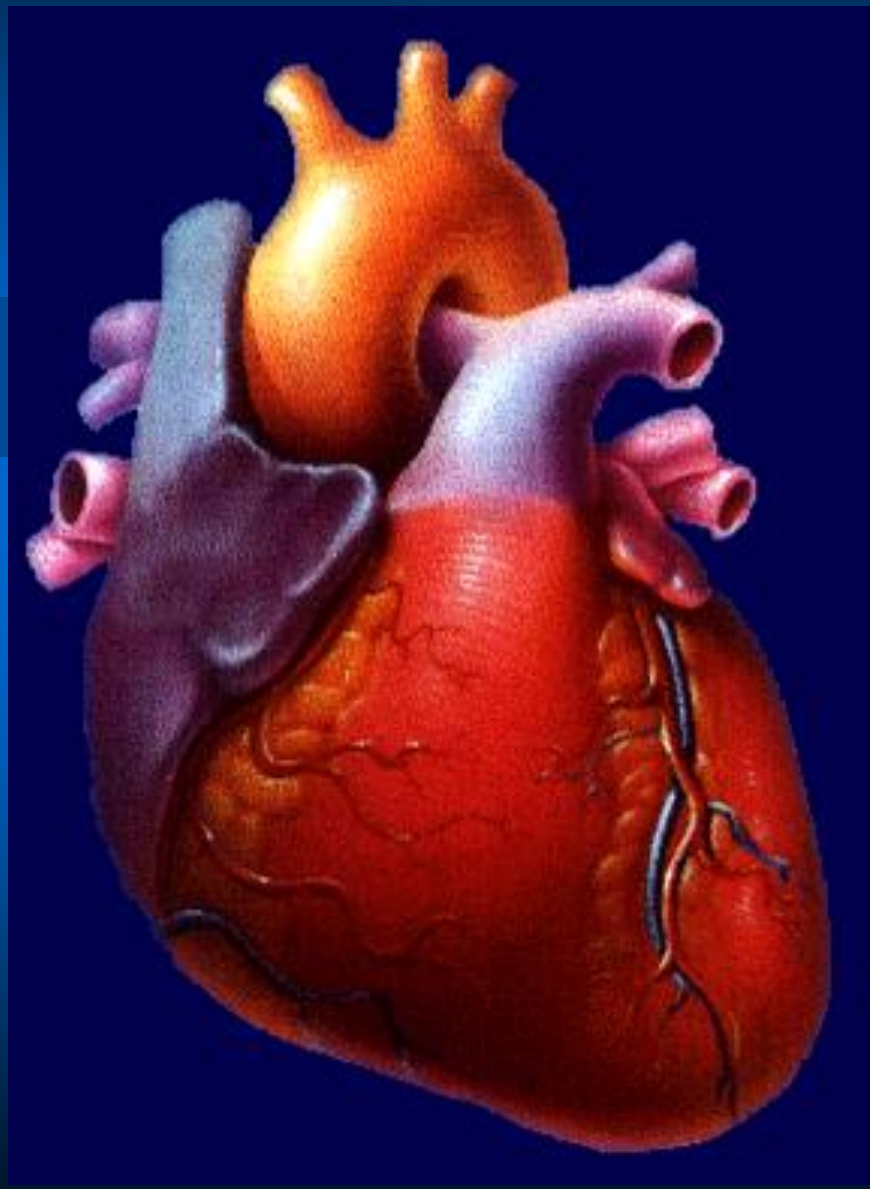
Left Atrial Enlargment: Clinical Implications



Dr. Manuel Paredes Horna
Hospital do Coração
Hospital Alemão Oswaldo Cruz
São Paulo - Brasil

Left Atrial Enlargment: Clinical Implications

" Nowadays when we are talking about left atrial enlargement … we are talking about the echocardiograpic finding of left atrial enlargement."

Hutter, D and Wood, M American College of Cardiology Conversations with de Experts, Sep 2004

Left Atrial Enlargment – Common Causes

- Elevation of LV filling pressures as a result of diastolic dysfunction leading to LA remodeling and dilatation.
- Atrial Fibrillation
- Severity of LV hypertrophy
- LV outflow tract obstruction
- Valvular disease (mitral stenosis, mitral reg., aortic stenosis).
- Left ventricular failure
- Constrictive pericarditis
- Cardiac transplantation

Yang et al. J AM Soc Echocardiogr, Vol 18 (10) Oct 2005. 1074-1082

Left Atrial Enlargment: Clinical Implications

- Important pathologic change in many forms of heart disease
- Close relationship with atrial fibrillation, systemic thromboembolic events , stroke and heart failure.
- Associated with increased morbity and mortality for patients with cardiovascular disease

Yang et al. J AM Soc Echocardiogr, Vol 18 (10) Oct 2005. 1074-1082

Left Atrial Enlargment: Clinical Implications

- How to define left atrial enlargement ?
- Does the observation indicate health or illness?
- What degree of pathology does it signify?

" Interpretation of Echocardiographic Measurements: A Call for Standardization"Vasan et al, Framingham Heart Study, Boston University School, National Heart, Lung and Blood Institute, Am Heart J 139(3):412-422, 2000

Left Atrial Enlargment: Clinical Implications

Published Echocardiographic Reference Values

- There was considerable variation in the values for the upper reference limits reported by the various studies. The ranges were as follows: left atrium, 36 to 47 mm; aortic root, 33 to 44 mm; left ventricular end-diastolic diameter, 52 to 70 mm; left ventricular end-systolic diameter, 30 to 40 mm; and left ventricular wall thickness, 11 to 13 mm. Whereas a few studies had small samples, the majority had modest though not ideal sample sizes (120 to 200 participants); only 3 studies were based on large samples. Besides the variation in sample sizes, differences in selection criteria and in measurement techniques (2-D vs M-mode) may have contributed to the variability of reference limits. The contribution of differences in statistical analyses to this heterogeneity in reference values was difficult to ascertain. Generally, the descriptions of the statistical methods (parametric vs nonparametric methods and the transformation of data) used for developing the reference limits in the studies were brief, and descriptions of the handling of outliers and the distribution of the data (gaussian vs nongaussian) were frequently lacking.
- This lack of consistency in echocardiographic reference values is comparable with the situation in clinical chemistry in the 1970s, before the adoption of measures to standardize reference limits. Furthermore, most echocardiographic reference values are based on cross-sectional observations and lack validation with outcome events.

" Interpretation of Echocardiographic Measurements: A Call for Standardization"Vasan et al, Framingham Heart Study, Boston University School, National Heart, Lung and Blood Institute, Am Heart J 139(3):412-422, 2000

Left Atrial Enlargment: Clinical Implications

Conclusions

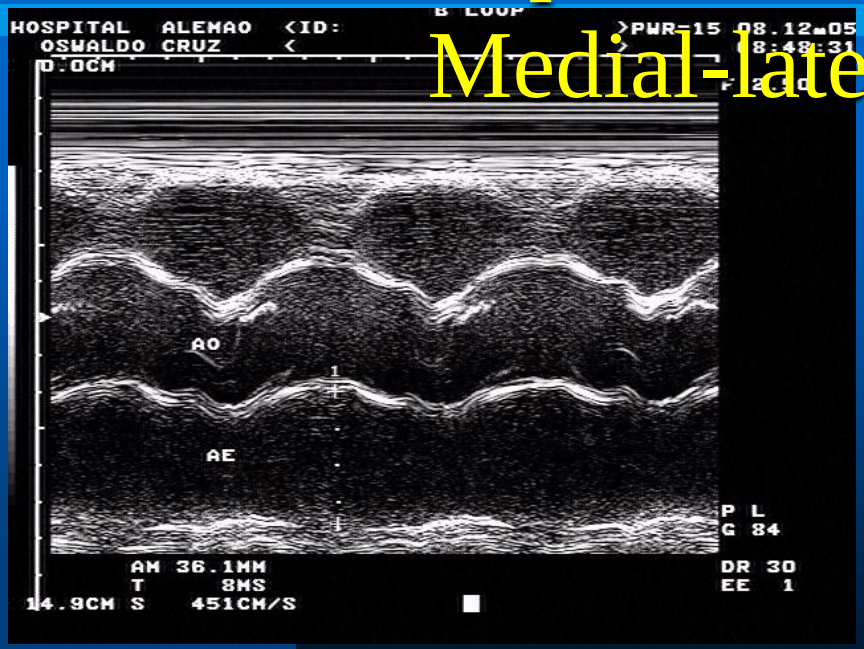
Despite the widespread use of echocardiography for diagnostic purposes, interpreting and reporting of echocardiographic measurements is seriously limited by a lack of standardization of reference values. Furthermore, there is no agreement among echocardiographers regarding the partitioning of reference values (by sex, ethnicity, or age), the anthropometric measure to be used for adjustment, or the choice of cut-points to categorize values within the abnormal range. The generation of a consensus regarding these controversial issues merits urgent attention to render more scientific and consistent the interpretation of echocardiographic measurements within and between laboratories.

