Echocardiography in Systemic Embolization

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UTHSCSA and STVHCS

Neurologic Events and Cardiac Source of Embolus

- "For patients who present with evidence of abrupt arterial occlusion, an embolic etiology is a relevant clinical consideration."

Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

Clinical Events with Potential Embolic Source

- Reasonable likelihood of causative cardiac etiology
  - Abrupt peripheral artery occlusion
  - Abrupt occlusion of organ vasculature (renal, mesenteric, etc.)
  - Cerebrovascular/transient ischemic accident in young patient (age <45 y)
  - Cerebrovascular/transient ischemic accident in older patient without "significant" cerebrovascular disease
- Low likelihood of causative cardiac embolic source
  - Seizure
  - Syncope
  - Dizziness
  - Headache
  - Nonfocal events

Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

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Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005. *ACC/AHA Practice Guideline, Echo 2003; p. 45.

- *Potential causes of these clinical scenarios
  - Intrinsic local vascular disease
  - Atheromatous emboli from proximal vessels
  - Cardiac source of emboli
- *Cause and effect may be hard to prove except in
  - Infective endocarditis
  - Prosthetic cardiac valves
- *Cardioembolic neurologic event: potential cardioembolic source in patient with nonlacunar stroke and no cerebrovascular disease

•Thrombus, mass, vegetation, tumor
•**Aortic atherosclerosis**
•**PFO** (Khandheria 11/06)

Neurologic Event Characteristics Likely Associated with Embolic Source

- Sudden onset neurologic event
- Previously asymptomatic individual
- Middle or anterior cerebral circulation
- Multiple events in peripheral territories
- Less likely: lacunar or hemorrhagic CVA
- BUT - "At this time there are no highly specific types of neurological events that should exclude the possibility of a cardioembolic source."

ACC/AHA Practice Guideline, Echo 2003; p. 45.

Cardiac Conditions Associated with Cardioembolic Source

- Definite:
  - Atrial fibrillation
  - Rheumatic heart disease
- Likely:
  - Cardiomyopathy
  - Anterior MI with aneurysm
- Link less well established:
  - Atrial septal aneurysm
  - Valvular strands
  - Mitral annular calcification

Table 12. Prevalence of Echocardiographic Abnormalities Based on Clinically Apparent Organic Heart Disease

	Potential Source of Embolus		
	(n)	(n)	%
All patients	370	164	44
Organic heart disease*	85	58	68
No organic heart disease	186	67	36

*Organic heart disease is defined variably as significant valvular or myocardial disease or evidence of reduced left ventricular function.

Data from references 289, 290, 296.

- However, the prevalence of a potential cardioembolic source in patients without clinically apparent cardiac disease is fairly high, suggesting "that echocardiographic screening may be applicable to patients other than those with clinically suspected disease".

ACC/AHA Practice Guideline, Echo 2003; p. 45-6.

Cardiac Conditions Associated with Cardioembolic Source

Table 10, abridged	Event patients		Control Patients	
	No. Pop.	Percent	No. Pop.	Percent
No potential source	1530	50.5		
Any potential source	1530	49.5		
LA thrombus	1153	8.5	877	3.2
Spontaneous Contrast	1081	17.3	1105	5.7
PFO	1292	19.1	1043	8.3
ASA	1131	13.3	1204	7.1
Ao atheroma	348	14.1	n/a	-
MVP	1131	5.0	927	8.9

ACC/AHA Practice Guideline, Echo 2003; p. 45.

No data for vegetation, tumor, myxoma, MV strands, etc.

Prevalence of Echo Abnormalities in Embolic Event

Table 11.	Cryptogenic (n=308)			Noncryptogenic (N=263)		
	Total	Echo+	Echo%	Total	Echo+	Echo%
PFO	308	100	32.5	263	64	24.3
Spont Contrast	104	17	16.3	74	10	13.5
ASA	168	38	22.6	110	14	12.7

ACC/AHA Practice Guideline, Echo 2003; p. 46.

Table 13. Transthoracic Versus Transesophageal Echocardiography for Detection of Potential Cardioembolic Source

Diagnosis by TTE*	Diagnosis by TEE (primarily or alone)
Mitral stenosis	Left atrial thrombus
Dilated cardiomyopathy	Left atrial spontaneous contrast
Left ventricular aneurysm	Atrial septal aneurysm
Left ventricular thrombus	Patent foramen ovale
Mitral valve prolapse	Aortic atheroma
Vegetation	
Atrial septal defect	

TEE indicates transesophageal echocardiography; TTE, transthoracic echocardiography.

