=Yes, 9=Unkn) |__|__|:|__|__| If yes, how many hours and minutes since your last cigarette? (99:99=Unknown)
	PAT SCAN
|__|__|/|__|__|/|__|__|	**Date of PAT scan?** (mo/day/yr)
|__|__|__|	**PAT Sonographer ID**
|__|__|.|__|	**Room temperature** (Celsius)
|__|__|__|	**Mean systolic baseline blood pressure**
|__|__|__|	**Cuff inflation pressure** (Baseline SBP + 50 or 250)
0 1 2 If no (0) or partial (2) ☞	**Was PAT protocol completed?** (Determined at time of scan or at time of interpreting) 0=No: protocol was not completed i.e. none of 3 parts completed of Baseline, Doppler, Deflation 1=Yes: protocol was done and completed i.e. all 3 parts completed of Baseline, Doppler, Deflation 2=Yes, Partial: protocol was partially completed i.e. 1 part of 3 completed, 2 of 3 completed of Baseline, Doppler, Deflation PAT scan deviations: **circle ALL that apply** 1: Subject refusal 2: Subject discomfort 3: Time constraint 4 Equipment problem (if not #5 or #6), specify _____ 5: Foot pedal problem/cuff sequence problem 6: Doppler problem 7: Other, specify

Appendix Item 6

Distribution & Categorization of Echocardiographic Measurements in Relation to Reference Limits

Distribution and Categorization of Echocardiographic Measurements in Relation to Reference Limits

The Framingham Heart Study: Formulation of a Height- and Sex-Specific Classification and Its Prospective Validation

Ramachandran S. Vasan, MD; Martin G. Larson, ScD; Daniel Levy, MD; Jane C. Evans, MPH; Emelia J. Benjamin, MD, ScM

Background Despite widespread categorization of echocardiographic measurements, there are no standardized guidelines for partitioning values exceeding reference limits.

Methods and Results We used regression analyses to develop sex- and height-specific reference limits for cardiac M-mode measurements (left ventricular [LV] mass, LV wall thickness, and LV and left atrial dimensions) in a healthy reference sample (n=1099) from the Framingham Heart Study. We then examined the distribution of measurements in a broad sample (n=4957) and classified the measurements according to increasing deviation from the height- and sex-specific reference limits and the 95th, 98th, and 99th percentile values for the broad sample (categories 0 through 4, respectively). To validate the categorization scheme, we used multivariable proportional-hazards regression to assess the relations of LV mass and LV wall thickness categories to risk of cardiovascular events and the relations of left atrial size to risk of atrial fibrillation. During a mean follow-up period of 7.7 years, 587 subjects developed new cardiovascular disease events, and 166 subjects developed new-onset atrial fibrillation. After adjustment for known risk factors, there was a 1.2- and 1.3-fold risk of cardiovascular disease events per category of LV wall thickness and LV mass, respectively, and a 1.6-fold risk of atrial fibrillation per category of left atrial size.

Conclusions Using a large community-based study sample, we propose a classification scheme that provides a standardized and validated framework for partitioning echocardiographic measurements. If adopted, the categorization scheme should promote uniformity in describing measurements among echocardiographic laboratories and enhance the comprehensibility of measurements to clinicians. (*Circulation*. 1997;96: 1863-1873.)

Key Words • echocardiography • cardiovascular diseases • ventricles • atrium • follow-up studies

Reference values, often referred to as the "upper limits of normal," have been proposed for echocardiographic dimensions of cardiac chambers.[1-10] The current practice in echocardiographic laboratories across the world is to categorize echocardiographic measurements as normal or into mild, moderate, or severe degrees of abnormality. For instance, the expressions "moderate concentric left ventricular hypertrophy" and "severe left atrial enlargement" are used widely to describe quantitative abnormalities of these cardiac structures. Despite the widespread use of such descriptive terms, there are no standardized guidelines in the echocardiographic literature regarding cut points for partitioning values exceeding reference limits. Furthermore, the current clinical practice of categorizing values exceeding reference limits is highly variable between and within institutions, neither height- nor sex-specific, and inadequately substantiated by scientific data.

The choice of cut points for classifying echocardiographic values (or any other quantitative clinical measurement) on an ordinal scale should be based on the distribution of these observations in relation to reference limits in a randomly selected noninstitutionalized sample of the general population.[11] Such a classification system may be useful for descriptive purposes, for prognostication, and for the prevention and treatment of diseases.[12] Previous publications from the Framingham Heart Study have evaluated the relations of echocardiographic variables as continuous measures to cardiovascular disease events. The objectives of the present investigation were twofold: (1) to develop a classification system of echocardiographic values exceeding reference limits in a community-based study sample and (2) to prospectively examine the utility of our categorization approach for predicting clinically important events during follow-up.

Methods

Study Sample

The selection criteria and study design of the FHS (both original and offspring study cohorts) have been detailed exten-

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From the National Heart, Lung, and Blood Institute's Framingham (Mass) Heart Study (all authors); the Divisions of Cardiology and Clinical Epidemiology, Beth Israel Hospital, Harvard Medical School, Boston, Mass (D.L.); the Cardiology Section (E.J.B.) and Department of Preventive Medicine and Epidemiology (R.S.V., M.G.L., D.L., E.J.B.), Boston (Mass) University School of Medicine; and the National Heart, Lung, and Blood Institute, Bethesda, Md (D.L.).

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E-mail emelia@fram.nhlbi.nih.gov

Selected Abbreviations and Acronyms

AF = atrial fibrillation
FHS = Framingham Heart Study
LA = left atrial
LV = left ventricular

sively.[13,14] Original subjects of the FHS who participated in the 16th biennial examination (1979 through 1981) and subjects of the Framingham Offspring Study who participated in the second offspring examination (1979 through 1983) constituted the study sample. The FHS examination has been approved by the Boston Medical Center Institutional Review Board, and all subjects gave informed consent before the examinations.

Of 6216 subjects who attended the index examinations, 1259 subjects (20.3%) with inadequate M-mode echocardiograms were excluded from the present investigation. The study sample included two groups. The larger group, called the broad sample, included all 4957 who had adequate M-mode echocardiograms. A healthy subgroup of 1099 subjects, henceforth called the reference sample, was selected from the broad sample to formulate reference limits. The reference sample included subjects between the ages of 20 and 45 years who were not obese (body mass index between 19 and 26 kg/m^2), who were of average height (1.5 to 1.9 m in men and 1.4 to 1.8 m in women), and who were free of cardiovascular disease, hypertension,[15] AF, diabetes mellitus, and cardiac medication use.

Echocardiographic Methods

All subjects underwent routine M-mode echocardiography. In >90% of subjects, two-dimensional guided M-mode echocardiograms were obtained from the left parasternal window.[16] All measurements were made according to the American Society of Echocardiography guidelines.[17] Three measurements were averaged for each value. The following echocardiographic variables were studied in the present investigation: LA dimensions, LV mass, LV wall thickness, and LV end-diastolic and end-systolic internal dimensions. LV mass was calculated thus: LV mass=0.8[1.04(LVIDD+IVST+PWT)^3−(LVIDD)^3]+0.6, where LVIDD represents LV end-diastolic internal dimension and IVST and PWT indicate the end-diastolic thicknesses of the interventricular septum and LV posterior wall, respectively.[18] End-diastolic LV wall thickness was calculated as IVST+PWT.

Analysis and Statistical Methods

Development of Classification for Values Exceeding Reference Limits

All analyses were sex-specific. Height was used for indexation of echocardiographic variables because the use of body surface area may inappropriately mask obesity-related alterations in cardiac structure.[19-22] For each echocardiographic variable Y, logarithmic regression analyses were performed using the reference sample with height as the predictor variable, thus: $\log Y=\beta_0+\beta_1 \log(\text{height})+E$, where β_0 is the Y-axis intercept, β_1 is the slope, and E is an error term. The predicted value of Y was calculated as $Y_p=\exp[\beta_0+\beta_1 \log(\text{height})]$. The 95th percentile value of Y was calculated for the reference sample as $Y_{95}=Y\times\exp(1.645\times\text{root mean square error})$. The values of Y_{95} represent the sex- and height-specific reference limits for the variable. Reference limits (regression coefficients and the values of [height]^k, k being sex-specific and echocardiographic variable–specific) for LV wall thickness, LV internal dimensions, and LV mass have been published previously.[19,20] The distribution of the ratio of the raw observation divided by the value predicted for height and sex, ie, Y/Y_p, in the broad sample was studied. The sex- and height-specific 95th, 98th, and 99th percentile values of the echocardiographic variable in the broad sample were determined subsequently from the corresponding percentiles of the ratio. We classified values of each echocardiographic variable into the following five categories based on sex- and height-specific percentiles (indicating increasing deviation from the reference limits): category 0 (reference limits), value ≤95th percentile of the reference sample; category 1, 95th percentile of reference sample<value≤95th percentile of broad sample; category 2, 95th percentile of broad sample<value≤98th percentile of broad sample; category 3, 98th percentile of broad sample<value≤99th percentile of broad sample; and category 4, value >99th percentile of broad sample.

Relations of Categories of Echocardiographic Variables to Clinical Outcomes

To assess the validity and prognostic significance of the proposed classification scheme, we evaluated the risk of adverse clinical outcomes among subjects in the five proposed categories of each echocardiographic variable (as defined at the baseline examination) during a follow-up period of up to 11 years. Category 0 served as the reference group with which the other categories were compared. The a priori hypothesis was that an increase in risk of adverse clinical events would be observed across the five categories of each echocardiographic variable. Analyses relating to categories of LV mass, LV wall thickness and LA dimensions are presented here. The relations of LV mass and LV wall thickness to the incidence of cardiovascular disease events and of LA dimensions to the incidence of new-onset AF were examined with sex-stratified Cox regression,[23] adjusted for known risk factors for these outcomes. The end points were selected a priori on the basis of previous studies reporting an association of increasing LV mass[24-29] and LV wall thickness[25,27] with risk of cardiovascular events and of increasing LA size with risk of AF.[30,31] All study subjects were under periodic surveillance for development of cardiovascular disease events with the aid of medical history, hospitalization records, and communication with personal physicians. All suspected new cardiovascular events were reviewed by a panel of three investigators who evaluated all pertinent available medical records. Cardiovascular disease events included coronary heart disease (angina pectoris, coronary insufficiency, myocardial infarction, and sudden or nonsudden death attributable to coronary heart disease), congestive heart failure, cerebrovascular disease (stroke or transient ischemic attack), and intermittent claudication. Criteria for these events have been detailed previously.[32] A diagnosis of AF on follow-up was made on the basis of documentation of AF or flutter on ECGs obtained from the FHS examination, hospital records, or private physician records. For examining the impact of LA size categories on risk of AF, we excluded subjects with AF at or before baseline (n=82).

Adjustment for Covariates

For multivariable analyses examining cardiovascular events as the outcome, hazard ratios were adjusted for the following covariates: sex, age (years), diastolic blood pressure (mm Hg), pulse pressure (mm Hg), the ratio of total to HDL cholesterol, body mass index (weight in kg/[height in m]^2), and the following dichotomous variables: hypertension, smoking, diabetes mellitus, and prior cardiovascular disease.[24] The covariates included in the multivariable models evaluating AF as the outcome event included age (years), hypertension status, diabetes mellitus, ECG LV hypertrophy, valve disease, and prior cardiovascular disease.[33] Hypertension was defined according to the JNC-V criteria as a systolic blood pressure value ≥140 mm Hg, a diastolic blood pressure value ≥90 mm Hg,[15] or current drug treatment for hypertension. Valve disease was defined as the presence of a diastolic murmur or a systolic murmur (grade 3/6 or more) on precordial auscultation at baseline. Criteria for other risk factors have been detailed previously.[34] Only subjects with complete information regard-

TABLE 1. Clinical and Echocardiographic Characteristics of Study Samples

	Reference Sample		Broad Sample	
	Men (n=387)	Women (n=712)	Men (n=2223)	Women (n=2734)
Clinical features				
Age, y (range)	35.7±6.1 (20-45)	36.1±5.5 (21-45)	49.8±13.9 (18-90)	51.6±15.0 (17-90)
Height, m	1.77±0.06	1.63±0.06	1.75±0.07	1.60±0.07
Weight, kg	74.0±6.9	58.9±6.1	81.1±12.0	64.1±12.3
Body surface area, m^2	1.91±0.11	1.63±0.10	1.96±0.16	1.66±0.15
Systolic blood pressure, mm Hg	116.9±9.3	109.6±10.3	128.8±17.2	125.0±20.6
Diastolic blood pressure, mm Hg	74.7±7.0	71.0±7.5	80.3±9.3	75.6±9.6
Coronary disease, %	...	...	8.3	5.3
Hypertension, %	...	...	35.0	31.6
Valve disease, %	...	...	2.8	3.1
Heart failure, %	...	...	0.8	1.0
AF, %	...	...	2.2	1.2
Diabetes mellitus, %	...	...	4.6	3.3
Echocardiographic features				
LV mass, g	173.9±39.7	114.5±23.5	202.1±61.8	135.9±44.3
Ventricular wall thickness, mm	18.1±2.0	15.5±1.5	19.8±3.0	17.4±3.0
LA dimension, mm	37.5±3.6	32.9±3.2	40.4±5.1	36.0±5.3
LV end-diastolic dimension, mm	50.9±3.5	46.1±3.1	51.1±4.4	45.7±4.0

Plus-minus values indicate mean±SD.

ing the covariates were included for the proportional-hazards analyses.

Choice of Statistical Models

We investigated whether the risk of adverse events differed among categories of echocardiographic variables using the several multivariable statistical models: models incorporating clinical variables only; multicategory models, in which risk of adverse outcome in each category was compared with that associated with category 0; trend models, in which we investigated whether there was a stepwise increase in risk of adverse outcome from one category to the next higher one; and threshold models, in which we tested whether there was a particular category above which there was increased risk of adverse outcomes (eg, risk of adverse events in subjects in categories 0 and 1 versus risk in subjects in categories 2, 3, and 4).

To explore the impact of sex on the risks associated with the echocardiographic categories, we performed secondary analyses incorporating interaction terms. All analyses were performed with the SAS System (SAS Institute Inc) procedures REG[35] and PHREG[36] on a SUNsparc 2 workstation; a two-sided value of $P<.05$ assessed statistical significance.

Results

Study Sample

The characteristics of the study subjects are summarized in Table 1. Compared with the reference sample, subjects in the broad sample were older, heavier, and had higher blood pressure, body mass index, and mean values for the echocardiographic measurements studied. In the broad sample, the prevalence of cardiovascular disease was as follows: hypertension, 33.1%; coronary disease, 6.7%; congestive heart failure, 0.9%; and AF, 1.7%. These conditions were grounds for exclusion from the reference sample.