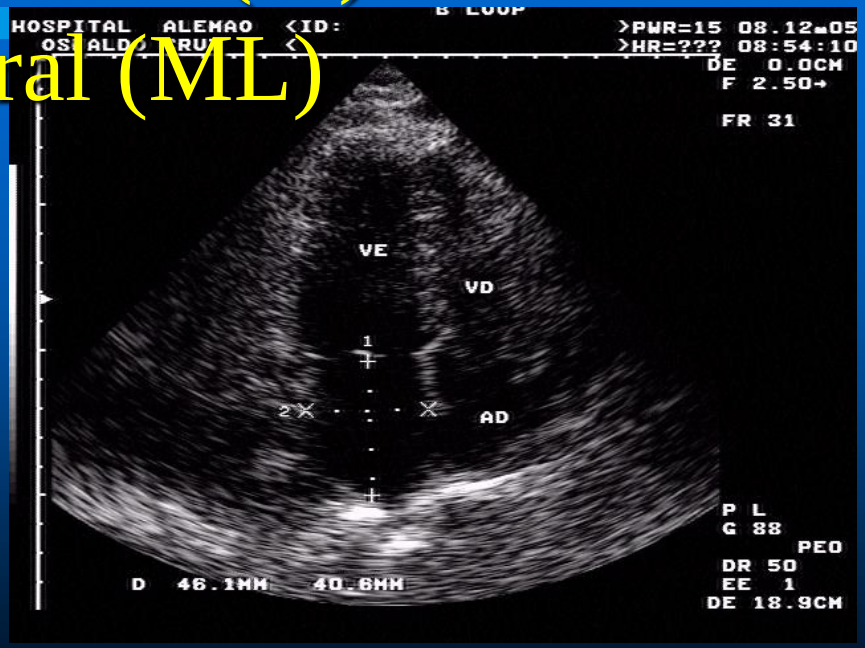
" Interpretation of Echocardiographic Measurements: A Call for Standardization"Vasan et al, Framingham Heart Study, Boston University School, National Heart, Lung and Blood Institute, Am Heart J 139(3):412-422, 2000

Left Atrial Measurement

Linear Dimensions

Anteroposterior (AP)
Superior-inferior (SI)
Medial-lateral (ML)





Left Atrial Anteroposterior Dimension

Mayo Clinic

	Female	Male
LAD,mm	33.1 +- 3.2	37.5 +- 3.6

	< 30 y	> 70 y
LAD,mm	34.3 +- 7.0	37.9 +- 7.0

Framingham Heart Study J Am Soc Echocardiogr 1995;8:793-800

Left Atrial Anteroposterior Dimension

Laboratory	Reference values used (mm)					Routine indexation		Partitioning by sex
	LA	Ao	LVIDed	LVIDes	IVS and LVPW	Height	BSA	
1	< 41	< 36	< 56	NA	<12	No	No	No
2	< 40	< 37	< 53	NA	< 11	No	No	No
3	19-40	20-37	35-56	NA	6-11	No	No	No
4	25-35	20-35	40-55	25-30	7-11	No	No	No
5	25-38	24-39	37-53	NA	7-11	No	No	No
6	19-40	10-32	35-53	NA	7-11	No	Yes	No
7	15-40	20-38	35-58	22-40	7-11	No	No	No
8	20-40	20-37	36-56	20-35	7-11	No	No	No
9	< 40	< 36	36-56	20-35	7-11	No	No	No
10	<45	< 35	35-58	< 40	7-11	No	No	No
11	15-40	20-37	40-56	25-40	7-11	No	No	No
12	<=40	<=40	<=55	<=45	< 12	No	No	No
13	25-40	22-37	35-57	NA	6-11	No	Yes	No
14	NA	NA	40-55	25-30	8-11	No	No	No
15	< 21/m²	< 22/m²	54-56	NA	< 12	No	Yes	No
16	< 41	<41	< 55	< 45	< 11	No	No	No
17	12-22/m² or < 40	12-22/m² or < 40	21-32/m²	NA	NA	No	No	No
18	19-40	20-37	35-57	23-45	6-11	No	No	No
19	20-40	20-37	36-56	20-35	7-11	No	No	No
20	19-39	20-35	35-55	23-39	6-12	No	No	No
21	< 44	< 40	< 56	20-35	6-11	No	No	No
22	20-40	20-37	33-55	25-42	NA	No	Yes	No
23	<=40	<=35	<=56	<=35	<=11	No	No	No
24	<=40	<=36	<=57	NA	<=11	No	No	No
25	19-40	20-37	37-56	NA	6-11	No	No	No
26	<=40	NA	<=57	NA	<=11	No	No	No
27	<=40	<=37	<=57	<=38	<=11	No	No	No
28	< 40	< 36	36-56	20-35	7-11	No	No	No
29	19-40	20-37	35-57	23-38	6-11	No	Yes	No

" Interpretation of Echocardiographic Measurements: A Call for Standardization"Vasan et al, Framingham Heart Study, Boston University School, National Heart, Lung and Blood Institute, Am Heart J 139(3):412-422, 2000

Left Atrial Anteroposterior Dimension

Normal Values

LAD < = 20 mm/m2 (Am.Soc.Echo)

< = 40 mm

Moyer Paula et al, Multinational Team of Investigators from Italy and Minnesota, J Am Coll Cardiol 2005;46:690-696

Left Atrial Anteroposterior Enlargement

	Mayo Clinic	BP / Incor	Arizona Heart Institute	
Mild, mm	40-48	40-45	40-50	Ao*1.2
Moderate	48-56	45-50	50-60	Ao*1.2 to 1.5
Severe, mm	>56	>50	60-70	Ao* > 1.5
Giant, mm			>70	

Left Atrial Measurement
Linear Dimensions

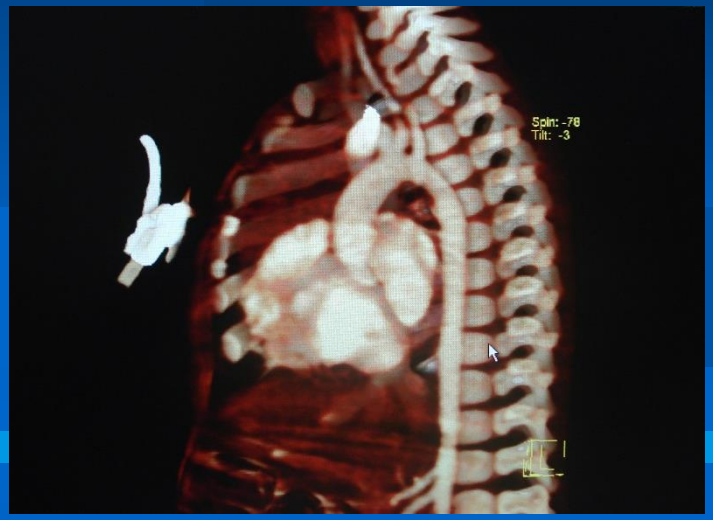
"In normal subjects a good correlation was found between SI and ML dimensions, while…

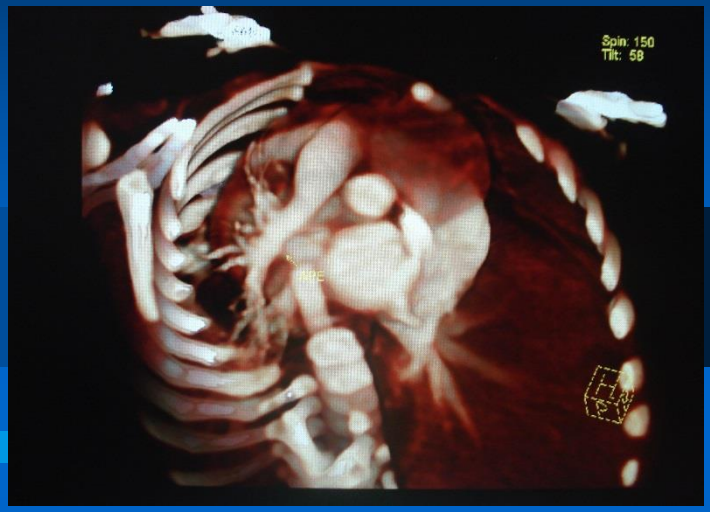
a lower correlation between SI and AP and between ML and AP "

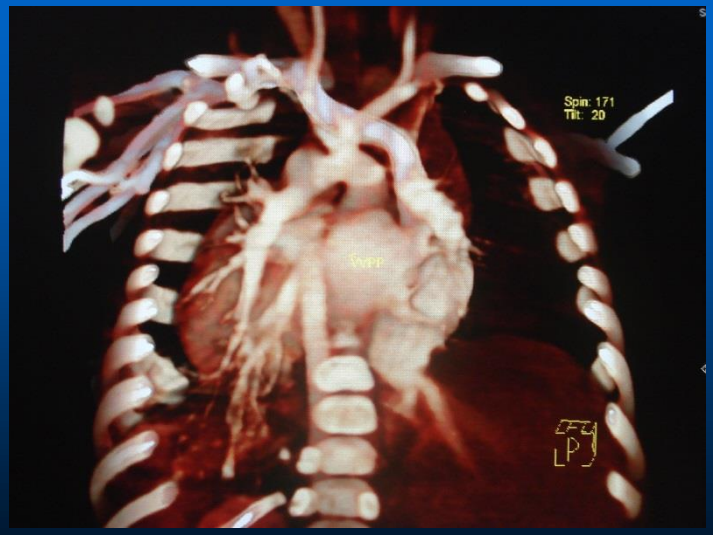
Loperfido et al, "Assesment of LA dimentions by Echo and Angiographic LA volumes in mitral valve disease"

British Heart Journal , 50(60):570-8, 1983 Dec

Left Atrial Measurement







Left Atrial Measurement
Linear Dimensions

"In patients with mitral valve disease a good correlation was found between SI and ML dimensions, while…

SI and ML dimensions had a low correlation with AP dimension"

Loperfido et al, "Assesment of LA dimentions by Echo and Angiographic LA volumes in mitral valve disease"

British Heart Journal , 50(60):570-8, 1983 Dec

Left Atrial Enlargment

LAD vs LAV

- Traditional M-mode method (temporal resolution) of determining LA diameter (LAD) may systematically underestimate LA volume (LAV) (spatial resolution).
- LAV index may be more sensitive and accurate to measure atrial size than anteroposterior LAD

Yang et al. J Am Soc Echocardiogr, Vol 18 (10) Oct 2005. 1074-1082

Left Atrial Enlargment

LAD vs LAV

- LAVolume index is preferred over linear measurements to determine LA size.