*TTE is sufficient; TEE may be additive but not essential. "TTE sufficient" identifies disease entities for which TTE is sufficient to establish a diagnosis and for which TEE is unlikely to provide additional information. When detected with TTE, further evaluation by TEE is not necessary in all patients. "TEE additive" identifies entities for which documented incremental diagnostic yield can be obtained by performing TEE after negative TTE or entities for which the likelihood of unique TEE-identified abnormalities is high enough to warrant TEE even after adequate TTE.

ACC/AHA Practice Guideline, Echo 2003; p. 46.

Table 14. Prevalence of Patent Foramen Ovale in Patients With Embolic Events

	(n)	PFO+	PFO%
Control	543	56	10.3
CVA/TIA	526	163	30.9
Known etiology	153	39	25.5
Cryptogenic	204	97	47.5

CVA/TIA indicates patients with documented cerebrovascular accident or transient ischemic attack; PFO indicates patent foramen ovale.

Known etiology refers to patients for whom an obvious primary neurological, cerebrovascular, or other etiology was present in a location adequate to explain the event. Cryptogenic refers to patients for whom a known etiology was not present.

Data from references 303, 307, 314, 317, 318.

ACC/AHA Practice Guideline, Echo 2003; p. 47.

Table 15. Prevalence of Aortic Atheroma in Patients With Prior Cerebrovascular Accident or Transient Ischemic Attack

	(n)	Atheroma	%
Control	574	23	4
CVA	677	139	20.5
Known etiology	217	31	14.3
Cryptogenic	123	29	23.6
	Mobile Atheroma		
	(n)	**Mobile**	**%**
Control	324	1	0.3
CVA/TIA	427	29	6.8

CVA/TIA indicates patients with documented cerebrovascular accident or transient ischemic attack.

Known etiology refers to patients for whom an obvious primary neurological, cerebrovascular, or other etiology was present in a location adequate to explain the event. Cryptogenic refers to patients for whom a known etiology was not present.

Data from references 309 through 313.

Table 16. Prevalence of Atrial Septal Aneurysm in Patients With Prior Embolic Events

	Total (n)	ASA Present	ASA (%)
Control	1213	53	4.3
All events	1635	213	13
Cryptogenic	168	38	22.6

ASA indicates atrial septal aneurysm.

Events refers to cerebrovascular accidents or transient ischemic attacks plus peripheral embolization. Cryptogenic refers to patients for whom a known etiology was not present.

ACC/AHA Practice Guideline, Echo 2003; p. 47.

Table 17. Prevalence of Neurological Events in Patients With and Without Spontaneous Contrast

	Left Atrial Clot			
	(n)	(%)	Event	%
All patients	713	90 (12.6)	87	12.2
Spontaneous contrast present	311	79 (25)	64	20.5
No spontaneous contrast	402	11 (3)	23	5.7

Data from references 302, 304, 305.

Recommendations for Echocardiography in Patients With Neurological Events or Other Vascular Occlusive Events

Class I

1. Patients of any age with abrupt occlusion of a major peripheral or visceral artery.
2. Younger patients (typically less than 45 years) with cerebrovascular events.
3. Older patients (typically more than 45 years) with neurological events without evidence of cerebrovascular disease or other obvious cause.
4. Patients for whom a clinical therapeutic decision (eg, anticoagulation) will depend on the results of echocardiography.

ACC/AHA Practice Guideline, Echo 2003; p. 47.

Recommendations for Echocardiography in Patients With Neurological Events or Other Vascular Occlusive Events

Class IIa

Patients with suspicion of embolic disease and with cerebrovascular disease of questionable significance.

Class IIb

Patients with a neurological event and intrinsic cerebrovascular disease of a nature sufficient to cause the clinical event.

Class III

Patients for whom the results of echocardiography will not impact a decision to institute anticoagulant therapy or otherwise alter the approach to diagnosis or treatment.

ACC/AHA Practice Guideline, Echo 2003; p. 47.