Classification of Values Exceeding Reference Limits

In general, we noted a significant relation between height and echocardiographic variables in both sexes. The distributions of the ratio of observed to sex- and height-predicted values were examined for each echocardiographic variable; the Figure displays the distribution of this ratio for LA dimension, LV mass, LV wall thickness, and LV end-diastolic dimension. Approximately one quarter of men and one third of women exceeded reference limits for LV wall thickness, LV mass, and LA dimension. Eleven percent of men and 9% of women exceeded reference limits for LV end-diastolic dimension. Tables 2 and 3 provide the sex- and height-specific cut points for the five proposed categories of each echocardiographic variable derived from the percentiles of the ratio of observed to sex- and height-predicted values in the reference (category 0) and broad (categories 1 through 4) samples.

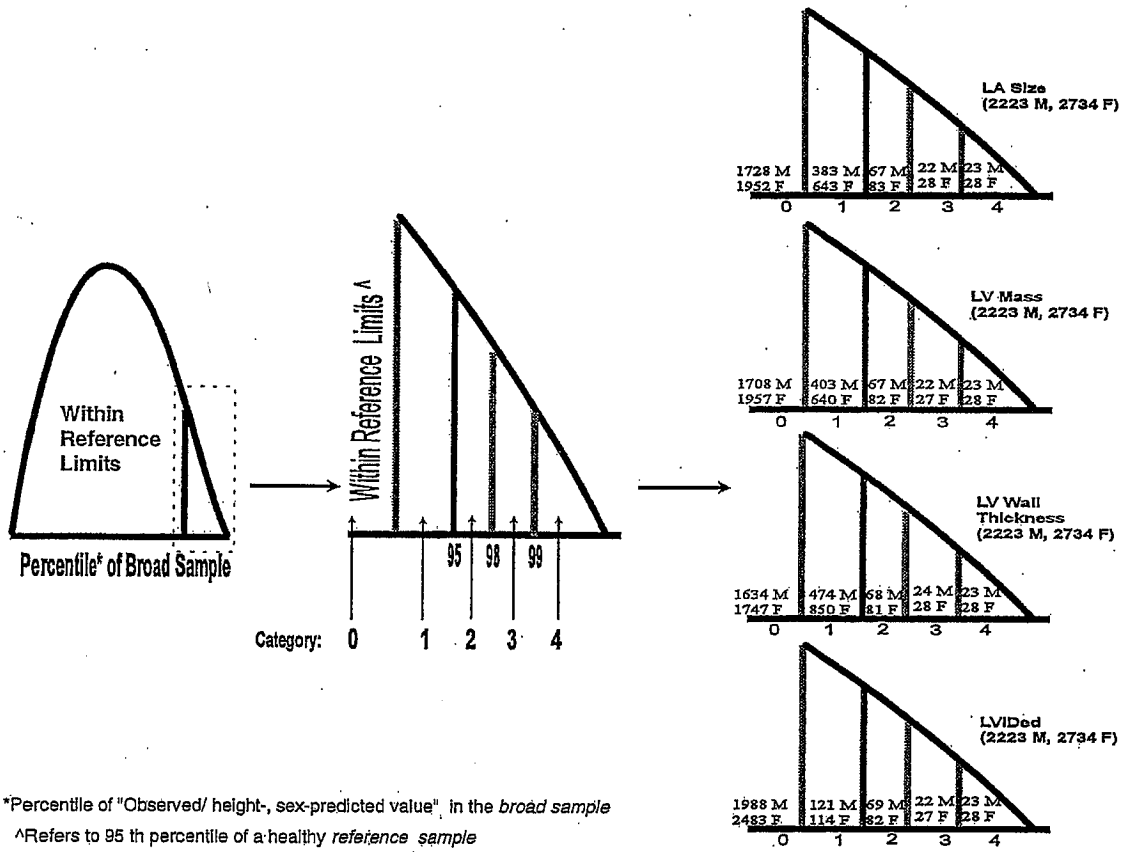
Relation of Category of Echocardiographic Variable to Clinical Outcome

Unadjusted Event Rates According to Category of Variable

Three subjects were lost to follow-up. During follow-up of the remaining 4954 subjects (mean age, 7.7 years; range, 0.4 to 11 years), 587 subjects experienced a new cardiovascular event; 55 of these new events were fatal. There were 166 subjects with new-onset AF among the 4872 subjects free of AF at baseline. Crude rates for new events increased across categories of LV mass, LV wall thickness, and LA size (Tables 4 through 6). Among men and women with a measurement of LV mass or LV wall thickness suggestive of extreme deviation from reference limits (category 4), >60% developed new cardiovascular disease events on follow-up; in comparison, <10% of the subjects in category 0 experienced a new event. Categories of LV mass or LV wall thickness between these two extremes (categories 1 through 3) had intermediate rates of new cardiovascular disease events. For categories of LA dimension, AF rates rose in stepwise fashion; >60% of subjects in category 4 developed AF, compared with 2% of subjects in category 0.

Multivariable Analyses

Irrespective of the choice of the statistical model, a significant risk gradient for adverse events was evident across the categories of LV mass, LV wall thickness, and LA dimensions for both sexes after adjustment for other



*Percentile of "Observed/ height-, sex-predicted value" in the *broad sample*

^Refers to 95 th percentile of a healthy *reference sample*

Distribution and categorization of echocardiographic variables in the broad sample of 4957 subjects based on deviation from height- and sex-specific reference limits. Categories were based on relations of 95th, 98th, and 99th percentile values of observed/predicted value for given height and sex in broad sample to reference limits. Reference limits were based on 95th percentile values in a healthy reference sample. Values for 22% of men and 29% of women exceeded reference limits for LA dimensions; values for 17% of men and 24% of women exceeded reference limits but were <95th percentile for broad sample. About 23% of men and 28% of women in broad sample exceeded reference limits for LV mass; LV mass values for 18% of men and 23% of women exceeded reference limits (height- and sex-specific) but were within 95th percentile of values for broad sample. Values for 26% of men and 36% of women exceeded reference limits for LV wall thickness; values for 21% of men and 31% of women were intermediate between reference limits and 95th percentile of values for broad sample. Values for 11% of men and 9% of women exceeded reference limits for LV end-diastolic internal dimensions (LVIDed); values for 5% of men and 4% of women were between reference limits and 95th percentile for broad sample. For LV end-systolic internal dimensions, distribution of male subjects was 2058, 53, 66, 23, and 23 for categories 0, 1, 2, 3, and 4, respectively; distribution of female subjects was 2545, 51, 83, 27, and 28 for categories 0, 1, 2, 3, and 4, respectively (not shown).

known risk factors. In general, trend models were roughly comparable to the five category models in terms of risk prediction but incorporated fewer variables (ie, were more parsimonious). The threshold models were inferior to the trend and five category models but were better than multivariable models that included only clinical predictors (data not shown). The results of the trend and five-category models are shown in Tables 4 through 6. There was a 1.2- to 1.3-fold increase in hazard for new cardiovascular disease events per increase in category of LV wall thickness and LV mass, respectively (trend model). There was a 1.6-fold increase in hazard of AF per increase in category of LA dimension (trend model); a 4.4-fold hazard was seen for subjects in the highest category of LA dimension compared with those in the lowest category. There were no significant sex differences in the risks associated with LV mass and LV wall thickness categories (probability values for the respective interaction terms were .29 and .68). There was a 29% greater risk for AF across LA size categories in women than in men (P=.08).

Discussion

Need for Classifying Echocardiographic Values in Relation to Reference Limits

Because of the plethora of tests in medicine, raw values of clinical measurements often are poorly comprehended by nonspecialists. Understandably, nonspecialists frequently cannot recall cut points for abnormality, much less retain a sense of how far an abnormal value has strayed from normal.[37] Clinical chemists have tried to resolve this dilemma by presenting any observed value in relation to its reference limits.[38] Classification of abnormal clinical measurements on an ordinal scale, ie, within reference limits and with increasing degrees of deviation from reference limits, is an attractive option because clinicians tend to think in terms of categories when they interpret quantitative clinical data.[39] Besides making clinical data more comprehensible to nonspecialists, classification also renders the available information more manageable.[40]

When standards for categorization of laboratory tests are absent, clinicians set their own informal criteria for

TABLE 2. Cut Points for Categorization of Echocardiographic LA Size, LV Mass, Wall Thickness, and LV Diameter in Women

Height		Category				
In	cm	0	1	2	3	4
			Left atrium, mm			
54	137	≤36.6	36.7-43.0	43.1-47.2	47.3-49.6	>49.6
55	140	≤36.8	36.9-43.3	43.4-47.5	47.6-49.9	>49.9
56	142	≤37.0	37.1-43.5	43.6-47.7	47.8-50.2	>50.2
57	145	≤37.2	37.3-43.7	43.8-48.0	48.1-50.4	>50.4
58	147	≤37.4	37.5-44.0	44.1-48.2	48.2-50.7	>50.7
59	150	≤37.6	37.7-44.2	44.3-48.5	48.6-51.0	>51.0
60	152	≤37.8	37.9-44.4	44.5-48.8	48.9-51.2	>51.2
61	155	≤38.0	38.1-44.7	44.8-49.0	49.1-51.5	>51.5
62	157	≤38.1	38.2-44.9	45.0-49.2	49.3-51.8	>51.8
63	160	≤38.3	38.4-45.1	45.2-49.5	49.6-52.0	>52.0
64	163	≤38.5	38.6-45.3	45.4-49.7	49.8-52.3	>52.3
65	165	≤38.7	38.8-45.5	45.6-50.0	50.1-52.5	>52.5
66	168	≤38.9	39.0-45.8	45.9-50.2	50.3-52.8	>52.8
67	170	≤39.1	39.2-46.0	46.1-50.4	50.5-53.0	>53.0
68	173	≤39.2	39.3-46.2	46.3-50.7	50.8-53.2	>53.2
69	175	≤39.4	39.5-46.4	46.5-50.9	51.0-53.5	>53.5
70	178	≤39.6	39.7-46.6	46.7-51.1	51.2-53.7	>53.7
71	180	≤39.8	39.9-46.8	46.9-51.3	51.4-53.9	>53.9
72	183	≤39.9	40.0-47.0	47.1-51.6	51.7-54.2	>54.2
			LV mass, g			
54	137	≤116	117-159	160-189	190-233	>233
55	140	≤119	120-163	164-194	195-240	>240
56	142	≤123	124-168	169-200	201-247	>247
57	145	≤126	127-173	174-205	206-254	>254
58	147	≤130	131-178	179-211	212-261	>261
59	150	≤133	134-183	184-217	218-268	>268
60	152	≤137	138-188	189-223	224-275	>275
61	155	≤141	142-193	194-229	230-282	>282
62	157	≤144	145-198	199-235	236-290	>290
63	160	≤148	149-203	204-241	242-297	>297
64	163	≤152	153-208	209-247	248-305	>305
65	165	≤155	156-213	214-253	254-312	>312
66	168	≤159	160-218	219-259	260-320	>320
67	170	≤163	164-223	224-266	267-328	>328
68	173	≤167	168-229	230-272	273-336	>336
69	175	≤171	172-234	235-278	279-344	>344
70	178	≤175	176-240	241-285	286-352	>353
71	180	≤179	180-245	246-291	292-360	>360
72	183	≤183	184-251	252-298	299-368	>368
			LV wall thickness, mm			
54	137	≤16.9	17.0-21.4	21.5-24.7	24.8-27.4	>27.4
55	140	≤17.0	17.1-21.6	21.7-24.9	25.0-27.6	>27.6
56	142	≤17.1	17.2-21.8	21.9-25.1	25.2-27.8	>27.8
57	145	≤17.2	17.3-21.9	22.0-25.3	25.4-28.0	>28.0
58	147	≤17.4	17.5-22.1	22.2-25.5	25.6-28.2	>28.2
59	150	≤17.5	17.6-22.2	22.3-25.6	25.7-28.4	>28.4
60	152	≤17.6	17.7-22.4	22.5-25.8	25.9-28.6	>28.6
61	155	≤17.7	17.8-22.5	22.6-26.0	26.1-28.8	>28.8
62	157	≤17.8	17.9-22.7	22.8-26.2	26.3-29.0	>29.0
63	160	≤18.0	18.1-22.8	22.9-26.3	26.4-29.2	>29.2
64	163	≤18.1	18.2-23.0	23.1-26.5	26.6-29.4	>29.4
65	165	≤18.2	18.3-23.1	23.2-26.7	26.8-29.6	>29.6
66	168	≤18.3	18.4-23.3	23.4-26.9	27.0-29.8	>29.8
67	170	≤18.4	18.5-23.4	23.5-27.0	27.1-29.9	>29.9
68	173	≤18.5	18.6-23.6	23.7-27.2	27.3-30.1	>30.1
69	175	≤18.6	18.7-23.7	23.8-27.4	27.5-30.3	>30.3
70	178	≤18.8	18.9-23.9	24.0-27.5	27.6-30.5	>30.5
71	180	≤18.9	19.0-24.0	24.1-27.7	27.8-30.7	>30.7
72	183	≤19.0	19.1-24.1	24.2-27.8	27.9-30.8	>30.8

RS indicates reference sample; BS, broad sample. Categories are 0, value≤95th percentile RS; 1, 95th percentile RS<value≤95th percentile BS; 2, 95th percentile BS<value≤98th percentile BS; 3, 98th percentile BS<value≤99th percentile BS; and 4, value>99th percentile BS. For women in category 0, the RS 95th percentile values correspond to the following percentiles of the broad sample: For LA size, 71%; for LV mass 72%, for LV wall thickness 64%, for LV internal diameter end diastole 91%, for LV diameter end systole 93%.