American Society of Echocardiography / European Society of Cardiology
Recommendations for Chamber Quantification
J Am Soc Echocardiogr Dec 2005;18:1440-63

Left Atrial Enlargment

LA Diameter vs Volume

	Women				Men			
	Reference	Mild	Moderate	Severe	Reference	Mild	Moderate	Severe
cm	27-38	39-42	43-46	>=47	30-40	41-46	47-52	>=53
cm/m2	15-23	24-26	27-29	>=30	15-23	24-26	27-29	>=30
ml	22-52	53-62	63-72	>=73	18-58	59-68	69-78	>=79
ml/m2	22+-6	29-33	34-39	>=40	22+-6	29-33	34-39	>=40

American Society of Echocardiography / European Society of Cardiology
Recommendations for Chamber Quantification
J Am Soc Echocardiogr Dec 2005;18:1440-63

Left Atrial Enlargment

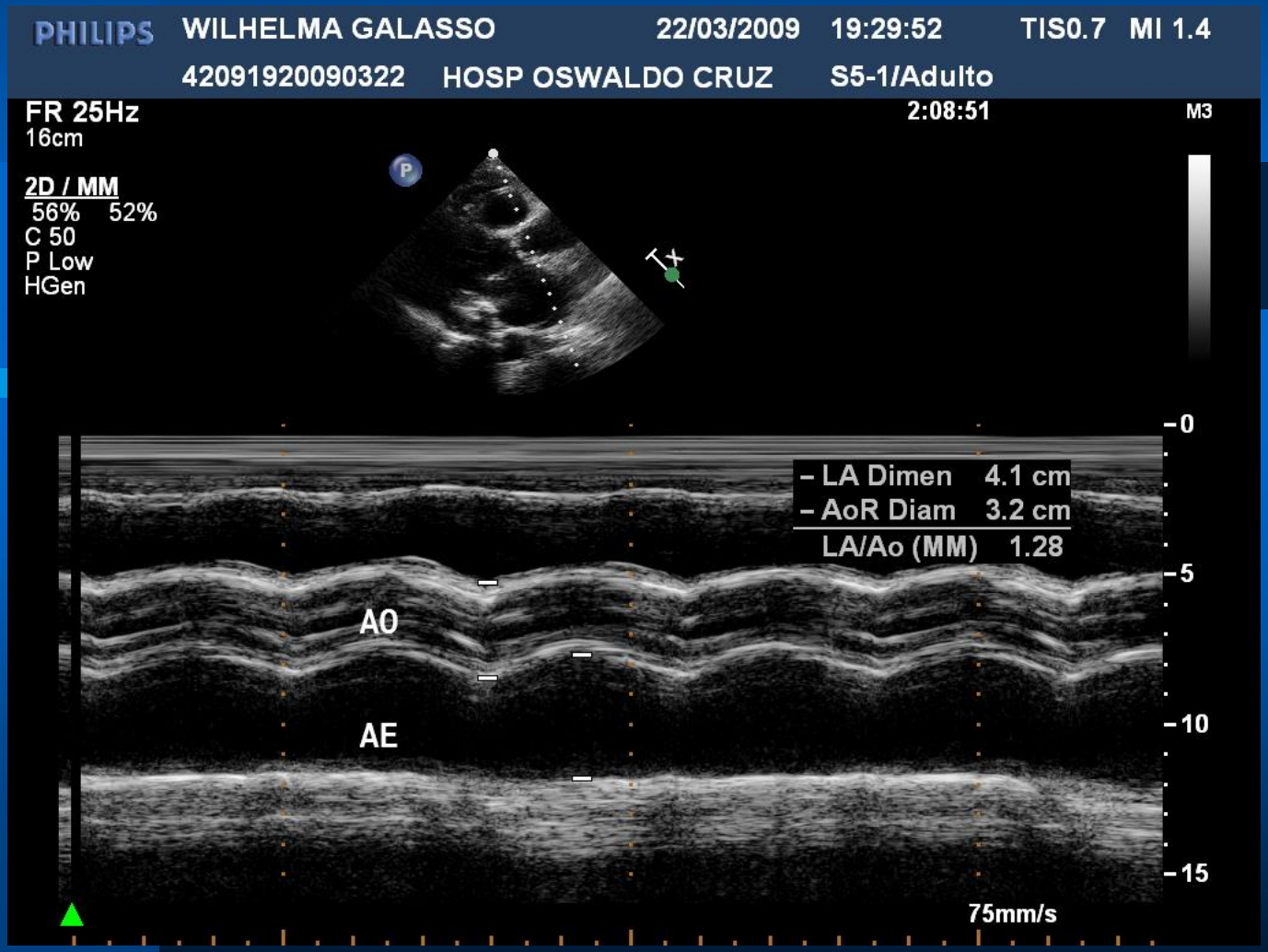
LA Diameter vs Volume

Left Atrium Reclassified N = 578 patients			LA Volume Index	
			Normal	Abnormal
LA Diameter	Normal	295	122 (41%)	173 (59%)
	Abnormal	283	15 (5%)	268 (95%)

LA Reclassified: Application of ASE/ESC Cutoffs to Unselected Outpatients Referred to the Ecocardiography Laboratory. Barbieri et al. Modena. Italy. J Am Soc Echocardiogr May 2008;21:433-38