SPARC Study: Stroke Prevention: Assessment of Risk in a Community

- Normal volunteers over 45 yo living in Olmstead County, MN – not patients, healthy people
- 1475 randomly selected residents – 588 consented to participate
- Clinical evaluation, BP measurements, TEE (successful in 581), Carotid US
- Publications:
  - Meissner, Khandheria et al. Mayo Clin Proc 1999
  - Meissner, Khandheria et al. Hypertension 1999
  - Agmon, Khandheria et al. Circulation 2000
  - Meissner, Khandheria et al. JACC 2004

SPARC Study: TEE Technique

- Agitated saline 5-10 ml; 2 injections at rest, 2 at Valsalva release, 2 at cough and count the number of microbubbles appearing in 3-5 cardiac cycles
- PFO – echo dropout in more than one plane
- R to L shunt – microbubbles in LA in 3-5 cardiac cycles
- Shunt definition: ≤ 10 bubbles called "trivial"; > 10 bubbles called small; dense opacification of LA called large
- ASA definition: bulging of septum in the region of the fossa ovalis extending ≥15 mm beyond the plane of the atrial septum
- LAA morphology and lobes, antegrade and retrograde PW velocities
- Aortic atheroma classified as simple (<4mm) or complex (disrupted or marked irregularities of the surface with focal increased echodensity and thickening of the adjoining intima and overlying shaggy echogenic material extending 4 mm or more from the aortic wall into the aortic lumen
- Valvular strands were small mobile filaments extending from a valve surface, often referred to as Lambl's excrescences

Meissner, Khandheria et al. Mayo Clin Proc 1999;74:862-869.

SPARC Study Population Comorbidities

Condition*	Men	Women	Overall
Congestive heart failure	3.4 (±0.9)	2.4 (±0.8)	2.9 (±0.6)
Ischemic heart disease	17.5 (±2.1)	9.3 (±1.6)	13.0 (±1.3)
Left ventricular hypertrophy	8.0 (±1.6)	8.6 (±1.5)	8.3 (±1.1)
Mitral valve disease	2.8 (±1.1)	4.1 (±1.4)	3.5 (±1.0)
Aortic valve disease	2.9 (±1.9)	3.0 (±1.7)	3.0 (±1.3)
Aortic stenosis	1.2 (±0.6)	1.3 (±0.6)	1.2 (±0.4)
Mitral valve prolapse	2.8 (±1.0)	7.1 (±1.5)	5.2 (±0.9)
Atrial fibrillation	4.6 (±1.1)	4.8 (±1.1)	4.7 (±0.8)
Hypertension	28.8 (±2.7)	34.1 (±2.6)	31.7 (±1.9)
Diabetes	8.4 (±1.5)	9.0 (±1.7)	8.7 (±1.1)
Stroke	2.4 (±0.8)	2.3 (±0.8)	2.4 (±0.6)
Transient ischemic attack	1.0 (±0.5)	3.1 (±0.9)	2.2 (±0.6)
Smoker (current)†	11.0 (±2.1)	11.4 (±1.9)	11.2 (±1.4)
Smoker (former)†	39.7 (±3.1)	17.2 (±2.3)	27.4 (±1.9)

*Identified by abstraction of medical records and defined in the "Appendix."
†Defined as 10 or more cigarettes daily; smoking was self-reported.