TABLE 2. Continued

Height		Category				
in	cm	0	1	2	3	4
			LV end-diastolic diameter, mm			
54	137	≤46.8	46.9-47.9	48.0-50.0	50.1-52.1	>52.1
55	140	≤47.3	47.4-48.3	48.4-50.4	50.5-52.6	>52.6
56	142	≤47.7	47.8-48.7	48.8-50.9	51.0-53.0	>53.0
57	145	≤48.1	48.2-49.2	49.3-51.4	51.5-53.5	>53.5
58	147	≤48.5	48.6-49.6	49.7-51.8	51.9-54.0	>54.0
59	150	≤49.0	49.1-50.0	50.1-52.2	52.3-54.4	>54.4
60	152	≤49.4	49.5-50.4	50.5-52.7	52.8-54.9	>54.9
61	155	≤49.8	49.9-50.8	50.9-53.1	53.2-55.3	>55.3
62	157	≤50.2	50.3-51.2	51.3-53.5	53.6-55.8	>55.8
63	160	≤50.6	50.7-51.7	51.8-54.0	54.1-56.2	>56.3
64	163	≤51.0	51.1-52.1	52.2-54.4	54.5-56.7	>56.7
65	165	≤51.4	51.5-52.5	52.6-54.8	54.9-57.1	>57.1
66	168	≤51.8	51.9-52.9	53.0-55.2	55.3-57.5	>57.5
67	170	≤52.1	52.2-53.3	53.4-55.6	55.7-58.0	>58.0
68	173	≤52.5	52.6-53.6	53.7-56.1	56.2-58.4	>58.4
69	175	≤52.9	53.0-54.0	54.1-56.5	56.6-58.8	>58.8
70	178	≤53.3	53.4-54.4	54.5-56.9	57.0-59.2	>59.2
71	180	≤53.7	53.8-54.8	54.9-57.3	57.4-59.7	>59.7
72	183	≤54.0	54.1-55.2	55.3-57.7	57.8-60.1	>60.1
			LV end-systolic diameter, mm			
54	137	29.9	30.0-30.6	30.7-32.3	32.4-33.9	>33.9
55	140	30.3	30.4-30.9	31.0-32.7	32.8-34.3	>34.3
56	142	30.7	30.8-31.3	31.4-33.1	33.2-34.7	>34.7
57	145	31.1	31.2-31.7	31.8-33.5	33.6-35.1	>35.1
58	147	31.4	31.5-32.1	32.2-33.9	34.0-35.6	>35.6
59	150	31.8	31.9-32.4	32.5-34.3	34.4-36.0	>36.0
60	152	32.2	32.3-32.8	32.9-34.7	34.8-36.4	>36.4
61	155	32.5	32.6-33.2	33.3-35.1	35.2-36.8	>36.8
62	157	32.9	33.0-33.5	33.6-35.5	35.6-37.2	>37.2
63	160	33.2	33.3-33.9	34.0-35.9	36.0-37.6	>37.6
64	163	33.6	33.7-34.3	34.4-36.2	36.3-38.0	>38.0
65	165	33.9	34.0-34.6	34.7-36.6	36.7-38.4	>38.4
66	168	34.3	34.4-35.0	35.1-37.0	37.1-38.8	>38.8
67	170	34.6	34.7-35.3	35.4-37.4	37.5-39.2	>39.2
68	173	35.0	35.1-35.7	35.8-37.8	37.9-39.6	>39.6
69	175	35.3	35.4-36.1	36.2-38.1	38.2-40.0	>40.0
70	178	35.7	35.8-36.4	36.5-38.5	38.6-40.4	>40.4
71	180	36.0	36.1-36.8	36.9-38.9	39.0-40.8	>40.8
72	183	36.4	36.5-37.1	37.2-39.2	39.3-41.2	>41.2

converting noncategorical data into categorical information. This was well illustrated by a study addressing the interpretation of objective measures by physicians; the larger the physician's own set of reference values was, the greater was the leniency in the interpretation of such data.[41] We searched the literature for cut points for classifying echocardiographic values exceeding the reference limits but failed to find standardized guidelines. Despite the routine use of descriptive categories in echocardiography laboratories, there is little scientific literature to support such practice.

Development and Validation of Our Classification

There is no universally accepted method for categorizing continuous variables.[42-44] In the present investigation, we developed a classification system for echocardiographic reference limits that attempted to meet two broad objectives: standardization of echocardiographic interpretation and clinical sensibility.[39] To achieve the latter goal, we sought to develop a classification system that was straightforward, user-friendly, evidence based, and based on appropriate physiological variables. Because echocardiographic measurements are dependent on sex as well as on body size,[19,20,45] echocardiographic variables should be classified with reference to sex and to anthropometric measurements. We chose height as a physiological obesity-independent determinant of echocardiographic measurements. Although age is an important determinant of cardiac dimensions,[21,46,47] we avoided formulating age-dependent cut points because of uncertainty in distinguishing the physiological from the pathological effects of aging on the heart.[48]

By examining the distribution of values in a broad study sample that included healthy and diseased individuals, we developed a classification in which each echocardiographic variable could be partitioned into four categories based on increasing degrees of deviation from reference limits (category 0). The present investigation suggested that echocardiographic measurements exceeding height- and sex-specific reference limits were

TABLE 3. Cut Points for Categorization of Echocardiographic LA Size, LV Mass, Wall Thickness, and LV Diameter in Men

Height		Category				
In	cm	0	1	2	3	4
			Left atrium, mm			
60	152	≤42.4	42.5-47.7	47.8-51.7	51.8-53.9	>53.9
61	155	≤42.5	42.6-47.9	48.0-51.9	52.0-54.1	>54.1
62	157	≤42.7	42.8-48.1	48.2-52.1	52.2-54.3	>54.3
63	160	≤42.8	42.9-48.3	48.4-52.3	52.4-54.5	>54.5
64	163	≤43.0	43.1-48.4	48.5-52.5	52.6-54.7	>54.7
65	165	≤43.1	43.2-48.6	48.7-52.6	52.7-54.9	>54.9
66	168	≤43.3	43.4-48.8	48.9-52.8	52.9-55.1	>55.1
67	170	≤43.4	43.5-48.9	49.0-53.0	53.1-55.3	>55.3
68	173	≤43.6	43.7-49.1	49.2-53.2	53.3-55.5	>55.5
69	175	≤43.7	43.8-49.3	49.4-53.4	53.5-55.6	>55.6
70	178	≤43.9	44.0-49.4	49.5-53.5	53.6-55.8	>55.8
71	180	≤44.0	44.1-49.6	49.7-53.7	53.8-56.0	>56.0
72	183	≤44.2	44.3-49.7	49.8-53.9	54.0-56.2	>56.2
73	185	≤44.3	44.4-49.9	50.0-54.0	54.1-56.4	>56.4
74	188	≤44.4	44.5-50.0	50.1-54.2	54.3-56.5	>56.5
75	190	≤44.6	44.7-50.2	50.3-54.4	54.5-56.7	>56.7
76	193	≤44.7	44.8-50.3	50.4-54.5	54.6-56.9	>56.9
77	196	≤44.8	44.9-50.5	50.6-54.7	54.8-57.0	>57.0
78	198	≤45.0	45.1-50.6	50.7-54.8	54.9-57.2	>57.2
			LV mass, g			
60	152	≤170	171-221	222-264	265-295	>295
61	155	≤175	176-228	229-272	273-305	>305
62	157	≤181	182-235	236-281	282-314	>314
63	160	≤186	187-242	243-289	290-324	>324
64	163	≤192	193-249	250-298	299-334	>334
65	165	≤198	199-257	258-307	308-344	>344
66	168	≤204	205-264	265-316	317-354	>354
67	170	≤210	211-272	273-325	326-364	>364
68	173	≤216	217-280	281-335	336-375	>375
69	175	≤222	223-288	289-344	345-385	>385
70	178	≤228	229-296	297-354	355-396	>396
71	180	≤234	235-304	305-363	364-407	>407
72	183	≤240	241-312	313-373	374-418	>418
73	185	≤247	248-320	321-383	384-429	>429
74	188	≤253	254-329	330-393	394-440	>440
75	190	≤260	261-337	338-403	404-451	>451
76	193	≤266	267-346	347-413	414-463	>463
77	196	≤273	274-355	356-424	425-475	>475
78	198	≤280	281-363	364-434	435-486	>486
			LV wall thickness, mm			
60	152	≤18.8	18.9-22.9	23.0-25.2	25.3-27.0	>27.0
61	155	≤19.1	19.2-23.2	23.3-25.6	25.7-27.4	>27.4
62	157	≤19.3	19.4-23.5	23.6-25.9	26.0-27.8	>27.8
63	160	≤19.6	19.7-23.8	23.9-26.3	26.4-28.1	>28.1
64	163	≤19.8	19.9-24.1	24.2-26.6	26.7-28.5	>28.5
65	165	≤20.1	20.2-24.4	24.5-27.0	27.1-28.9	>28.9
66	168	≤20.4	20.5-24.8	24.9-27.3	27.4-29.3	>29.3
67	170	≤20.6	20.7-25.1	25.2-27.7	27.8-29.6	>29.6
68	173	≤20.9	21.0-25.4	25.5-28.0	28.1-30.0	>30.0
69	175	≤21.1	21.2-25.7	25.8-28.3	28.4-30.4	>30.4
70	178	≤21.4	21.5-26.0	26.1-28.7	28.8-30.7	>30.7
71	180	≤21.6	21.7-26.3	26.4-29.0	29.1-31.1	>31.1
72	183	≤21.9	22.0-26.6	26.7-29.4	29.5-31.5	>31.5
73	185	≤22.2	22.3-26.9	27.0-29.7	29.8-31.8	>31.8
74	188	≤22.4	22.5-27.2	27.3-30.1	30.2-32.2	>32.2
75	190	≤22.7	22.8-27.5	27.6-30.4	30.5-32.6	>32.6
76	193	≤22.9	23.0-27.8	27.9-30.7	30.8-32.9	>32.9
77	196	≤23.2	23.3-28.2	28.3-31.1	31.2-33.3	>33.3
78	198	≤23.4	23.5-28.5	28.6-31.4	31.5-33.6	>33.6

Abbreviations and categories as in Table 2. For men in category 0, the RS 95th percentile values correspond to the following percentiles of the broad sample: For LA size, 78%; for LV mass, 77%; for LV wall thickness, 74%; for LV internal end-diastolic diameter, 89%; and for LV end-systolic internal diameter, 93%.

TABLE 3. Continued

Height		Category				
In	cm	0	1	2	3	4
			LV end-diastolic diameter, mm			
60	152	≤52.1	52.2-54.2	54.3-56.6	56.7-60.1	>60.1
61	155	≤52.6	52.7-54.7	54.8-57.1	57.2-60.7	>60.7
62	157	≤53.0	53.1-55.2	55.3-57.7	57.8-61.2	>61.2
63	160	≤53.5	53.6-55.8	55.9-58.2	58.3-61.8	>61.8
64	163	≤54.0	54.1-56.3	56.4-58.7	58.8-62.3	>62.3
65	165	≤54.5	54.6-56.8	56.9-59.3	59.4-62.9	>62.9
66	168	≤55.0	55.1-57.3	57.4-59.8	59.9-63.5	>63.5
67	170	≤55.5	55.6-57.8	57.9-60.3	60.4-64.0	>64.0
68	173	≤55.9	56.0-58.2	58.3-60.8	60.9-64.5	>64.5
69	175	≤56.4	56.5-58.7	58.8-61.3	61.4-65.1	>65.1
70	178	≤56.9	57.0-59.2	59.3-61.8	61.9-65.6	>65.6
71	180	≤57.3	57.4-59.7	59.8-62.3	62.4-66.2	>66.2
72	183	≤57.8	57.9-60.2	60.3-62.8	62.9-66.7	>66.7
73	185	≤58.2	58.3-60.7	60.8-63.3	63.4-67.2	>67.2
74	188	≤58.7	58.8-61.1	61.2-63.8	63.9-67.7	>67.7
75	190	≤59.2	59.3-61.6	61.7-64.3	64.4-68.3	>68.3
76	193	≤59.6	59.7-62.1	62.2-64.8	64.9-68.8	>68.8
77	196	≤60.0	60.1-62.5	62.6-65.3	65.4-69.3	>69.3
78	198	≤60.5	60.6-63.0	63.1-65.8	65.9-69.8	>69.8
			LV end-systolic diameter, mm			
60	152	35.3	35.4-36.3	36.4-39.4	39.5-42.0	>42.0
61	155	35.7	35.8-36.7	36.8-39.8	39.9-42.4	>42.4
62	157	36.0	36.1-37.0	37.1-40.2	40.3-42.8	>42.8
63	160	36.4	36.5-37.4	37.5-40.6	40.7-43.2	>43.2
64	163	36.7	36.8-37.7	37.8-41.0	41.1-43.6	>43.6
65	165	37.1	37.2-38.1	38.2-41.4	41.5-44.0	>44.1
66	168	37.4	37.5-38.4	38.5-41.8	41.9-44.4	>44.4
67	170	37.8	37.9-38.8	38.9-42.1	42.2-44.8	>44.9
68	173	38.1	38.2-39.1	39.2-42.5	42.6-45.2	>45.2
69	175	38.4	38.5-39.5	39.6-42.9	43.0-45.6	>45.6
70	178	38.8	38.9-39.8	39.9-43.3	43.4-46.0	>46.0
71	180	39.1	39.2-40.2	40.3-43.6	43.7-46.4	>46.4
72	183	39.4	39.5-40.5	40.6-44.0	44.1-46.8	>46.8
73	185	39.8	39.9-40.8	40.9-44.4	44.5-47.2	>47.2
74	188	40.1	40.2-41.2	41.3-44.7	44.8-47.6	>47.6
75	190	40.4	40.5-41.5	41.6-45.1	45.2-48.0	>48.0
76	193	40.7	40.8-41.8	41.9-45.5	45.6-48.4	>48.5
77	196	41.1	41.2-42.2	42.3-45.8	45.9-48.7	>48.7
78	198	41.4	41.5-42.5	42.6-46.2	46.3-49.1	>49.1

associated with an adverse prognosis; furthermore, the greater the extent of deviation, the worse the prognosis. Results of trend models indicated a stepwise increase in hazard per category increase in LV mass (1.3-fold risk of cardiovascular disease events), LV wall thickness (1.2-fold risk of cardiovascular events), and LA size (1.6-fold risk of AF). The adverse impact associated with values in categories 1 through 4 (compared with category 0) was evident in both sexes, persisted in multivariable analyses adjusting for the impact of other known risk factors, and was generally consistent within the various statistical models explored.

Strengths and Limitations

Any classification may be justified on the basis of its peremptory assignment, its consensual validation, or external documentation.[40] Peremptory assignment is desirable when data have no inherent meaning (eg, zip codes). A consensual approach involves establishing a standard by common agreement of experts in the field. External documentation (validation by application) requires providing independent evidence that justifies the creation of the proposed categories. We chose the latter method because we believe that it was unbiased and scientifically more rigorous. Furthermore, the ability of any classification system to predict risk of adverse events considerably enhances its utility to the clinician. The longitudinal design of the FHS facilitated such prospective validation.

To the best of our knowledge, except for LV mass,[49] the present investigation is the first systematic attempt at classifying echocardiographic values exceeding reference limits. The a priori definition of cut points based on the distribution of the echocardiographic measurements instead of post hoc generation based on clinical outcome events is an additional strength of our study.[44] The large, community-based study sample used for deriving our reference limits and for developing and validating our classification approach makes the present investigation unique. In comparison, previous reports of echocardio-

TABLE 4. Relations of Categories of LV Mass to Incidence of New Cardiovascular Disease Events: Results of Cox Proportional-Hazards Models

	Men			Women			Hazards Ratio (95% CI)†	
Proposed Category	No. in Category	No. of Events on Follow-up	Rate per 1000 Person-Years*	No. in Category	No. of Events on Follow-up	Rate per 1000 Person-Years*	Trend Models	5-Category Models
Value ≤95 percentile reference sample (category 0)	1707	189	15.1	1955	107	7.2	1.0 (Reference)	1.0 (Reference)
95 percentile reference sample<value≤95 percentile broad sample (category 1)	403	89	32.3	640	96	20.7	1.32 (1.20-1.44)	1.27 (1.03-1.56)
95 percentile broad sample<value≤98 percentile broad sample (category 2)	67	29	71.1	82	23	45.3	1.73 (1.44-2.08)	1.75 (1.26-2.45)
98 percentile broad sample<value≤99 percentile broad sample (category 3)	22	10	92.7	27	8	51.9	2.28 (1.74-3.00)	2.05 (1.20-3.49)
Value >99 percentile broad sample (category 4)	23	19	181.7	28	17	149.0	3.00 (2.09-4.32)	3.10 (2.08-4.63)

*Based on 587 new cardiovascular events among 4954 subjects in the broad sample. Cardiovascular events include coronary disease (angina, myocardial infarction, coronary insufficiency, and sudden cardiac death), heart failure, stroke, transient ischemic attacks, and intermittent claudication.