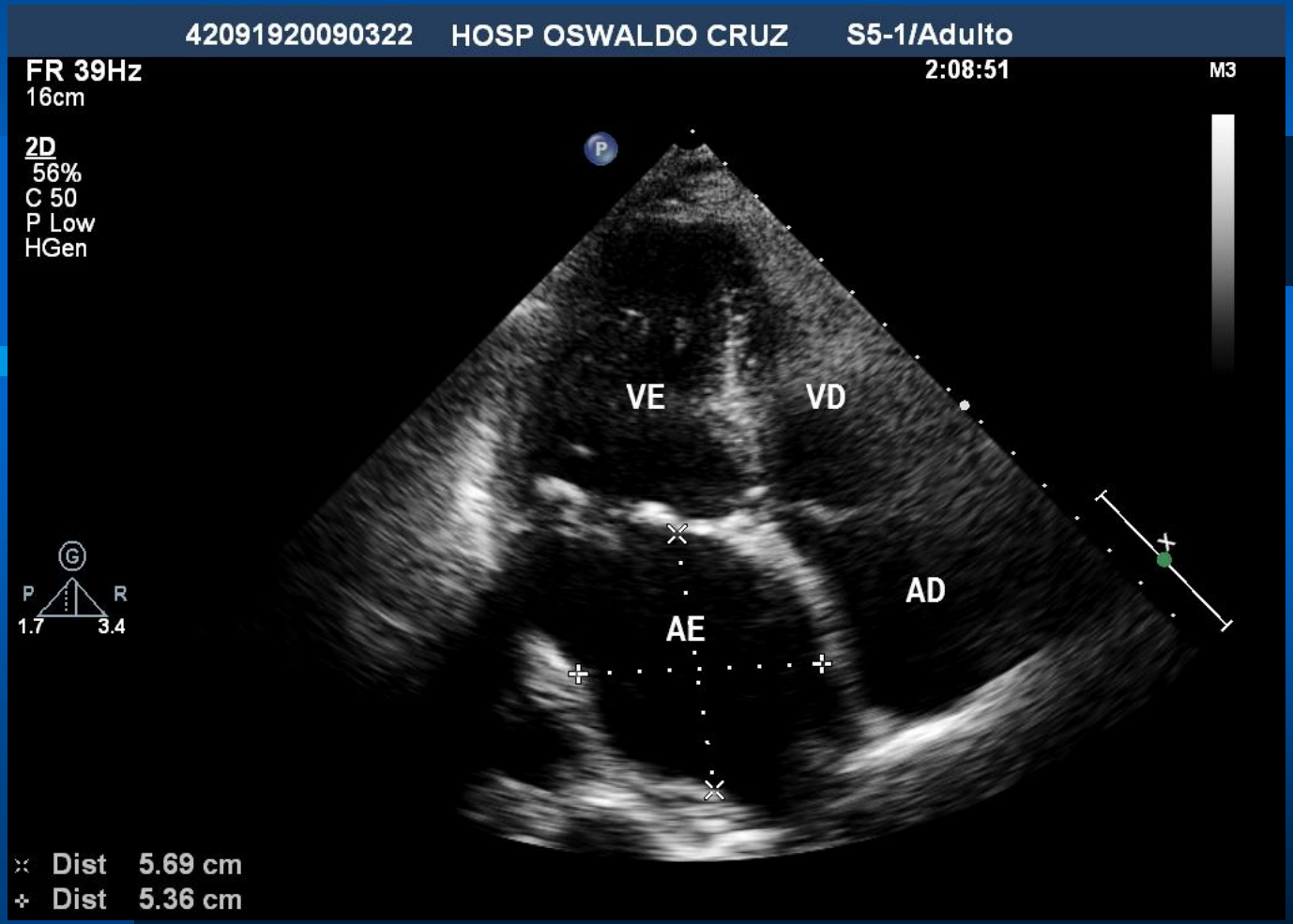
Left Atrial Enlargment

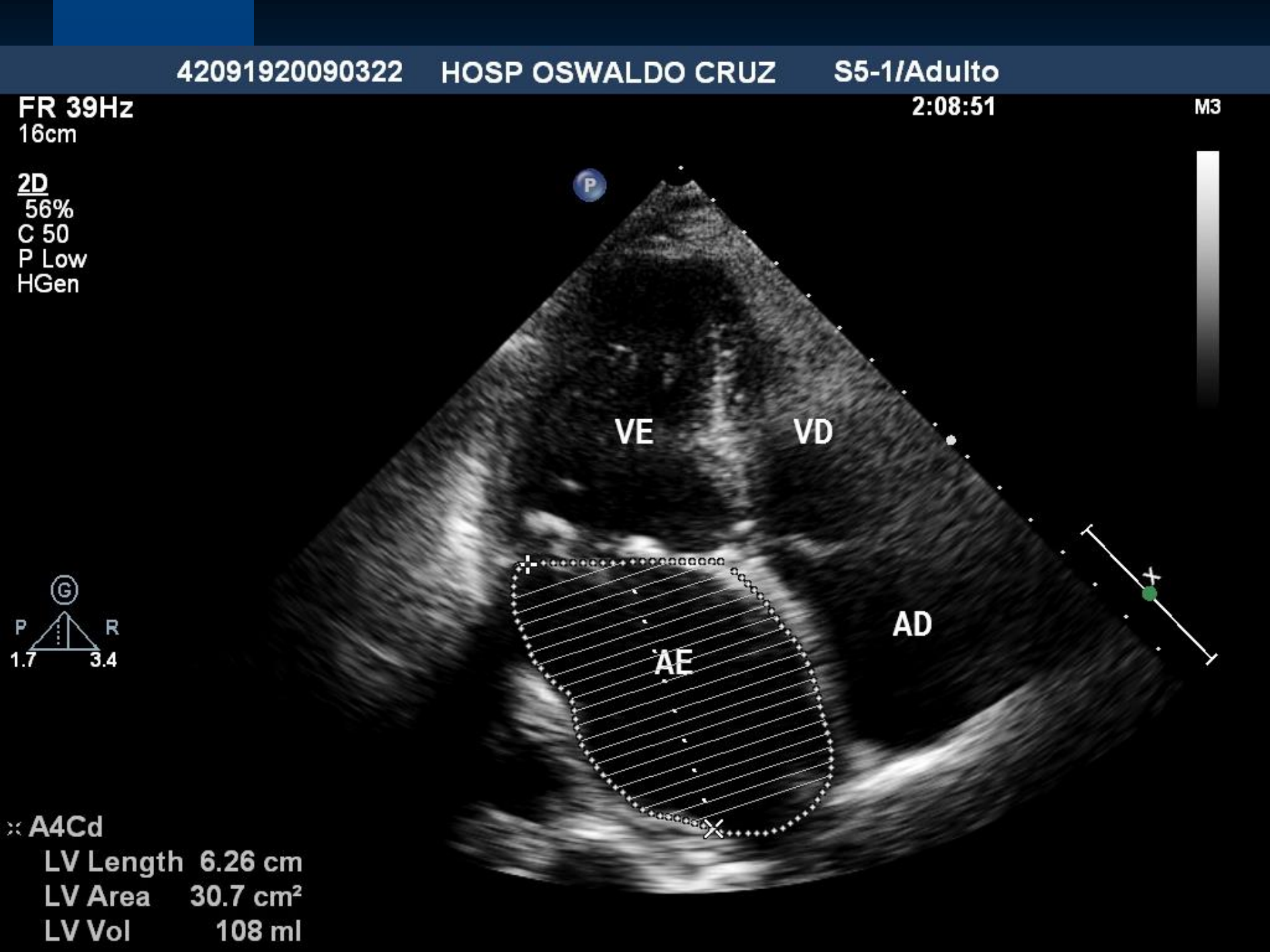
LA Diameter vs Volume

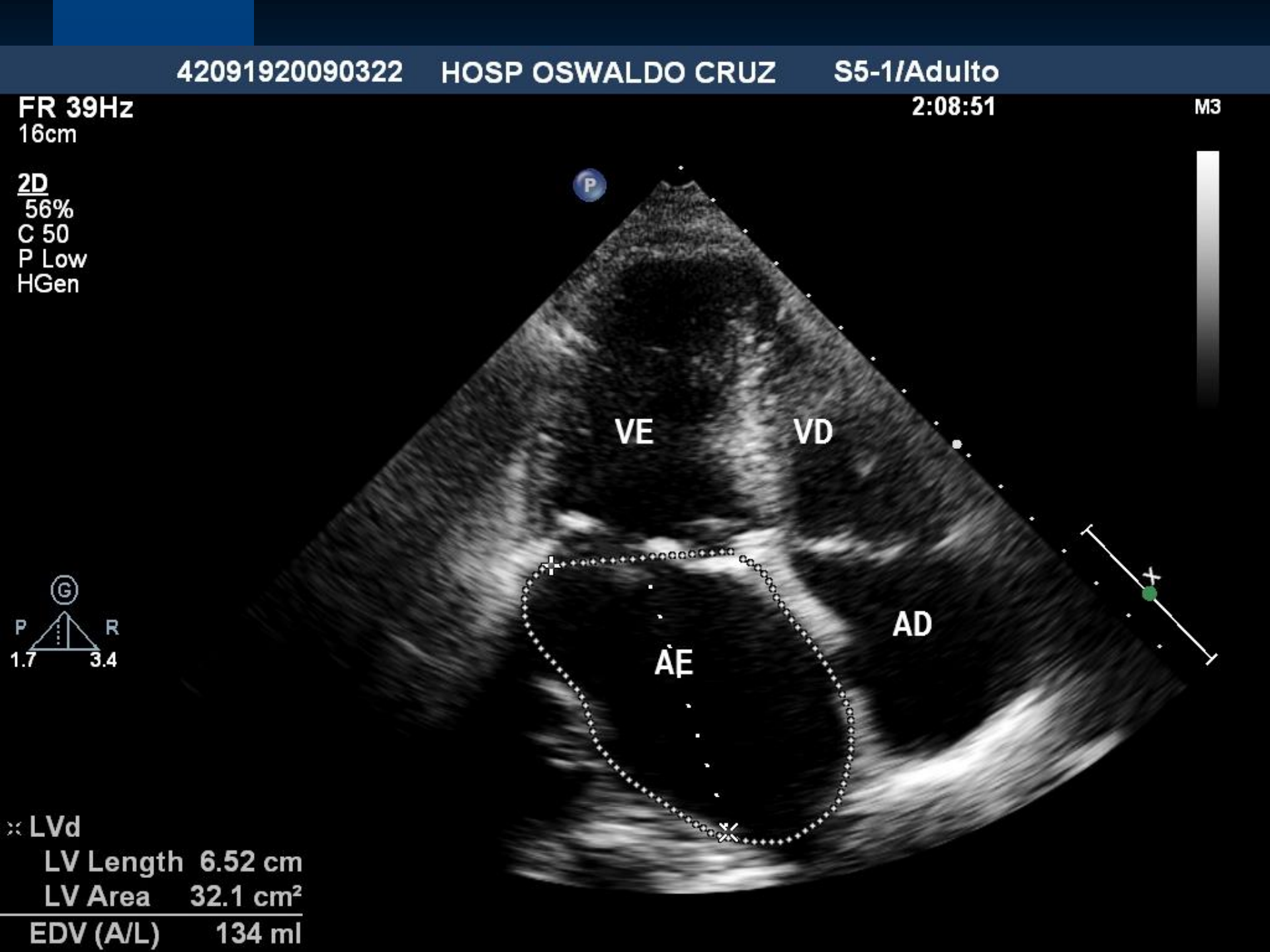


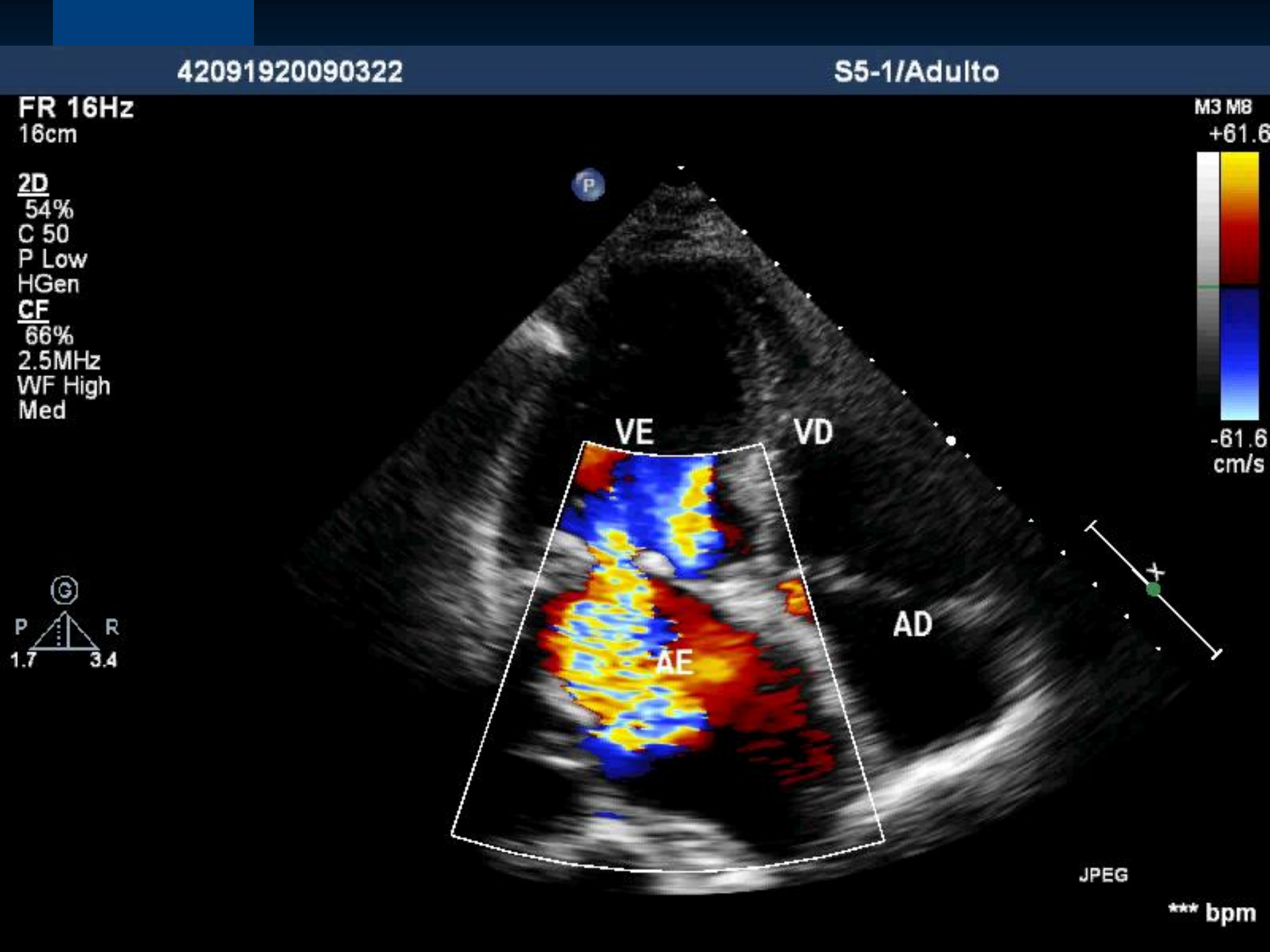
Left Atrial Enlargment

LA Diameter vs Volume




42091920090322 HOSP OSWALDO CRUZ S5-1/Adulto
FR 39Hz
16cm
2:08:51
M3
2D
56%
C 50
P Low
HGen
VE
VD
AD
AE
G
P
R
1.7
3.4
A4Cd
LV Length 6.26 cm
LV Area 30.7 cm²
LV Vol 108 ml