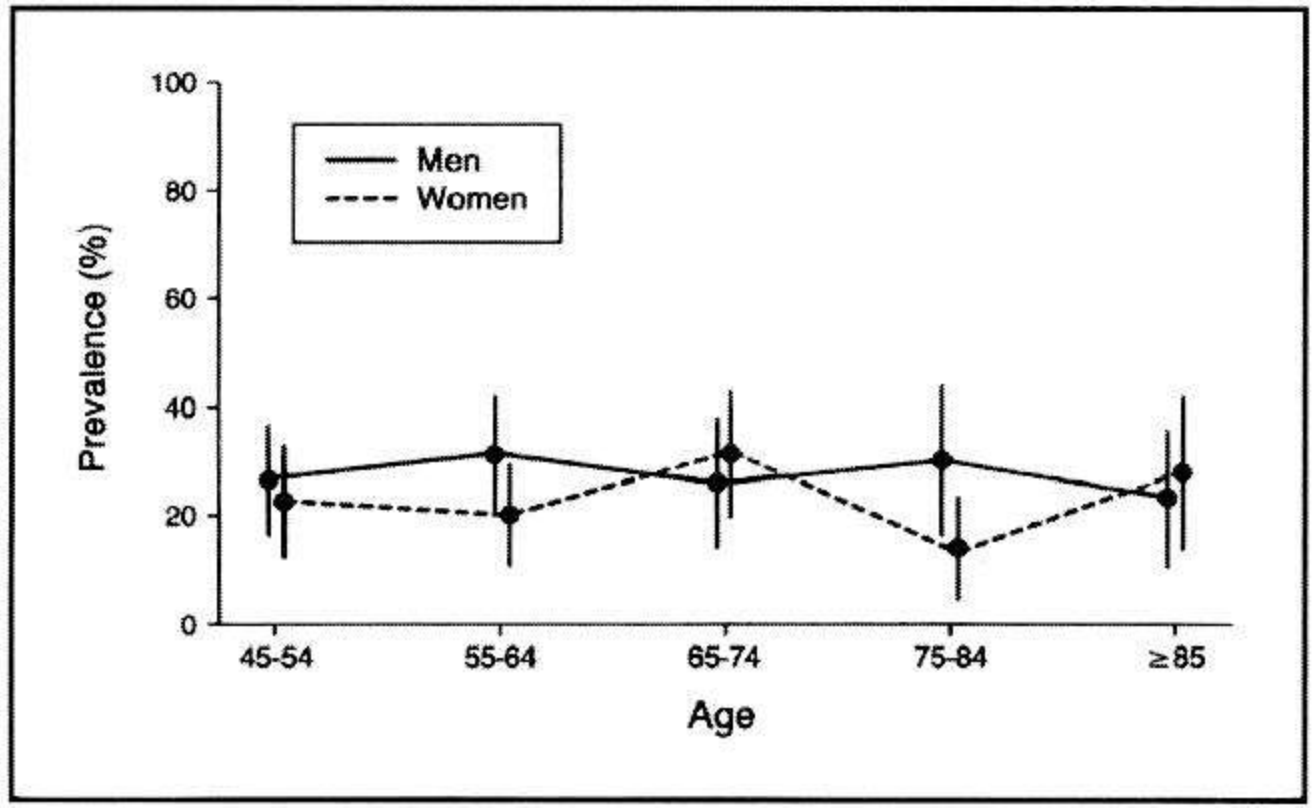
Table 1. Prevalence (±SE) (%) of Comorbid Conditions in Subjects Participating in a TEE Study. After adjustment for multiple comparisons, there was no statistical difference between participants and 20% of refusers with respect to 16 comorbid conditions in the medical record, including Htn, HF, DM and stroke, among others. Meissner, Khandheria et al. Mayo Clin Proc 1999;74:862-869.

SPARC Study: Stroke Prevention: Assessment of Risk in a Community

	Number	Percent
AFib	23	4
Aflutter	1	0.2
LAA thrombus	1	0.2
LA/LAA spont echo contrast	21	3.6
LA thrombus	0	
Card Tumor	4	0.7

Meissner, Khandheria et al. Mayo Clin Proc Sept 1999

SPARC Study: PFO Prevalence



ASA prevalence was 2.2% (12 pts). 6 patients had PFO also.

The prevalence (±SE) of patent foramen ovale, defined as visualization of the defect or shunt, was 25.6% (±1.9%). Of the 148 subjects with patent foramen ovale, 68 (46%) had defects 1 mm or more in size. Eighty-four subjects (57%) had shunts at rest, and 136 (92%) had shunts with maneuvers (Valsalva, cough).

Meissner, Khandheria et al. Mayo Clin Proc 1999;74:862-869.

PFO Diagnostic Pitfalls

- False-positive
  - Transpulmonary shunting
  - Extraneous background echoes/noise
- False-negative
  - Incomplete RA opacification with contrast
  - LA pressure > RA pressure (provokation: Valsalva, cough)
  - Site of injection (need good venous access, brachial if needed)
  - Insufficient number of injections

Feigenbaum: It appears that a PFO with 5 mm or more of separation or with more right-to-left shunts confer the greatest risk of embolic events