†Hazards ratio adjusted for age, sex, hypertension, diastolic blood pressure, pulse pressure, smoking, total cholesterol/HDL cholesterol, diabetes mellitus, and previous cardiovascular disease. These proportional-hazards analyses are based on 555 subjects with new cardiovascular events among 4775 subjects with complete information regarding covariates.

graphic reference limits[1-10] have been based on percentile estimates drawn from cross-sectional samples of smaller numbers of healthy subjects. Previous investigations from the FHS[19,50] and elsewhere[1-10] have not subdivided the values exceeding reference limits for practical use by clinicians.

The exclusion of subjects without satisfactory echocardiograms (who are generally sicker) may have resulted in the lowering of thresholds for abnormal values. The use of M-mode measurements presents other potential limitations. Cardiac disease may result in distorted LV geometry with the possibility of underestimating or overestimating LV mass.[51] Furthermore, M-mode technology (transducer sensitivity, etc) has changed over the past two decades because the echocardiograms were performed. In addition, categories based on M-mode measurements may not be generalizable to two-dimensional echocardiographic measurements. Nonetheless, previous investigations have found reasonable agreement between measurements made by the two techniques.[6,52] Finally, it is possible for a patient to shift between categories simply on the basis of limitations in the reproducibility of echocardiographic measurements.[53]

Because the generation and validation of our classification are based on ambulatory subjects, its prognostic relevance in hospitalized subjects is unknown. A related potential limitation is that in addition to age, the cut points are largely dependent on the prevalent pattern and severity of cardiac disease in the study participants. For instance, cut points for varying degrees of LV hypertrophy and LV dilatation obtained from our study sample may differ substantially from those obtained from subjects in hypertension and heart failure clinics, respectively. Nonetheless, it is heartening to note that the prevalence of cardiovascular disease in our study sample was consistent with that observed in the general US population.[54] Furthermore, although we have demonstrated significant prognostic value of this categorization scheme, the therapeutic implications of our classification, if any, are unknown. Last, given the largely white racial composition of the Framingham sample, readers should exercise caution in extrapolating the study results to other racial groups.

TABLE 5. Relations of Categories of LV Wall Thickness to Incidence of New Cardiovascular Disease Events: Results of Cox Proportional-Hazards Models

	Men			Women			Hazards Ratio (95% CI)†	
Proposed Category	No. in Category	No. of Events on Follow-up	Rate per 1000 Person-Years*	No. in Category	No. of Events on Follow-up	Rate per 1000 Person-Years*	Trend Model	5-Category Model
Value ≤95 percentile reference sample (category 0)	1633	184	15.4	1745	69	5.1	1.0 (Reference)	1.0 (Reference)
95 percentile reference sample<value≤95 percentile broad sample (category 1)	474	101	31.2	850	137	22.5	1.18 (1.08-1.30)	1.27 (1.03-1.55)
95 percentile broad sample<value≤98 percentile broad sample (category 2)	68	22	49.1	81	20	37.2	1.39 (1.17-1.69)	1.33 (0.92-1.92)
98 percentile broad sample<value≤99 percentile broad sample (category 3)	24	14	109.4	28	10	67.8	1.64 (1.26-2.20)	2.20 (1.40-3.48)
Value >99 percentile broad sample (category 4)	23	15	138.7	28	15	107.0	1.94 (1.36-2.86)	1.72 (1.10-2.69)

*Based on 587 new cardiovascular events in 4954 subjects of the broad sample. Cardiovascular events include coronary disease (angina, myocardial infarction, coronary insufficiency, and sudden cardiac death), heart failure, stroke, transient ischemic attacks, and intermittent claudication.

†Hazards ratio adjusted for age, sex, hypertension, diastolic blood pressure, pulse pressure, smoking, total cholesterol/HDL-cholesterol, diabetes mellitus, and previous cardiovascular disease. These proportional-hazards analyses are based on 555 subjects with new cardiovascular events among 4775 subjects with complete information regarding covariates.

TABLE 6. Relations of Categories of LA Dimension to Incidence of AF: Results of Cox Proportional-Hazards Models

Proposed Category	Men			Women			Hazards Ratio (95% CI)†	
	No. in Category	No. of Events on Follow-up	Rate per 1000 Person-Years*	No. in Category	No. of Events on Follow-up	Rate per 1000 Person-Years*	Trend Model	5-Category Model
Value ≤95 percentile reference sample (category 0)	1720	49	3.7	1947	26	1.7	1.0 (Reference)	1.0 (Reference)
95 percentile reference sample<value≤95 percentile broad sample (category 1)	371	23	8.4	638	21	4.3	1.64 (1.37-1.96)	1.32 (0.89-1.96)
95 percentile broad sample<value≤98 percentile broad sample (category 2)	59	11	25.9	78	15	26.3	2.69 (1.88-3.84)	2.42 (1.43-4.08)
98 percentile broad sample<value≤99 percentile broad sample (category 3)	17	3	30.1	22	7	49.2	4.41 (2.57-7.53)	4.84 (2.72-8.63)
Value >99 percentile broad sample (category 4)	7	4	91.9	13	7	109.0		

*Based on 166 new onset AF events in 4872 subjects in the broad sample who were free of AF at baseline.

†Hazard ratio adjusting for age, sex, hypertension, valve disease, ECG LV hypertrophy, diabetes mellitus, and previous cardiovascular disease. These proportional-hazards analyses are based on 164 subjects with new-onset AF among 4851 subjects free of AF at baseline and who had complete information regarding covariates. For LA size hazard ratios, categories were combined because of small numbers.

Clinical Implications

Scrutiny of our cut points reveals that there are some challenges to currently used thresholds for quantitative echocardiographic abnormalities. For example, a sum of septal and posterior LV wall thicknesses of 20 mm is regarded as normal by most clinicians. Nonetheless, we would classify this value as above reference limits in a woman or in a short man; such a value for wall thickness (category 1) is associated with a 1.2-fold risk of cardiovascular disease events compared with values within reference limits. These observations underscore the weaknesses inherent in the use of traditional reference limits that establish an arbitrary dichotomous threshold (mean±2 SD or 95th percentile) without providing insights into risks associated with various levels of the echocardiographic variable.

By classifying echocardiographic values on an ordinal scale reflecting an increasing hazard for morbid events across categories, we have reported a framework that will promote greater consistency in echocardiographic interpretation and will provide prognostic information. Such a standardized classification is particularly important in an era when the nonspecialist not only orders echocardiograms but also is expected to interpret and act on the results of the studies.

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Appendix Item 7

Quality Assurance Protocol

Quality Assurance Protocol for Offspring Exam 8

Element	Frequency	Procedure	Statistics
Reproducibility	Annual	• Intra- Inter-observer measurement variability • Intra- Inter-observer qualitative assessment variability* Interpreters measure 20 scans twice	• Continuous measures: Mean ± sd • Qualitative measures: Kappa statistics? • Correlation coefficients • Mean ± sd $\lvert y - y \rvert$ • Range $\lvert y - y \rvert$ • Components of variability • Subject • Within sonographer • Between sonographer
	Annual	• Temporal variability • Interpreters measure calibration scan set	
	Once	• Sonographer variability • Sonographers scan 20 FHS personnel	
Descriptive statistics	Quarterly	• Generated by data management staff • Assessment of differences in quantitative & qualitative* variables across sonographers and observers for routine scans	• Measurement variability • Mean ± sd
Data cleaning	Monthly	• Generated by data management staff	• Out of range data • Missing data
QA reports	Quarterly	• Generated by data management staff • Reproducibility statistics included in reports	• Descriptive statistics • Data cleaning
Lab meetings	Bi-weekly	• FHS sonographers measure random or difficult studies together	
	Monthly	• FHS review QA reports • FHS Review lab flow, issues	
	Quarterly	• Review FHS reports with key personnel	

QA = quality assurance; sd = standard deviation; FHS = Framingham Heart Study

***Note: we have NOT assessed reproducibility on qualitative echo data before. This is essential to enhance integrity of data & usability of data set.**

Appendix Item 8

Tonometry Echo PAT Logsheet Complications & Premature Termination of Studies

TONOMETRY / ECHO/ PAT ADVERSE REACTION LOG

To be filled out when a test was administered and adverse reaction occurred.**

NAME: _____ **ID:** _____

DATE OF CLINIC VISIT: ___-___-____ (mm/dd/yyyy)

PAT TEST - SKIN REACTION - PETECHIAE

Fill in and circle all that apply

Abnormality Location	Time Course	Skin Reaction Pain?	Patient Upset?	Prior Occurrence?	Easy Bruising?
Hand Forearm Upper arm	**Onset** Date: ___-___-____ Time: ___:___ AM PM	YES NO Describe:	YES NO *Describe:*	YES NO *Describe:*	YES NO *Describe:*
Describe:	**Offset** Date: ___-___-____ Time: ___:___ AM PM				

OTHER ADVERSE REACTIONS

Fill in an circle all that apply

Pain	Other
Date: ___-___-____	Date: ___-___-____
Describe:	*Describe:*

**Note: If test was not administered due to adverse reaction, then all information should be recorded in the log book. Adverse reaction is defined by MD/Tech group.

Appendix Item 9

2-D + M-Mode Illustrations

FHS Offspring Exam 8 Echocardiography Scanning Protocol Overview

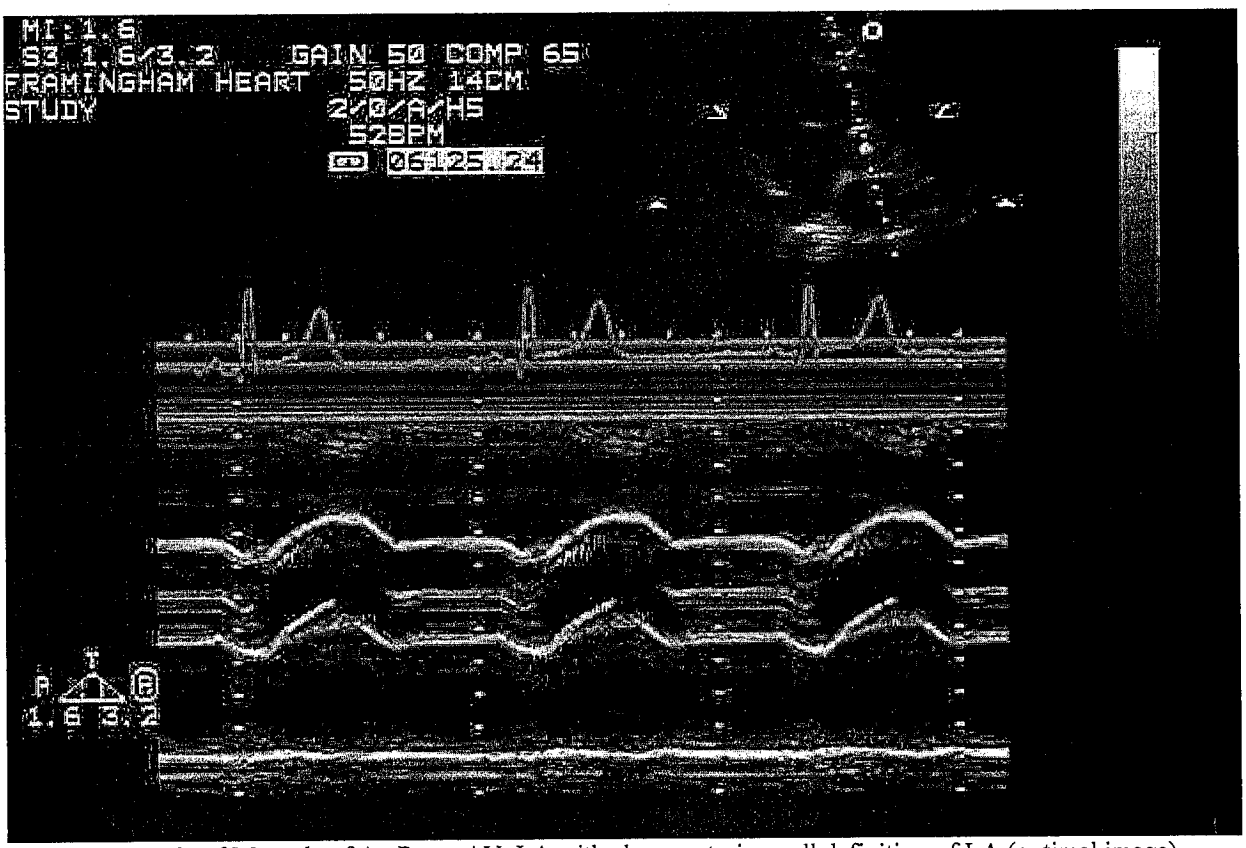

Fig. 1a – Example of M-mode of Ao Root, AV, LA with clear posterior wall definition of LA (optimal image).

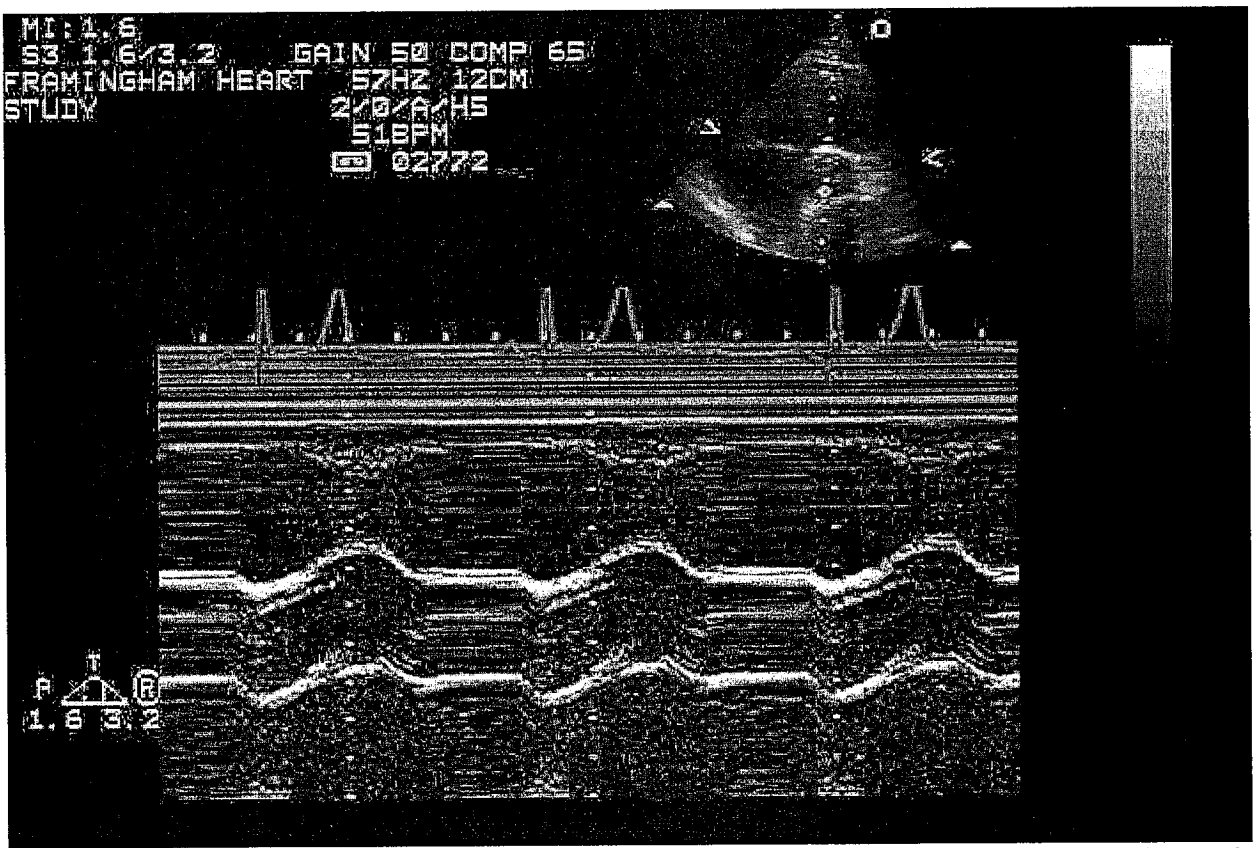

Fig. 1b – Example of M-mode of Ao Root, AV, LA, with posterior wall of LA not showing due to overly decreased depth (suboptimal image).