42091920090322 HOSP OSWALDO CRUZ S5-1/Adulto
FR 39Hz
16cm
2:08:51
M3
2D
56%
C 50
P Low
HGen
VE
VD
AD
AE
P
R
1.7
3.4
LVd
LV Length 6.52 cm
LV Area 32.1 cm²
EDV (A/L) 134 ml


420919200903 22
S5-1/Adulto
FR 16Hz
16cm
2D
54%
C 50
P Low
HGen
CF
66%
2.5MHz
WF High
Med
M3 M8
+61.6
-61.6
cm/s
VE
VD
AD
AE
P
R
1.7
3.4
JPEG
*** bpm

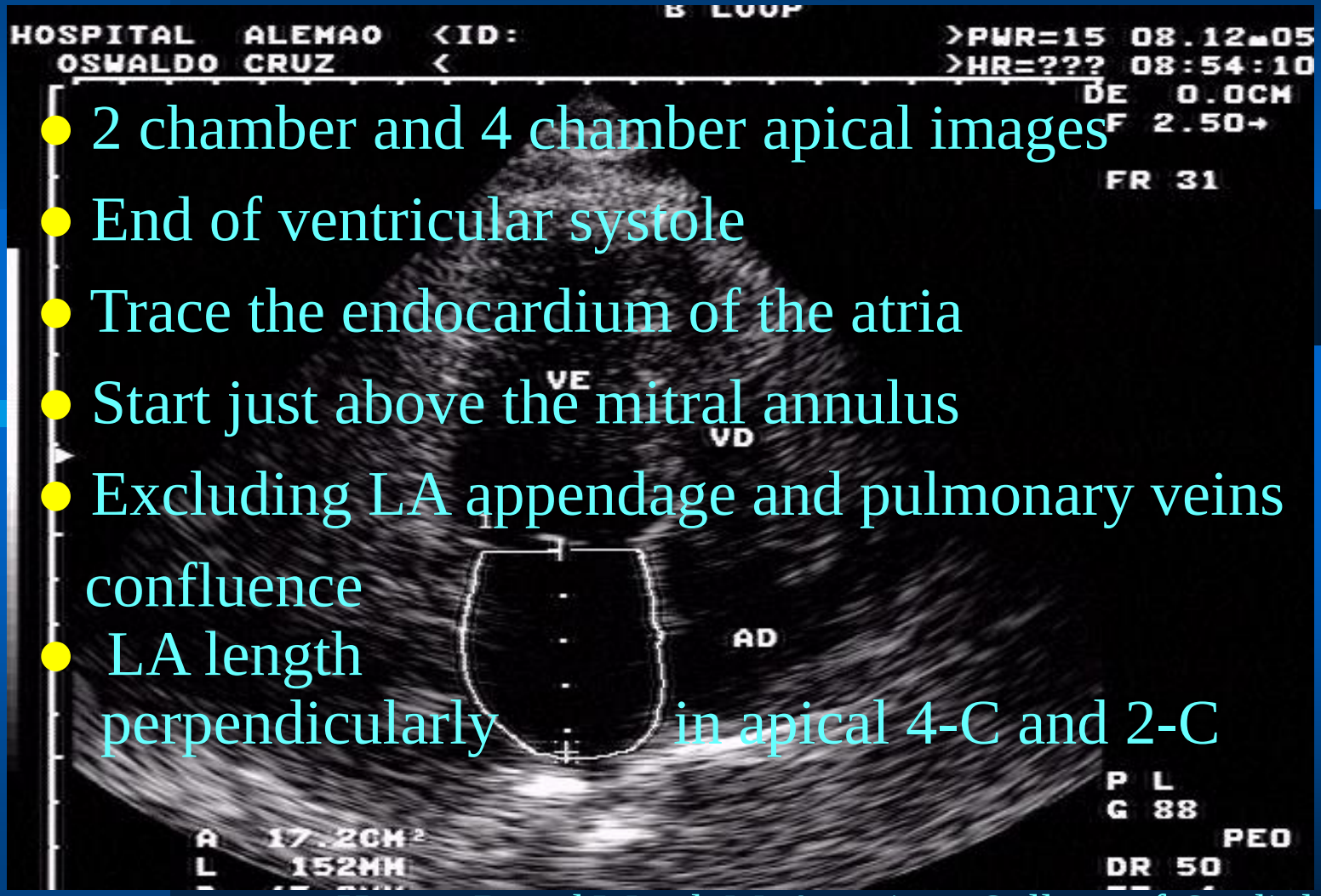
Left Atrial Measurement

LAVolume

Ellipse formula
Area-length 4C technique
Simpson biplane method
Echo 3D

Left Atrial Measurement

LA Volume



- 2 chamber and 4 chamber apical images
- End of ventricular systole
- Trace the endocardium of the atria
- Start just above the mitral annulus
- Excluding LA appendage and pulmonary veins confluence
- LA length perpendicularly in apical 4-C and 2-C

Hutter, D and Wood, M American College of Cardiology Conversations with de Experts, Sep 2004

Left Atrial Volume Measurement

Ellipse formula

$$LAV = \frac{\pi}{6} (D1 * D2 * D3)$$

$$= 0{,}523 (D1 * D2 * D3)$$

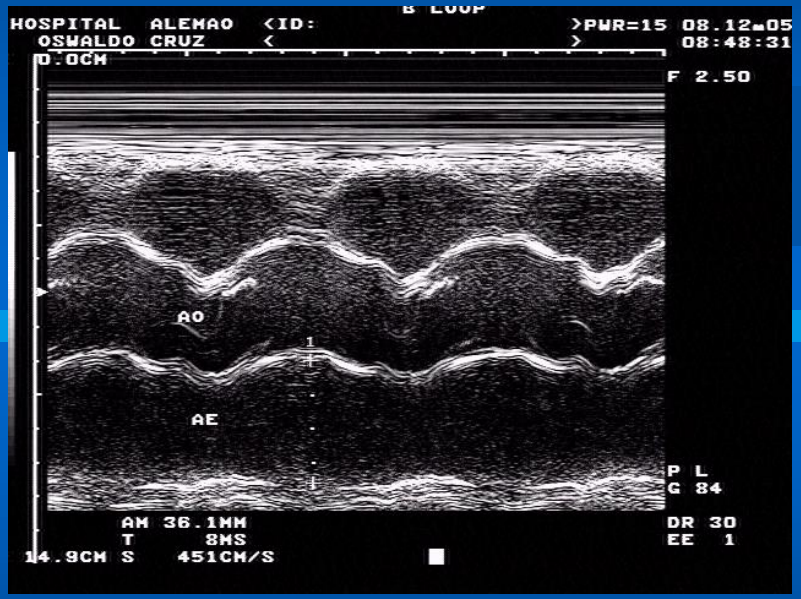
where, D1 = AP diameter PLAX
D2 = short-axis apical 4 chamber
D3 = long-axis apical 4 chamber

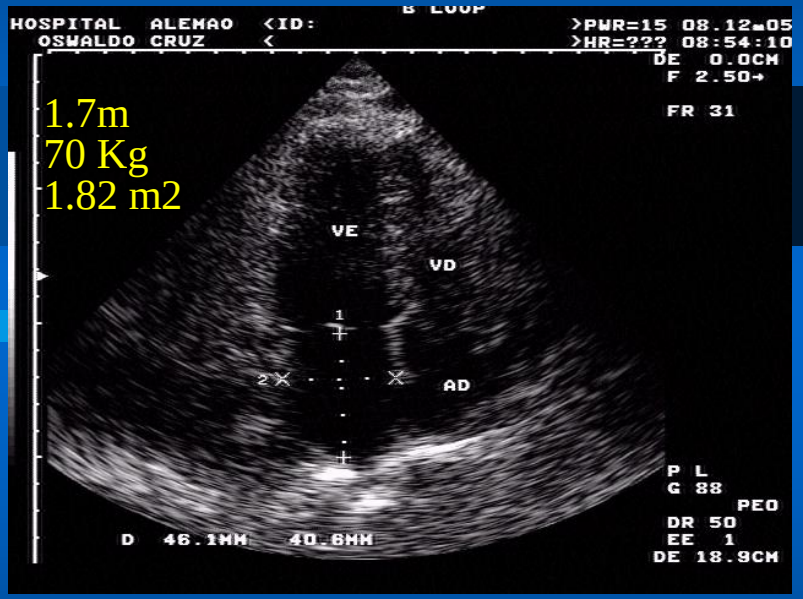
Normal value = 21 ml/m2 women, 22 ml/m2 men

Pritchett et al, Mayo Clinic, JACC 2003:1036-43

Left Atrial Volume Measurement

Ellipse formula





LAV Index = 0.523*AP*SI*ML

= 0.523*3.6*4.6*4.0

= 34.6 ml/1.82m2

= 19 ml/m2

Left Atrial Volume Measurement

Area-Length technique

$$LAV = (0.85 * A1 * A2) / L$$

Arcilla et al
Wang et al

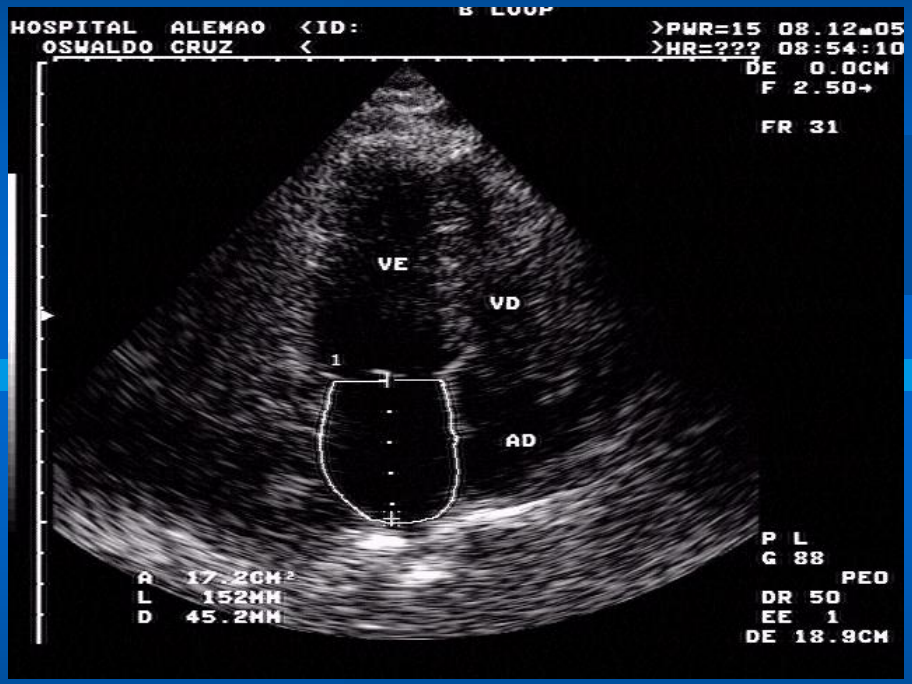
where, A1= Apical 4-C area
A2 = Apical 2-C area
L = common length