Khandheria BK. "Cardioembolic Disease." AHA Scientific Sessions 11/06

PFO Prognosis

- In healthy population, incidental PFO was not a risk factor for a cardioembolic event
- …"The amount of speculation has exceeded the availability of new data to provide insights into the relationships between PFO and stroke."*
- "A recent statement on the prevention of stroke concluded that antiplatelet agents are a reasonable selection and that warfarin could be used when patients with PFO have a predisposing hypercoagulable disorder."*
- "In 2004, the American Academy of Neurology issued a practice parameter that concluded that PFO is not associated with an increased risk of stroke death among medically treated patients with cryptogenic stroke. Recent guidelines conclude that data are insufficient to make a recommendation about placement of PFO-occluding devices."*

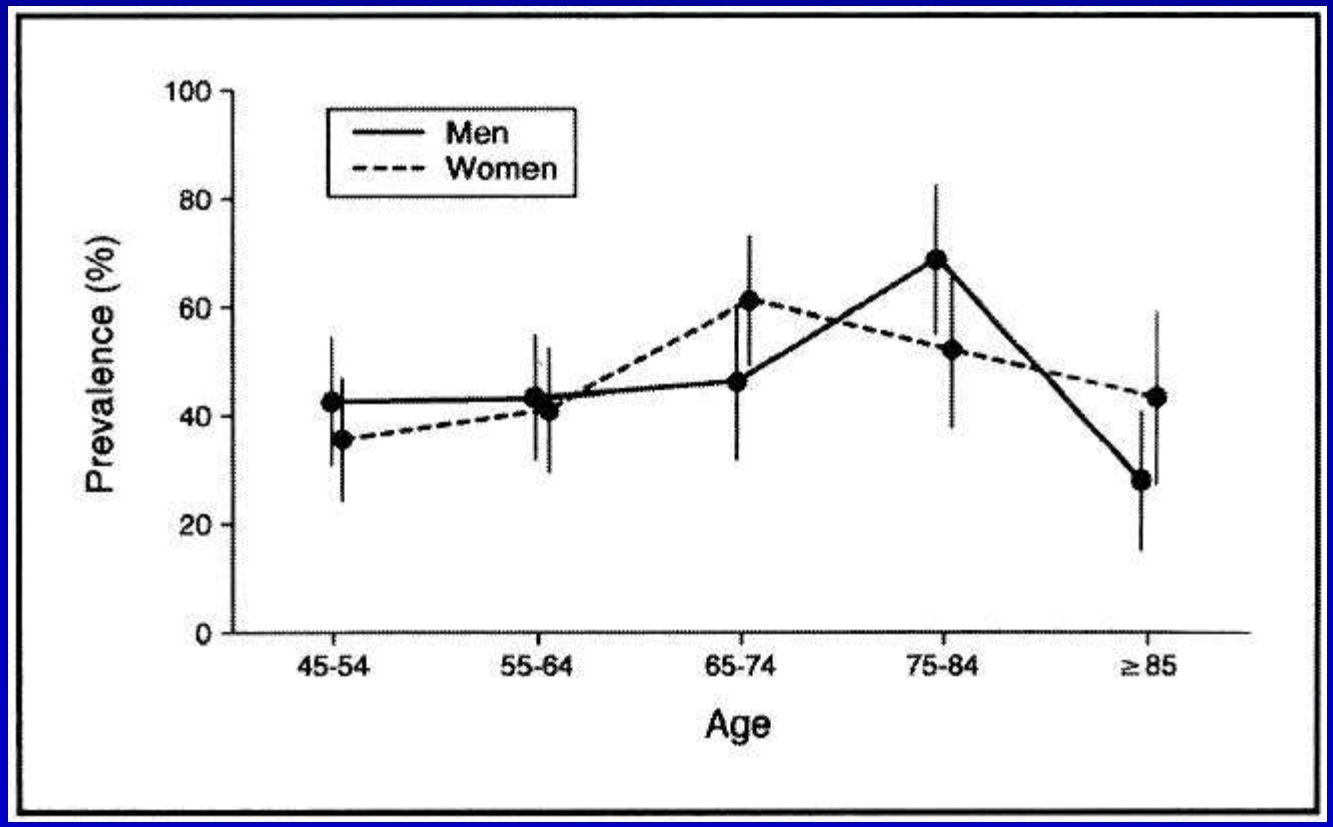
Meissner I et al. J Am Coll Cardiol. 2006;47:440.
Petty GW et al. Mayo Clin Proc. 2006;81:602.
*Adams HP. Mayo Clin Proc. 2006;81:597.