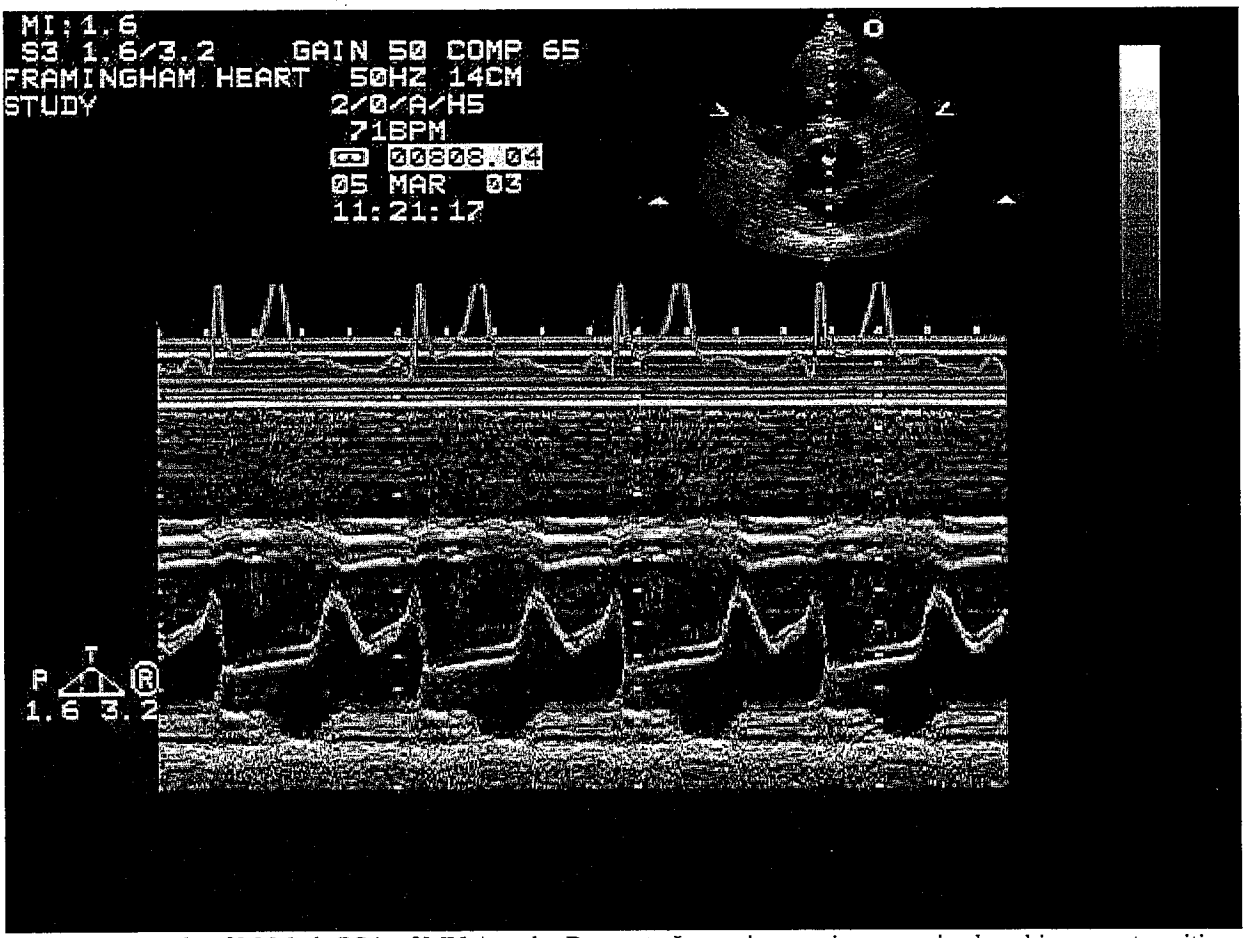

Fig. 7a – Example of M-Mode PSA of MV Annular Descent. Image is on-axis, cursor is placed in correct position on MV with E-Point Septal Separation (EPSS) clearly visualized and easily measurable (optimal image).

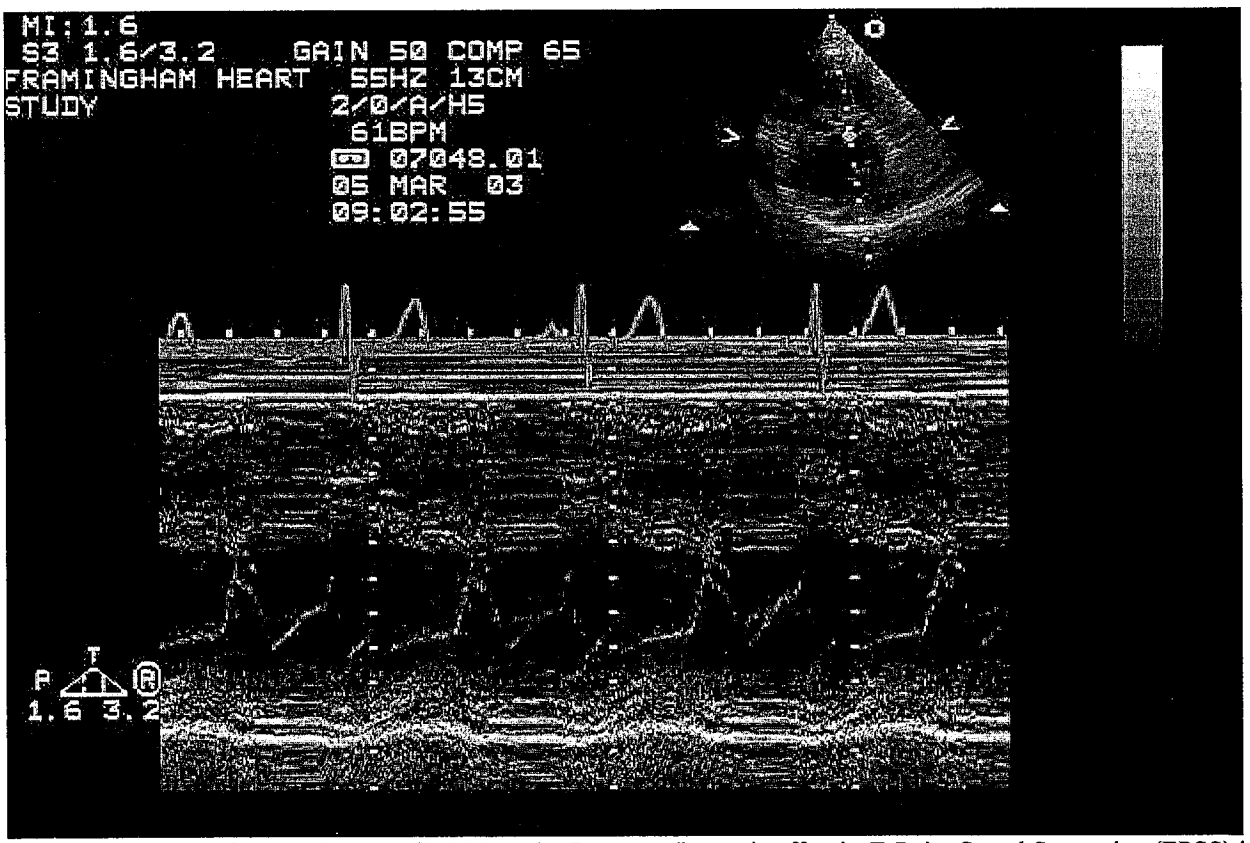

Fig. 7b – Example of M-Mode PSA of MV Annular Descent. Image is off-axis, E-Point Septal Separation (EPSS) is neither clearly visualized nor easily measurable (sub-optimal image).

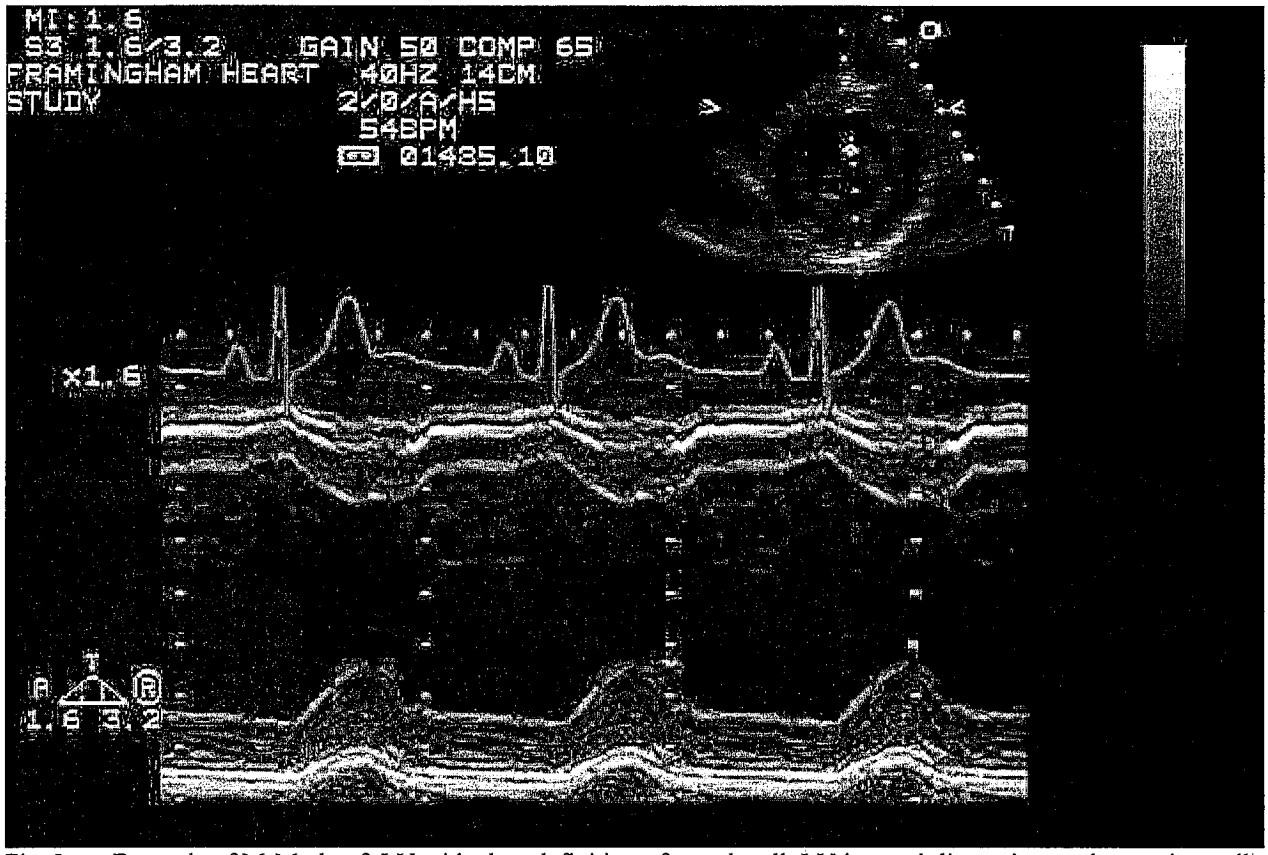

Fig. 2a – Example of M-Mode of LV with clear definition of septal wall, LV internal dimension, and posterior wall (optimal image).

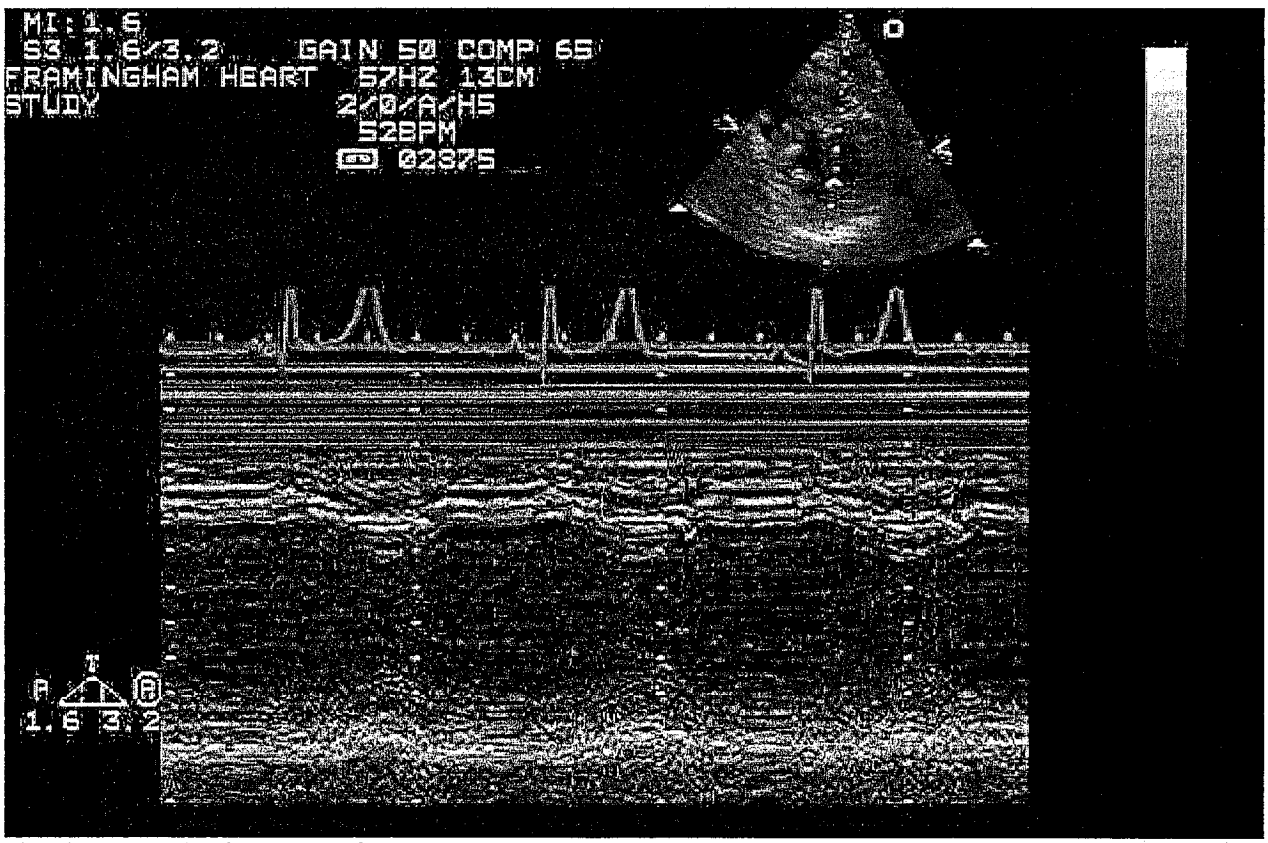

Fig. 2b – Example of M-Mode of LV with unclear definition of septal wall and posterior wall. LV is somewhat "eggy" because window is too low (suboptimal image).