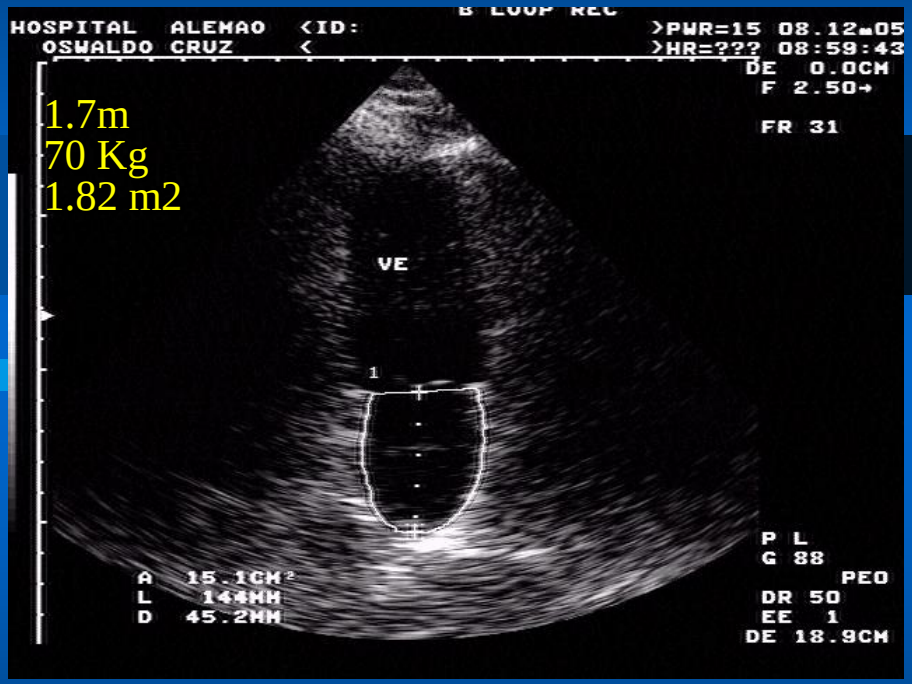
Normal value = 21+-7ml/m2 both gender

Arcilla et al, Chest 1973; Wang et at, Chest 1984;86:595-601

Left Atrial Volume Measurement

Area-Length technique





LAV Index = 0.85*A1*A2 / L

= 0.85*17.2*15.1 / 4.5

= 49.0 ml/1.82m2

= 26.7 ml/m2

Left Atrial Volume Measurement

Simpson Method
(disk summation method)

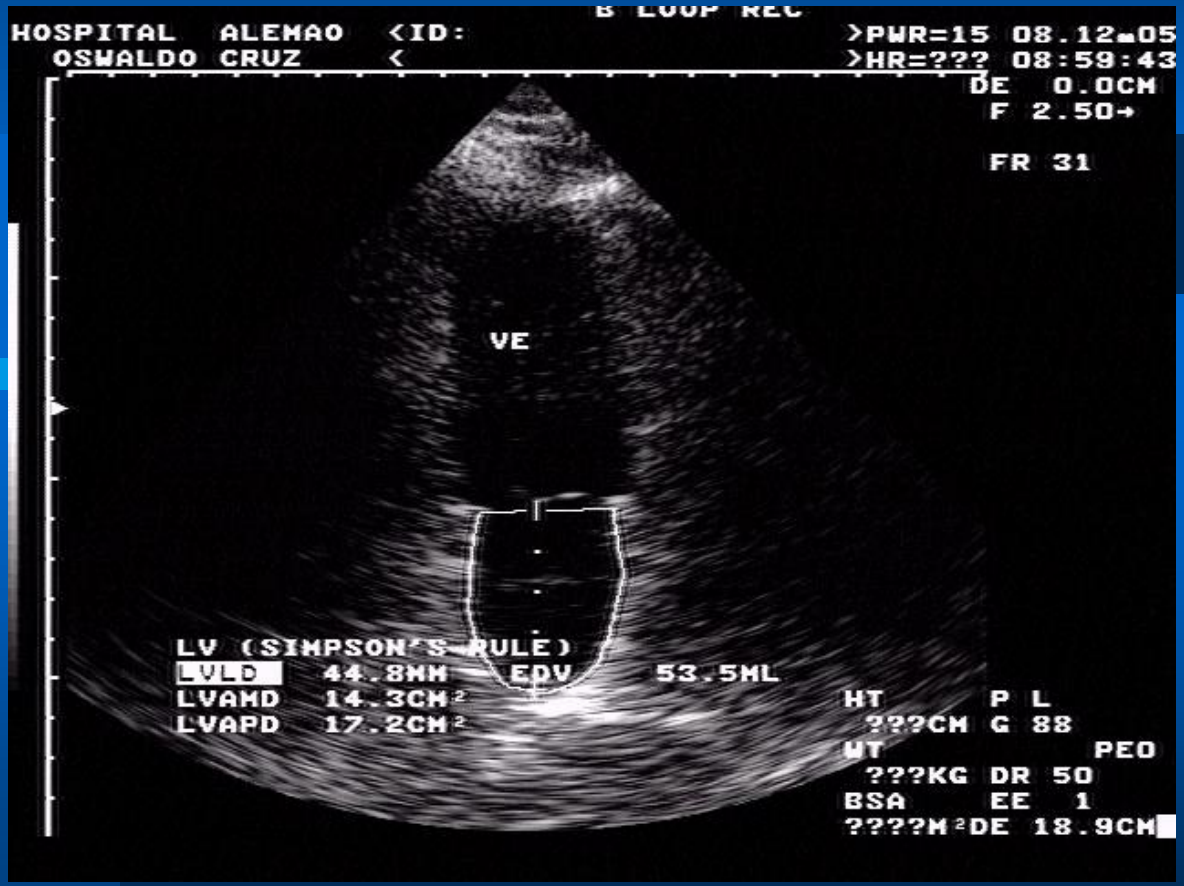
Normal value = 20+-6ml/m2 both gender Wang et al

22+-4ml/m2 both gender Tsang et al

Tsang et al, JACC 2002;40:1636-44

Left Atrial Volume Measurement

Simpson Method



LAV Index = 53.5 ml/1.82m2
= 29.4 ml/m2

Left Atrial Volume Index

Normal Values (ml/m2)

	Female	Male
Ellipse formula	21	22
Area/Length technique	21+-7	21+-7
Simpson method	22+-4	22+-4
Echo 3D		

Left Atrial Volume Index

Limit (normal) Values

LA volume index = 32 ml/m2 (2 SD above normal)

Moller, J et al, Mayo Clinic, USA, Circulation 2003 May 6

Left Atrial Measurement

Mayo Clinic (2042 participants, 767 normal subjects)

	Percentile	5%	50%	95%
LAD,cm	Female	2,80	3,50	4,20
	Male	3,00	3,90	4,60
LAD/BSA, cm/m2	Female	1,58	2,00	2,52
	Male	1,49	1,88	2,30
LAV,ml	Female	23	36	54
	Male	29	45	69
LAV/BSA,ml/m2	Female	14	21	30
	Male	14	22	33

LAV: elliptical model

Pritchet et al, “Left Atrial Volume” JACC, 2003:1036-43

Left Atrial Enlargement: Prevalence in Cardiovascular Disease

Mayo Clinic (2042 participants, 767 normal subjects)

		LA Diameter /BSA LA Enlargement %	LA Volume /BSA LA Enlargement %
Hypertension	Yes	22	27
Coronary disease	Yes	38	38
Congestive heart failure	Yes	71	74
Valve disease	Yes	59	61
Atrial fib/flutter	Yes	54	56

LAV: elliptical model

Pritchet et al, "Left Atrial Volume" JACC, 2003:1036-43

Left Atrial Enlargement: Prevalence in Population

Mayo Clinic (2042 participants, 767 normal subjects)

	LA diam /BSA	LA vol /BSA
	LAE%	LAE%
Male	18	16
Female	12	16

LAV: elliptical model

Pritchet et al, “Left Atrial Volume” JACC, 2003:1036-43

Left Atrial Enlargment

LA Diameter vs Volume

	Women				Men			
	Reference	Mild	Moderate	Severe	Reference	Mild	Moderate	Severe
cm	27-38	39-42	43-46	>=47	30-40	41-46	47-52	>=53
cm/m2	15-23	24-26	27-29	>=30	15-23	24-26	27-29	>=30
ml	22-52	53-62	63-72	>=73	18-58	59-68	69-78	>=79
ml/m2	22+-6	29-33	34-39	>=40	22+-6	29-33	34-39	>=40

American Society of Echocardiography / European Society of Cardiology
Recommendations for Chamber Quantification
J Am Soc Echocardiogr Dec 2005;18:1440-63

Left Atrial Enlargment

LA Quantification

- Quantification LA size by biplane volumetric 2-D echocardiography
- Either Simpson method or area-length method

American Society of Echocardiography / European Society of Cardiology
Recommendations for Chamber Quantification
J Am Soc Echocardiogr Dec 2005;18:1440-63