Fig. 2b – Example of M-Mode of LV with unclear definition of septal wall and posterior wall. LV is somewhat "eggy" because window is too low (suboptimal image).

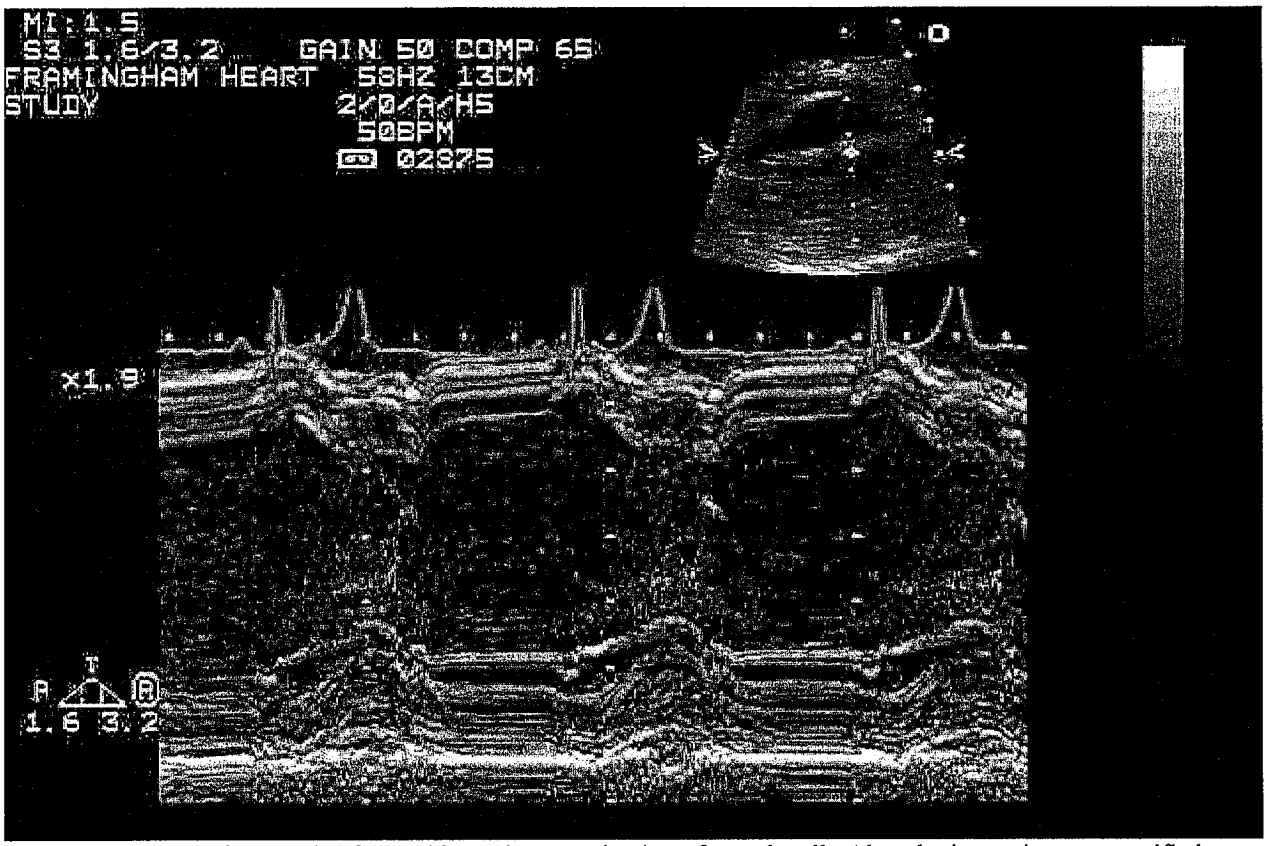

Fig. 2c – Example of M-Mode of LV with EKG contamination of septal wall. Also, the image is overmagnified (suboptimal image).

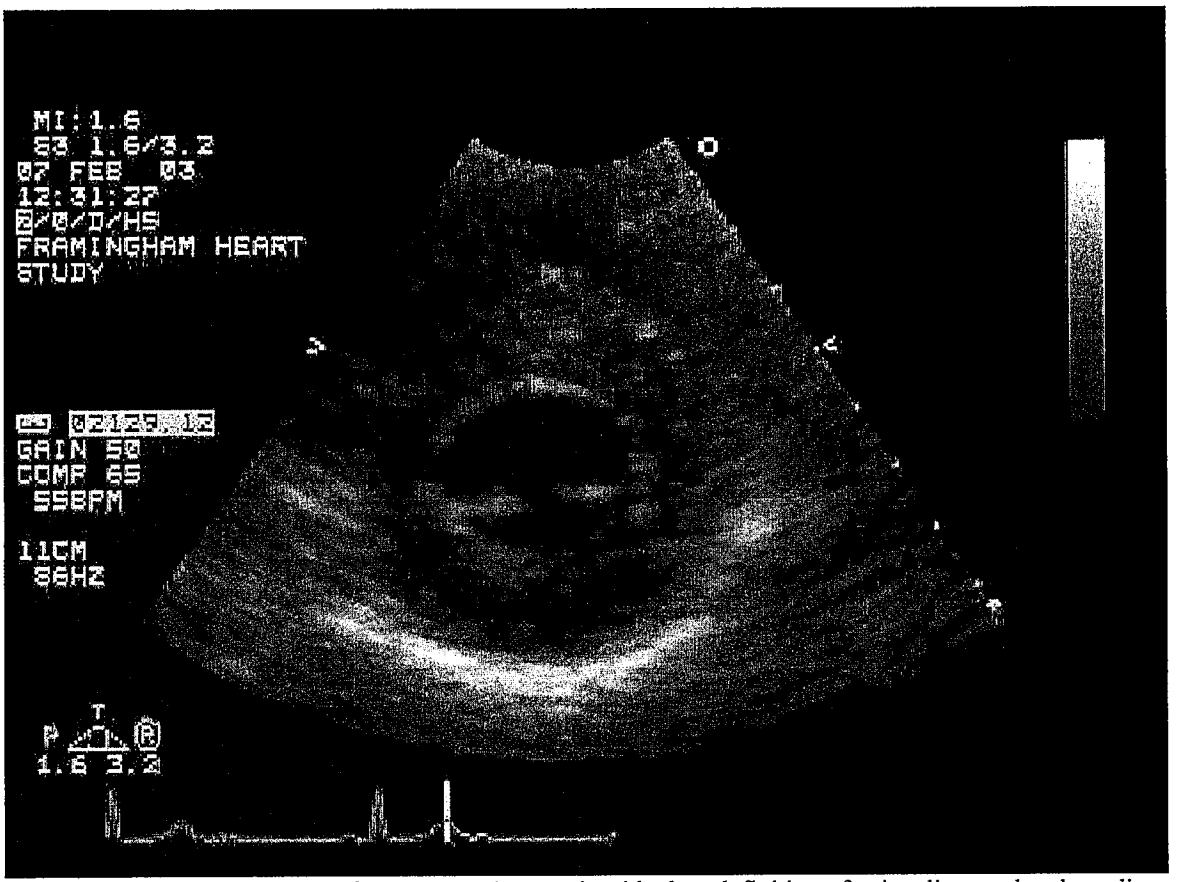

Fig. 4a - Example of 2-D PSA of LV. Image is on-axis with clear definition of epicardium and endocardium (optimal image).

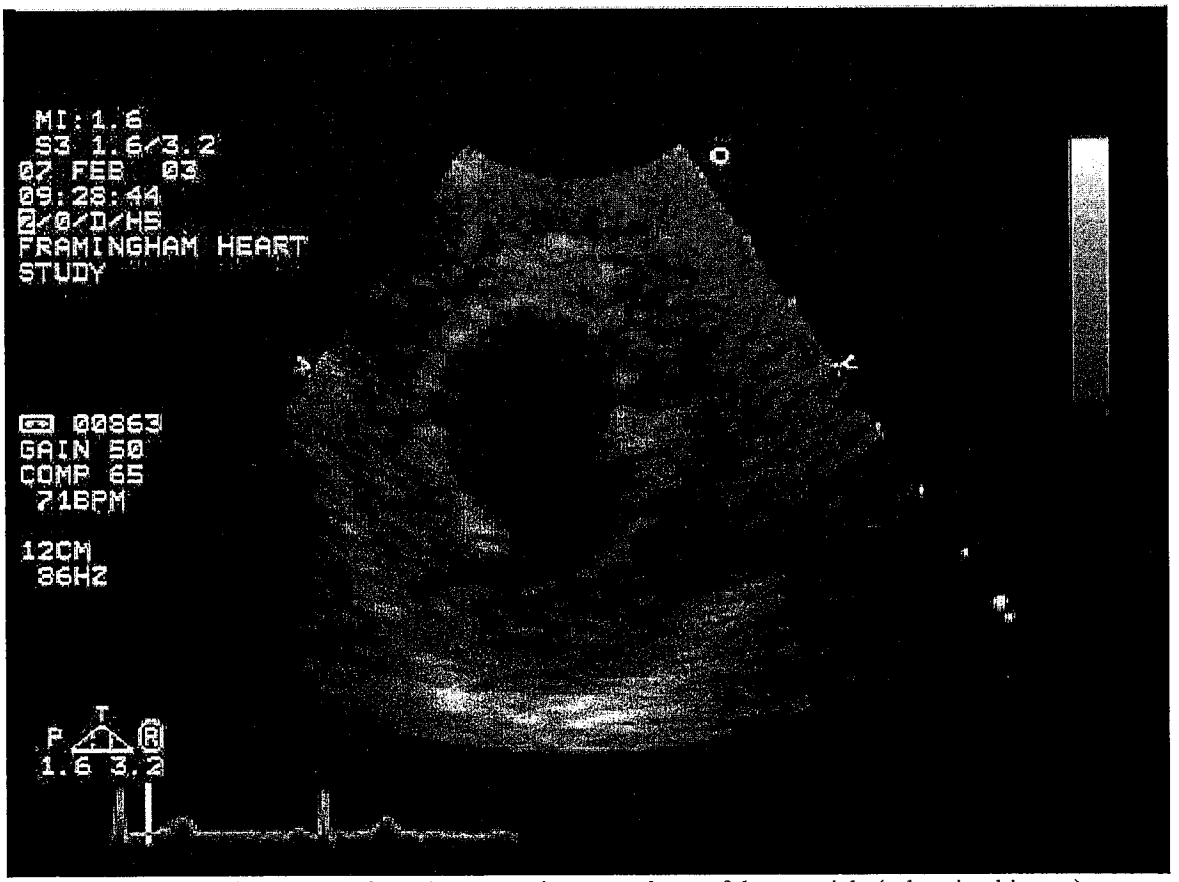

Fig. 4b. – Example of 2-D PSA of LV demonstrating eggy shape of the ventricle (suboptimal image).

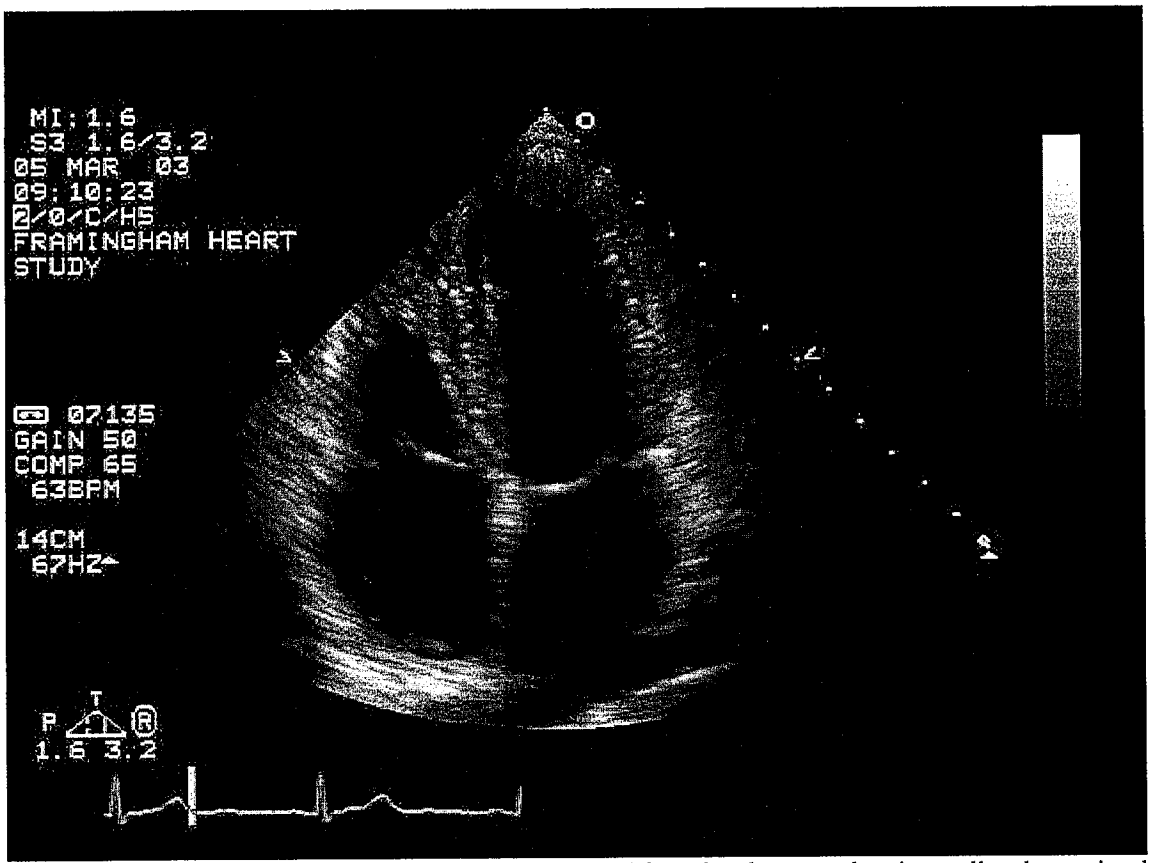

Fig. 3a – Example of 2-D Apical Four-Chamber view. All four chambers are showing well and on-axis; clear wall definition, mitral valve as well as tricuspid valve are showing well. Septum is in a vertical line and the entire heart is on-axis (optimal image)

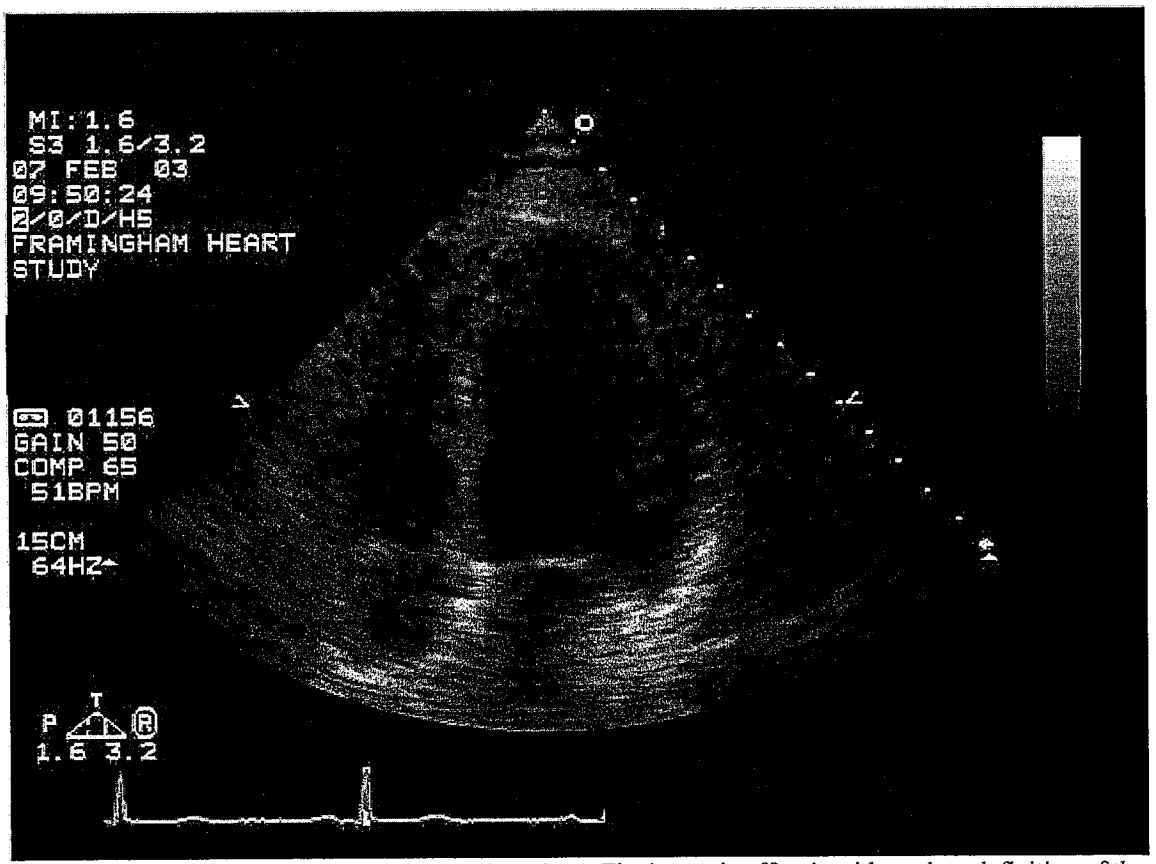

Fig. 3b - Example of 2-D Apical Four-Chamber view. The image is off-axis with unclear definition of the endocardium. The right atrium and ventricle are not fully open (suboptimal image).

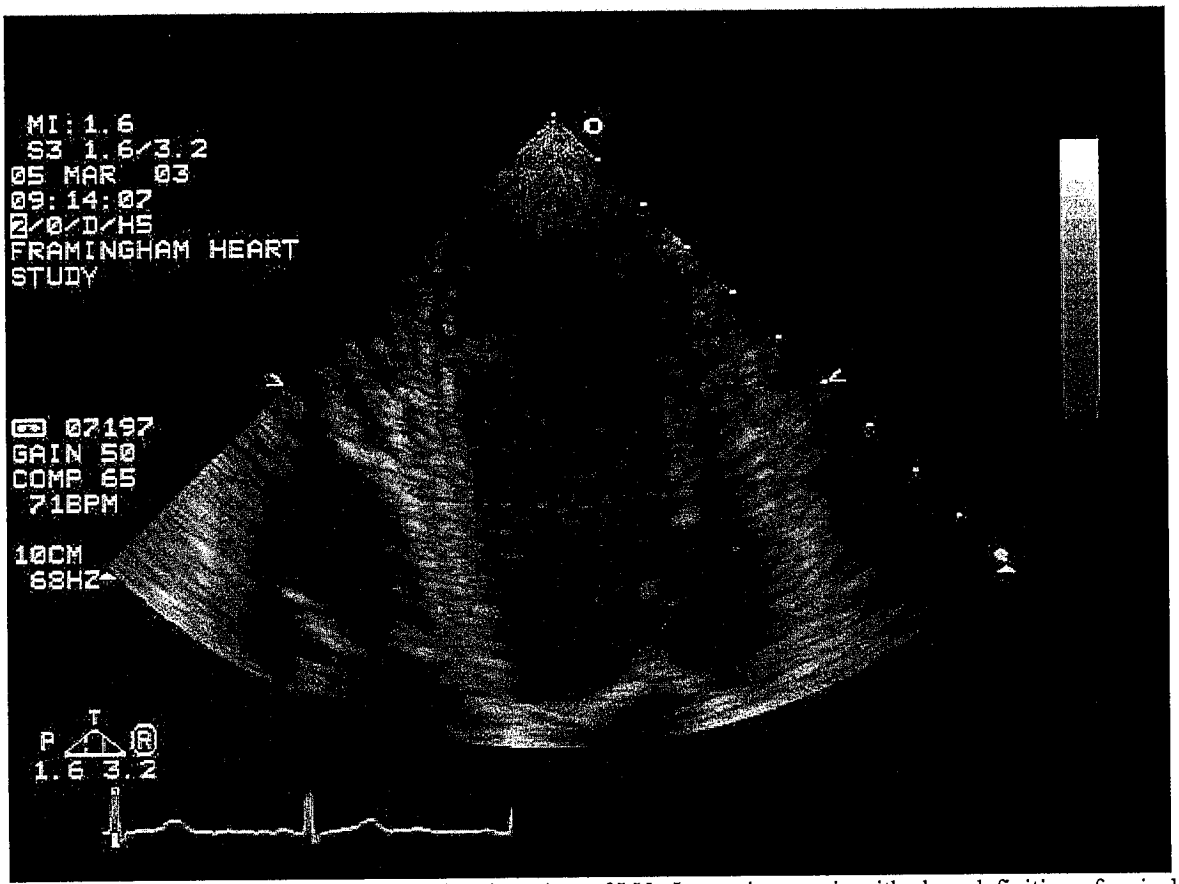

Fig. 5a – Example of 2-D Apical Four-Chamber view of LV. Image is on-axis with clear definition of apical endocardium and mitral valve annulus and leaflets are clearly shown. Longitudinal measurement is made from apex to imaginary line across mitral annulus. (optimal image)

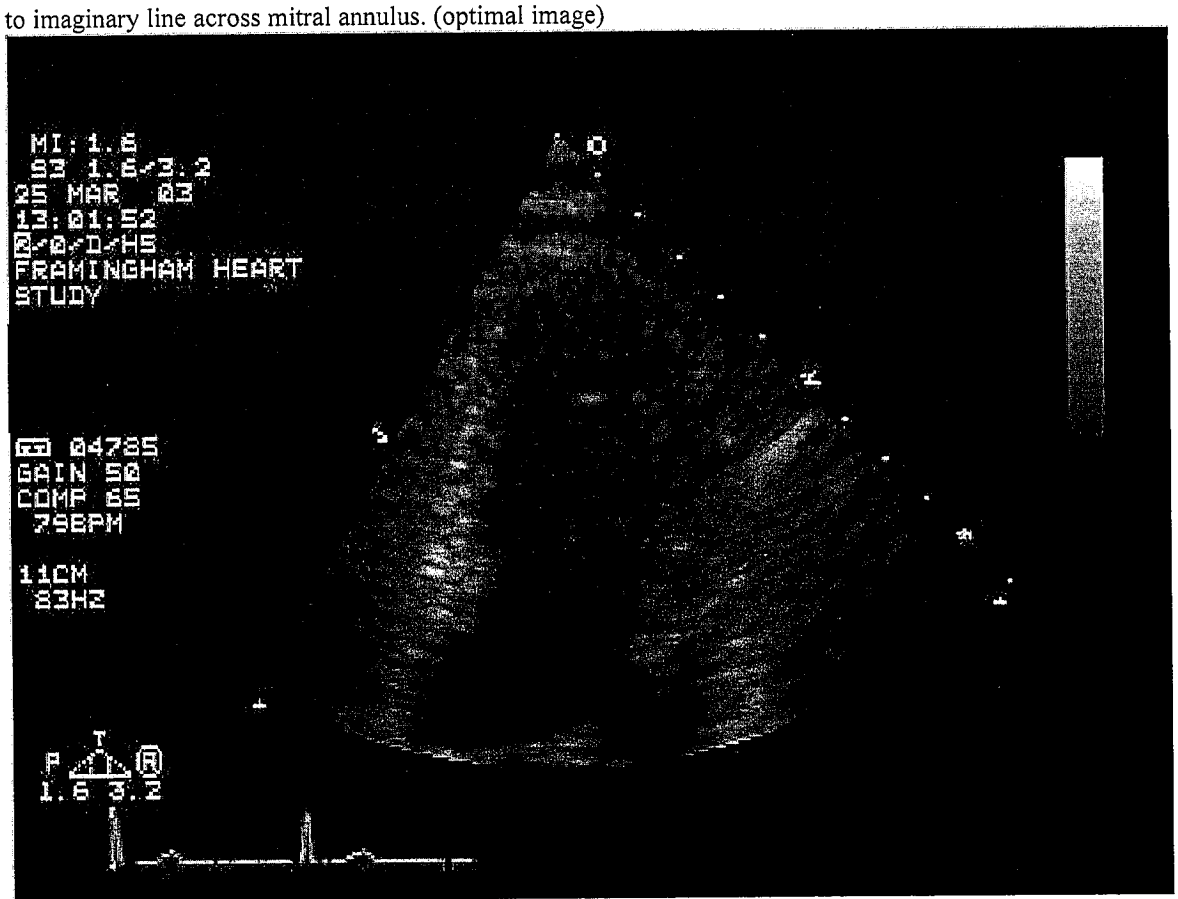

Fig. 5b – Example of 2-D Apical Four-Chamber view of LV. LV is off-axis and apical endocardium is not clearly visualized. Mitral valve annulus is not visible. (sub-optimal)

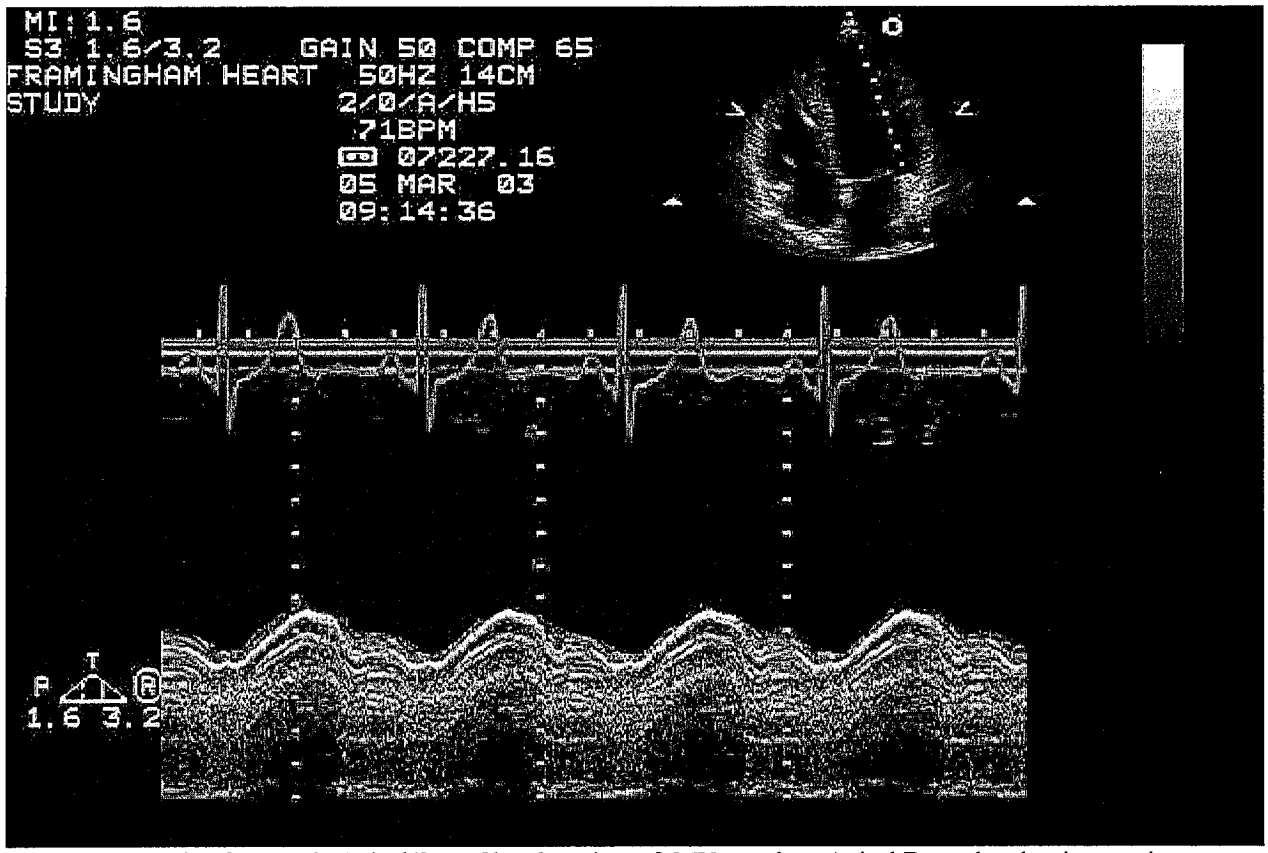

Fig. 6a – Example of M-Mode Apical Four-Chamber view of MV annulus. Apical Four-chamber is on-axis, cursor placed in correct position at MV annulus. Clear echoes of MV annulus movements (optimal image).