Left Atrial Enlargment

LA Volume: clinical outcome

- reflects the severity of diastolic dysfunction
- reflects subacute or chronic diastolic function
- provides prognostic information
- independent risk factor for cardiovascular events
- powerful predictor of survival for patients with acute myocardial infarction and dilated cardiomyopathy

Yang et al. J Am Soc Echocardiogr, Vol 18 (10) Oct 2005. 1074-1082

LA volume and Cardiovascular Risk

LA volume index > 32 ml/m2

Independently associated with:

Cardiovascular Risk score ($p<0.001$)

Congestive heart failure ($p=0.014$)

Vascular disease ($p=0.012$)

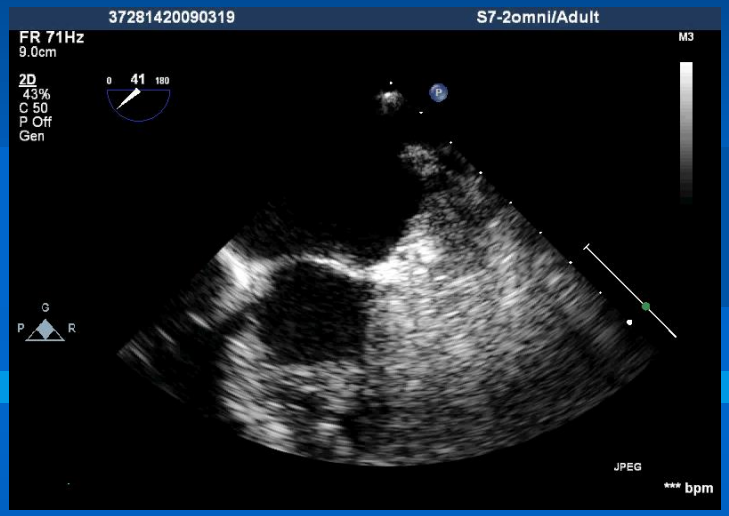
Transient ischemic attack or stroke ($p=0.021$)

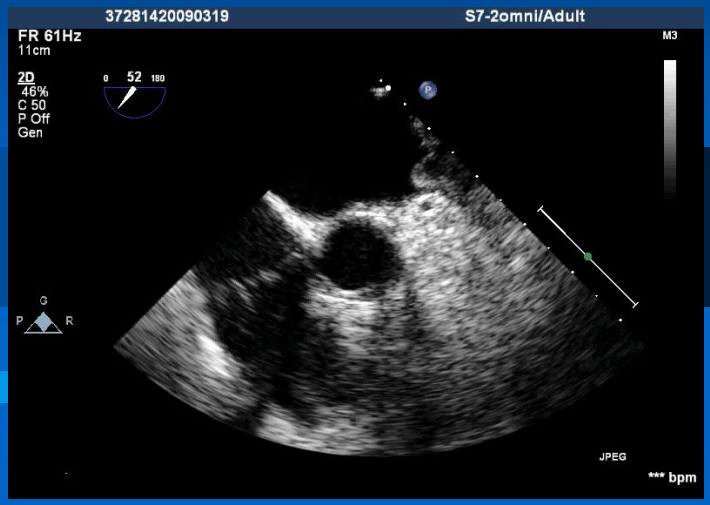
Clinical and echocardiographic model:

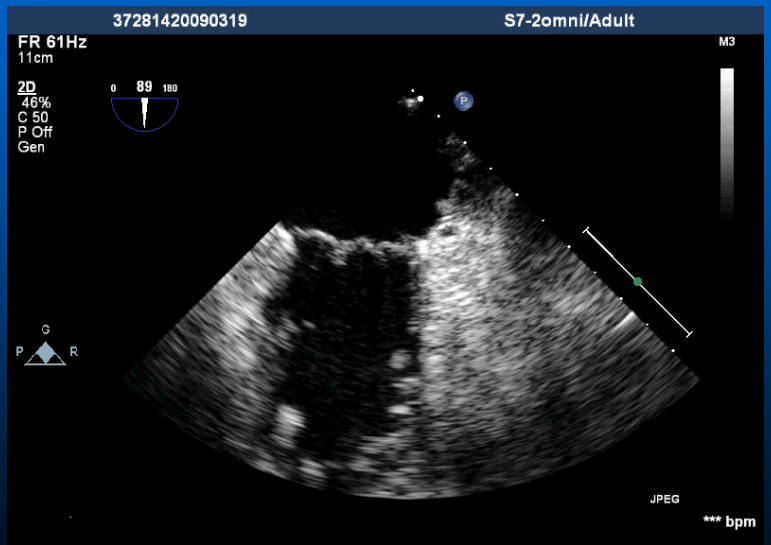
Diastolic function grade ($p<0.001$)

Tsang, TS, et al., 140p, Mayo Clinic, Am J Cardiol 2002 Dec 15, 90(12):1284-9

Left Atrial Enlargment
Clinical Implications in *Atrial Fibrilation*







Left Atrial Enlargment
Clinical Implications in *Atrial Fibrilation*

- LA size is important for clinical decisions
- SPAF study showed that if LA size was grater than 44 mm the risk of stroke was higher so you should use Coumadin in those people as opposed to aspirin.

Stroke Prevention in Atrial Fibrillation Study; *Stroke* 1990;21;538-545

Hutter, D and Wood, M American College of Cardiology Conversations with de Experts, Sep 2004

Left Atrial Enlargment
Clinical Implications in *Atrial Fibrilation*

SPAF Study

- Aspirin 325 mg vs Warfarin in non-rheumatic AF
- Ischemic stroke and systemic embolism
- 1330p, constant or intermittent AF, 1.3y follow-up.
- 42% Aspirin vs 67% warfarin reduced events

Stroke Prevention in Atrial Fibrillation Study; *Stroke* 1990;21;538-545

Left Atrial Enlargment
Clinical Implications in *Atrial Fibrilation*

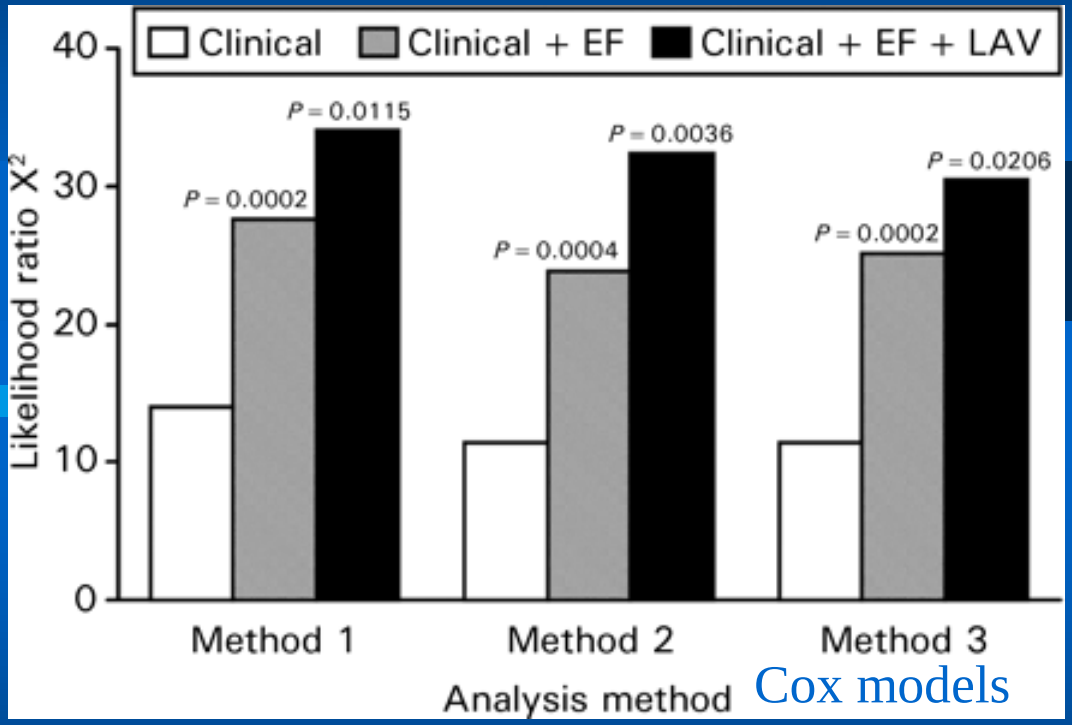
"Left atrial volume predicts cardiovascular events in patients originally diagnosed with lone atrial fibrillation: three-decade follow-up"

- Olmsted County, USA, Mayo Clinic healthcare.
- Among 3623 residents, since 1950-1980 to 2002
- Lone AF with exclusion criteria: >60y.old, CHD, Hyperthyroidism, Valvular Heart Disease, CHF, CMP, COPD, Cardiome-galy, HBP, DM, trauma, surgery, acute medical illness
- Eco 2D since 1976, LAV biplane area-length method

Martin, O. et al. Mayo Clinic. European Heart Journal 2005; 26 ; 2556-2561

Left Atrial Enlargment
Clinical Implications in *Atrial Fibrilation*

Predictors of adverse cardiovascular events



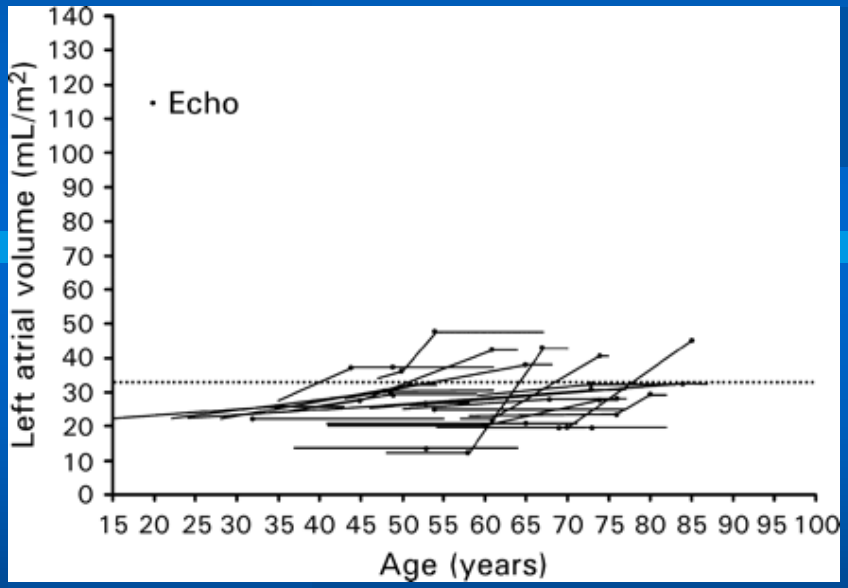
Clinical data: age, number of risk factors