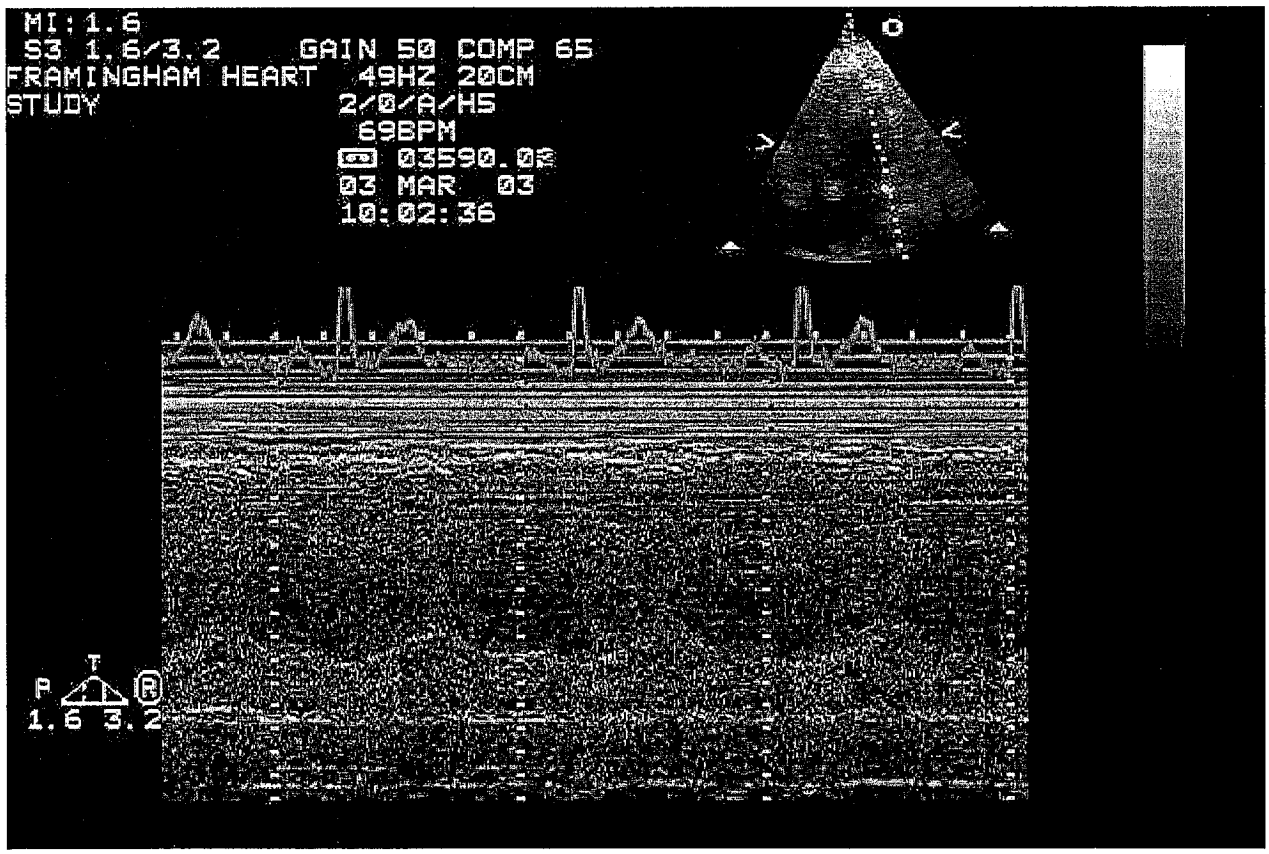

Fig. 6b – Example of M-Mode Apical Four-Chamber view of MV annulus. 2-D four-chamber view is not clear. Echoes of MV annulus movements are not well-defined and has a grainy appearance (suboptimal image).

Appendix Item 10

FHS Exam Components

Offspring Exam 8 Components-Clinic

Section I: Informed Consent & Tracking Procedures

1) Informed Consent
2) Waiver of Informed Consent
3) HIPPA - Release of Health Information for Research Purposes
4) FHS Follow-up by Proxy
5) Tracking Information Form

Section II: Clinical Measurements & Procedures

1) Lab
   a. Blood
   b. Urine
2) Anthropometrics
   a. Weight
   b. Height
   c. Waist Girth
   d. Waist Girth at Iliac Crest
   e. Sagittal Abdominal Diameter
3) ECG
4) Ankle-Brachial Blood Pressure Measurement
5) Observed Physical Performance
   a. Hand Grip Test
   b. Measured Walks

Section III: Tech-Administered Questionnaires

1) Cognitive Function
   a. MMSE
2) Physical Function
   a. KATZ-ADL Scale
   b. Rosow-Breslau
   c. NAGI
3) Depressive Symptoms
   a. CES-D
4) Physical Activity Questionnaire
   a. Exercise
5) Other
   a. Living Arrangement
   b. Use of Nursing and Community Services
   c. Fractures
   d. Proxy Form

Section IV: Physician-Administered Medical History and Physical Exam

1) Medical History
2) Resting Blood Pressure
3) Physical Exam

Section V: Self-Administered Questionnaires

1) Socio-demographics
2) SF12 Health Survey
3) Sleep Questionnaire
4) Willett Food Frequency Questionnaire

Section VI: PFT-Spirometry and Diffusion Capacity (full sample)

1) Spirometry
2) Diffusion Capacity
3) Post Bronchodilator Spirometry (Sub-sample)
   a. Albuterol
4) Respiratory Disease Questionnaire

Section VII: Non-Invasive Vascular Testing**

1) Echocardiogram
2) Carotid
3) Tonometry
4) PAT

Section VIII: Exam Completeness

1) Exit Interview
2) Referral Tracking & Adverse Events
3) Participant Letter
4) MD Letter to Personal Physician

Appendix Item 11

FHS Echo Specific Reading Guidelines

FHS Echo Specific Reading Guidelines 2005					
LA enlargement*	□ no	□ borderline	□ mild	□ moderate	□ severe
Mitral Valve					
MV thickening	□ no **<0.5 cm**	□borderline>0.4-0.5cm	□ mild **0.5-0.7 cm**		□ mod/severe □ **0.8 cm**
Mitral stenosis	□ no	□ possible **2.5-3.9 cm^2**	□ likely **<2.5 cm^2**		
MAC	□ no		□ mild **M-mode < 3 mm 2-D focal**	□ mod. **MM 3-5 2-D >1/3 ring**	□severe **MM >5 mm 2D □½ circumference**
MVP	□ no	□ MSD **2mm behind annulus**	□ mild **>2 to <4 mm**		□ mod/severe □ **4 mm**
AorticValve/Root					
AV thickening	□ no		□ mild **focal/limited**	□ mod. **diffuse, some thin leaflet seen**	□ sev. **diffuse, 'white-out' AV**
Ao cusp excursion (MM+2-D sense)	□ no□**1.5 cm**		□ mild **1.-1.4 cm**	□ mod. **0.5-0.9cm**	□ sev. **<0.5 cm**
Aotic root dilation	□ no		□present_ **3.6 ♀; 3.8♂cm**		
Aortic root calcium	□ no		□ mild **focal <½ ring**	□ moderate **>½ ring**	□ severe **entire ring**
LV Structure*					
LV enlargement	□ no	□ borderline	□ mild	□ moderate	□ severe
□ LVWT,	□ no	□ borderline	□ mild	□ moderate	□ severe
□ LVWT, other	□ no		□ ASH **sw:pw >1.3 & sw□1.3**	□ ISH **not ASH & sw □ 1.2 cm_ 1.1_ pw □ 1.2 cm_ 1.1_**	□ DUSK **discrete upper septal knuckle (visual)**
LV Systolic Fxn					
LV ejection fraction	□ normal □ **55%**	□ borderline **50-54%**	□ mild □□**40-49%**	□ moderate □**30-39%**	□ severe □□**29%**
RA/RV/TV/peric.§					
RA enlargement	□ LA nl **RA<LA**		□ mild **grade cf. w/ LA**	□ mod. **c/w LA**	□ sev c/w **LA**
RV enlargement	□ no **0.9-2.6 cm**		□ mild **>2.7 PLA**	□mod LV□**LV**(LVnl)	□ sev **RV** □**LV** (LV nl)
RV hypertrophy	□ no □**0.6 cm**		□ mild **0.7-0.9 cm**	□ mod □**1.0 cm**	□ sev □**1.0 cm**
Pericardial fluid	□ no/sys.		□ mild **localized**	□ med **surrounds □ > .5 cm**	□ large **surrounds □ > .5 cm**
Valve Regurg.					
Mitral {Helmke}	□ none	□ trace **w/in 1 cm valve**	□ mild **RJA/LAA □19%**	□ moderate **20-40%**	□ severe **□41%**
Aortic {Perry}	□ none	□ trace	□ mild **JH/LVOH 10-24%**	□ moderate **JH/LVOH 25-49%**	□ severe **JH/LVOH □50%**
Tricuspid	□ none	□ trace **w/in 1 cm valve**	□ mild **RJA/RAA □19%**	□ moderate **20-40%**	□ severe □□**1**□
Mitral Stenosis·	□ none **4-6 cm^2**	□ trace **2.5-3.9 cm^2**	□ mild **1.5-2.5 cm^2**	□ mod. **1.0-1.5 cm^2**	□ severe **< 1 cm^2**
Aortic Stenosis·	□ none**3-5 cm^2**	□ trace **2-3 cm^2 g10-15 mm Hg**	□ mild **1.1-2 cm^2; g16-29 mmHg**	□ mod. **.75-1.1cm^2; g30-49 mm Hg**	□ severe □**0.75 cm^2; g□50 mm Hg**

*NOTE: For LA/LVwt/LVID check height & sex specific nomograms; delete MM measure if off-axis &/or doesn't make sense.
For LA consider both parasternal & apical views;
For LVID if eccentric (short/long axis dimension >1.3 don't measure MM), overrule if dilated in apical views.

§Note R □ morphology is subjective & should take into account height, sex & relation to L □ size

NOTE: Assessment of valvular regurgitation is based on subjective impressions of jet area.

NOTE: Assessment of valvular stenosis should consider LV function and body size

Appendix Item 12

Echo Bibliography

Framingham Heart Study: Bibliography Related to Echocardiography

1. Levy D, Anderson KM, Plehn JF, Savage DD, Christiansen JC, Castelli WP: Echocardiographically determined left ventricular structural and functional correlates of complex or frequent ventricular arrhythmias on one-hour ambulatory electrocardiographic monitoring. Am.J.Cardiol. 1987;59:836-830.
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18. Manolio TA, Levy D, Garrison RJ, Castelli WP, Kannel WB: Relation of alcohol intake to left ventricular mass: the Framingham Study. JACC 1991;17:717-721.
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Appendix Item 13

NIHem Noninvasive Hemodynamics Workstation Data Acquisition Notes and Instructional Poster

NIHem Noninvasive Hemodynamics Protocol Flowsheet

Phase	Time (min) Total	Phase	Instrumentation	Computer	Verbal	Misc.
Setup **Record signal averaged P-wave**	0-5	5	• Place BP cuff on R arm, microphone over brachial artery, pressure hose behind arm • Apply 4 ECG leads to chest; arm leads under L & R collarbones, leg leads on lower L & R ribcage • Place PPG sensor along spine	• Machine on, [Register] • Enter Pt initials • Enter Center ID & Pt ID • Study date (default) • Select Study Type • Select Operator(s) • Click [OK] • Record SA P-wave	• 'Please lie down and make yourself comfortable' • 'I am going to place ECG electrodes on your chest and a BP cuff on your right arm'	• Participant should change into hospital gown (open in front), undershorts OK, remove bra or T-shirt • If gown is tight on arm, remove RA from sleeve before applying BP cuff
Acquire BP1	5-7	2	• Check volume setting, put on headphones • Cuff will automatically inflate/deflate • Remove BP cuff and headphones and store after BP complete	• Click [Waveforms] on toolbar • Click [BP] • Set Max Cuff Pressure • Click [BP1] • Click [Sys] on first beat with K-sound and [Dia] on first beat without K-sound; repeat clicks OK • Click [Close]	• 'Now I'm going to check your blood pressure' • 'The cuff will inflate and deflate automatically' • 'Lie and breathe quietly and try not to talk'	• Make sure there is space between cuff and chest to avoid respiratory artifact • Watch for motion artifact on red and orange traces. • If major motion artifact or clicked [Systole] or [Diastole] too late, [Abort] and redo. • May replay and edit current BP, but only before moving on to next BP.
Acquire Tonometry and PPG-PWV	7-11	4	• Find maximal pulsation with fingertips first • Place tonometer over artery • Sweep across artery to find center, adjust pressure, maximize waveform amplitude and features • Record PPG-PWV	• Click [Bra] • Optimize brachial waveform • Click [Save] to freeze tracing • Repeat for femoral [Fem] & carotid [Car] • Click site again to replace data, but complete each site before moving to next • Click [PPG-PWV] on toolbar • Click [PPG1]	• 'Now I'm going to check your pulses with the tonometer' • Before Femoral: 'I'm going to check the pulse at the top of your leg' • 'Now I'm taking recordings from the sensor on your back. It will feel warm like a heating pad, but not hot'	• Put on gloves • Place a small dot at each pulse site just after tonometry is acquired • Remove gloves
Acquire Aortic Imaging	11-13	2	• Optimize image • Minimize depth • Use 2:1 zoom	• Click [Aortic US] • Click [LVOT] to initiate acquisition into a 5 sec circular buffer • Click [Save] as soon as a continuous 5 sec loop of satisfactory images is obtained Click [Close]	• 'I'm placing cold gel on your chest'	• Place participant in the left lateral decubitus position • Use pillows as props for participant comfort • Confirm that ECG tracing is intact after moving participant • Minimal depth setting:10-12 cm

NIHem Noninvasive Hemodynamics Protocol Flowsheet

Phase	Time (min) Total	Phase	Instrumentation	Computer	Verbal	Misc.
Acquire Aortic Pressure-Flow	13-15	2	• HP Filter: 300Hz-400Hz • Prepare to use tonometer • Disconnect ECG from participant	• Click [Aortic PQ] • Click [Flow] • Obtain 20 sec of good flow waveforms • Click [Car] • Obtain 20 sec of good pressure waveforms • Click [Close]	• Verify 'Are you comfortable?' • 'The sonographer will take pictures of your heart. Then I will record the pulse in your neck'	• Pulsed Doppler from apical 5-chamber • Max. peak velocity in LVOT • Minimize wall filters • Adjust scale (not zero) if aliasing

Transit Distances and Wrap Up	15-16	1	• For SSN-F measurement, open calipers wider than SSN-F distance. Use right thumb as leverage to adjust calipers to size of measurement.	• Click [Distances]
				• Enter values in mm, e.g.,
				  • SSN-B = 380-490
				  • SSN-F = 480-650
				  • SSN-C = 65-110
				• Click [OK]
					• 'I'm going to take a few measurements'
					• Thank participant
						• Measure Bra with arm out at 90°
						• Each distance from SSN to site