Cut – Off > 32 ml/m2

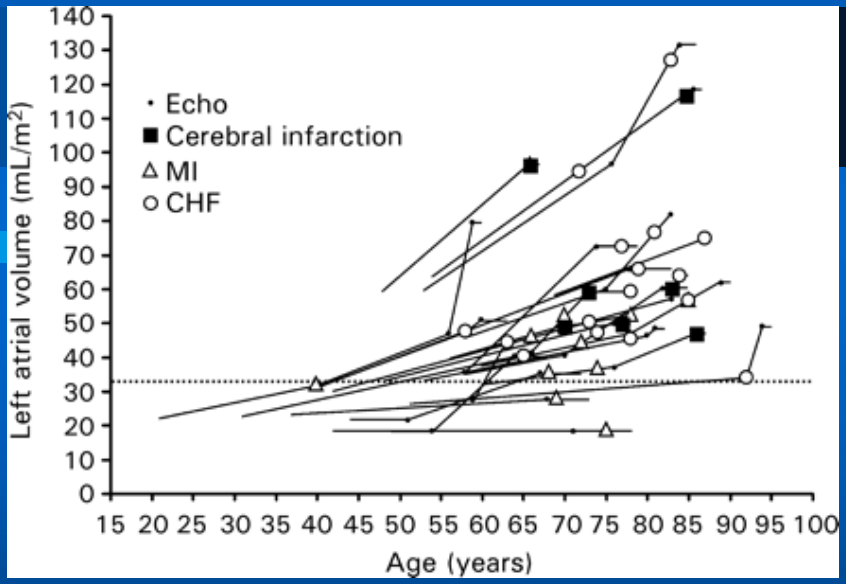
Martin, O. et al. Mayo Clinic. European Heart Journal September 1, 2005

Left Atrial Enlargment
Clinical Implications in *Atrial Fibrilation*

Left atrial volume predicts cardiovascular events in patients originally diagnosed with lone atrial fibrillation: three-decade follow-up



LAV over time for 23 patients without events



LAV over time for 23 patients with events.

Cut – Off > 32 ml/m2

Martin, O. et al. Mayo Clinic. European Heart Journal September 1, 2005

Left Atrial Enlargment
Clinical Implications in *Atrial Fibrilation*

"Left atrial volume predicts cardiovascular events in patients originally diagnosed with lone atrial fibrillation: three-decade follow-up"

- 46 patients fit inclusion criteria
- Twenty-three (50%) patients developed events.
- In a multivariable analysis, patients with indexed LAV 32 mL/m^2 had a significantly worse event-free survival
- All cerebral infarctions occurred in patients with na indexed LAV >32 mL/m^2.
- Patients with lone AF and normal sized atria had a benign clinical course throughout the long-term follow-up.

Martin, O. et al. Mayo Clinic. European Heart Journal 2005; 26 ; 2556-2561

Left Atrial Enlargment
Clinical Implications in *Acute Myocardial Infarction*

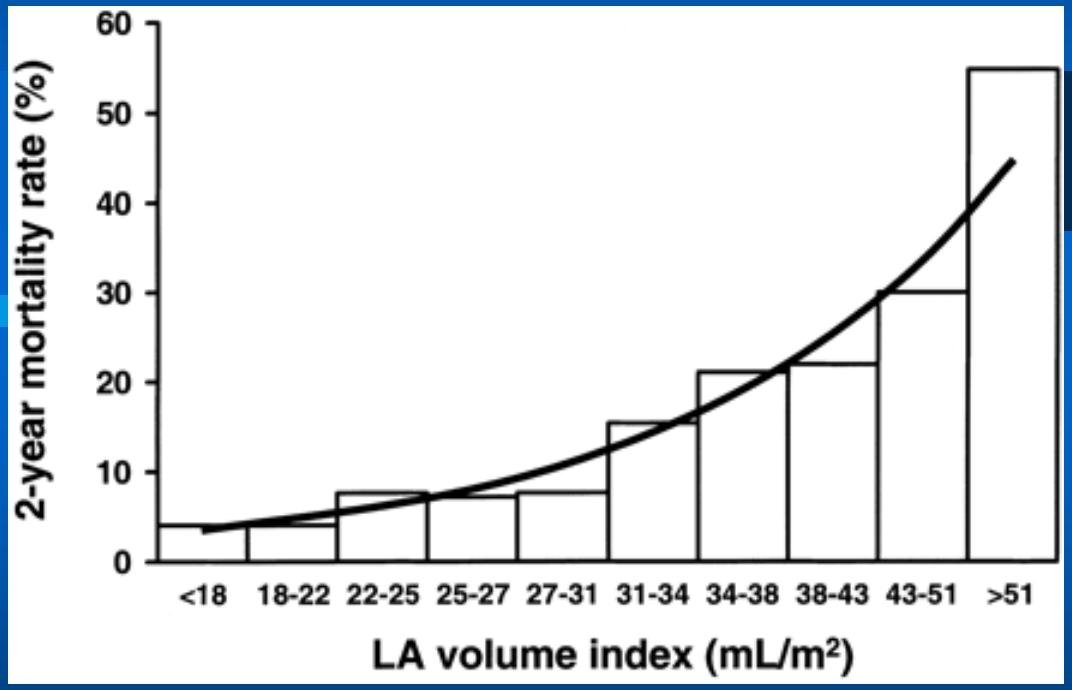
Left Atrial Volume Index (Cut – Off > 32 ml/m2)

"Increased LA volume index is a powerful predictor of mortality after AMI and provides prognostic information incremental to clinical data and conventional measures of LV systolic and diastolic function"

Moller, J, Patricia Pellikka, et al, " Left Atrial Volume: A Powerful Predictor of Survival After Acute Myocardial Infarction" 340p, Mayo Clinic, Circ. 2003 May 6

Left Atrial Enlargment
Clinical Implications in *Acute Myocardial Infarction*

Left Atrial Volume Index (Cut – Off > 32 ml/m2)

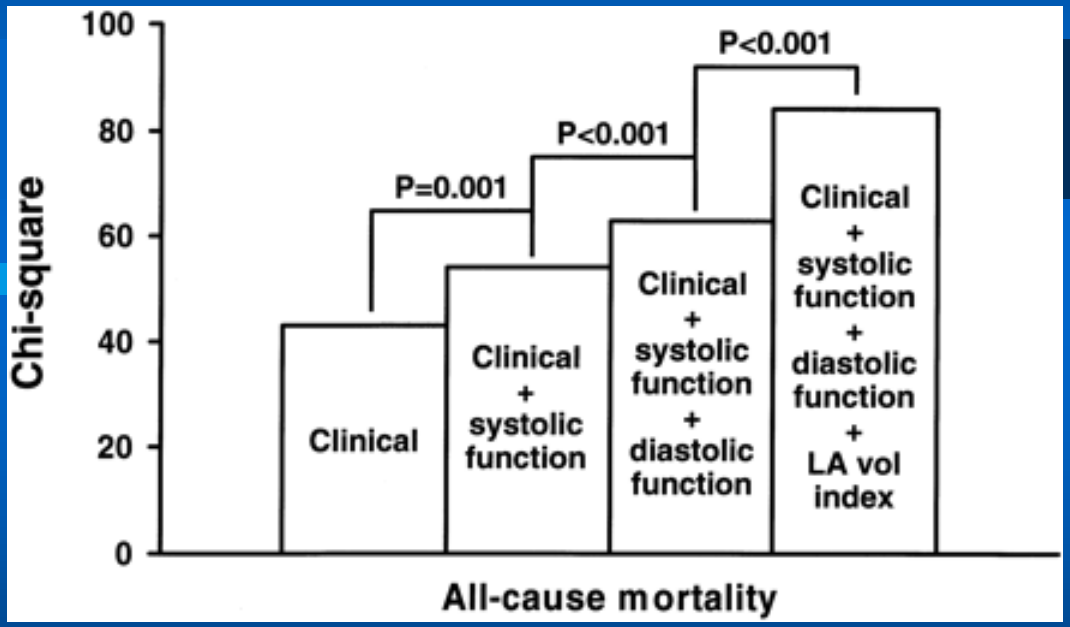


Unadjusted 2-year mortality rates in 10 equal groups of patients according to LA volume index

Moller, J, Patricia Pellikka, et al, " Left Atrial Volume: A Powerful Predictor of Survival After Acute Myocardial Infarction" 340p, Mayo Clinic, Circ. 2003 May 6

Left Atrial Enlargment
Clinical Implications in *Acute Myocardial Infarction*

Left Atrial Volume Index (Cut – Off > 32 ml/m2)



Incremental value of assessment of LA volume in predicting mortality.

Moller, J, Patricia Pellikka, et al, " Left Atrial Volume: A Powerful Predictor of Survival After Acute Myocardial Infarction" 340p, Mayo Clinic, Circ. 2003 May 6

Left Atrial Enlargment
Clinical Implications in *Ischemic Stroke*

Left atrial volume in the prediction of first ischemic stroke in an elderly cohort without atrial fibrillation.

- Of 1554 residents (59% women) aged 75+/-7 years,
  92 (6%) had experienced at least 1 ischemic stroke over 4.3+/-2.7 years
- Left atrial volume of 32 mL/m2 or greater was independent of age, diabetes, myocardial infarction, and hyperlipidemia for the prediction of first ischemic stroke.
- Left atrial volume of 32 mL/m2 or greater was also an independent predictor of death.

Barnes, ME. et al. Mayo Clin Proc. 2004 Aug;79(8):1008-14