SPARC Study: LAA Study

- Single lobe in 169 (29%)
- Two lobes in 284 (49%)
- Multiple lobes in 127 (22%)
- Velocities measured in 96%
  - Mean velocity in NSR was 66 cm/s (18-167 range)
  - Velocity <30 cm/s in 2.9%
  - Mean velocity in AFib was 57 cm/s

Meissner, Khandheria et al. Mayo Clin Proc 1999;74:862-869.

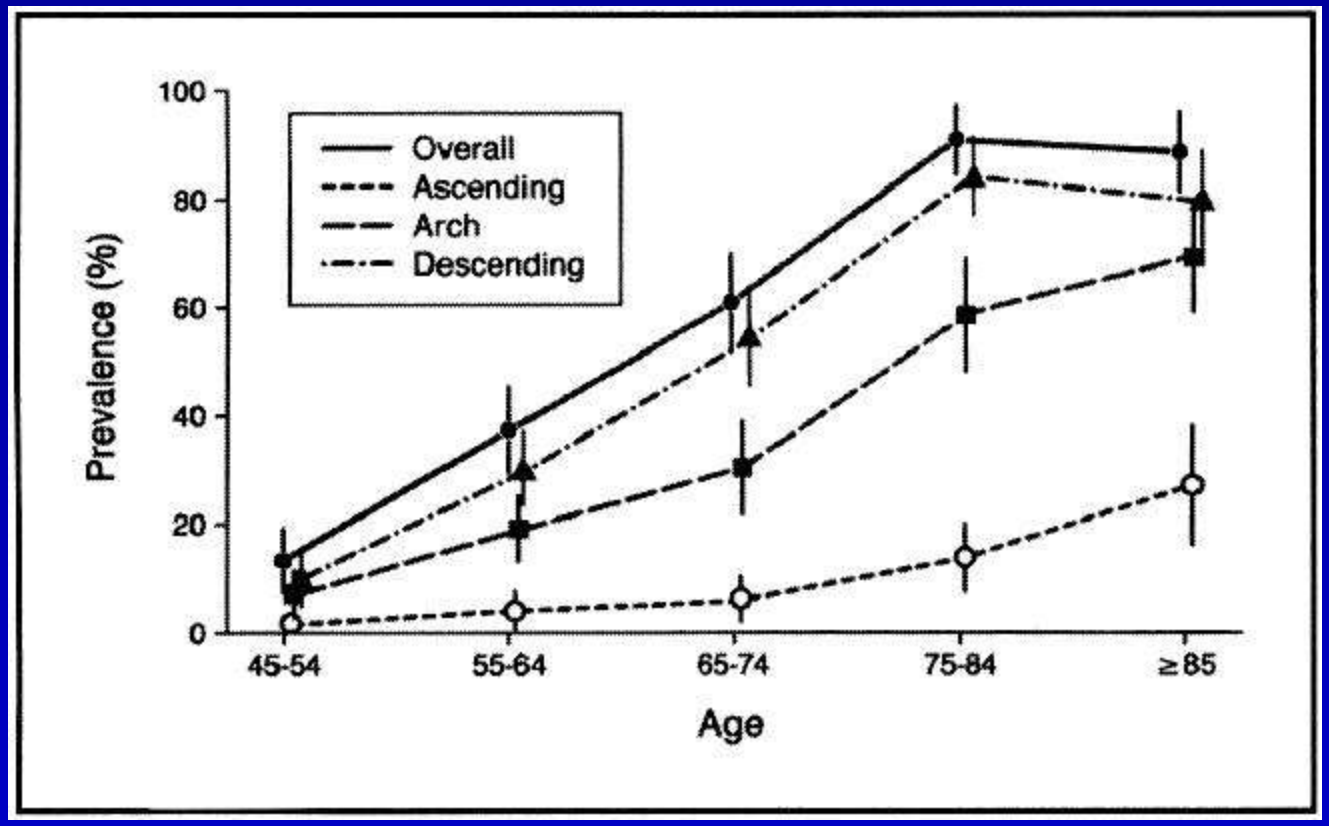
SPARC Study: Stroke Prevention: Assessment of Risk in a Community



Age- and sex-specific prevalence and 95% confidence interval of strands on native valves in random sample of Olmsted County population, 45 years or older .

Meissner, Khandheria et al. Mayo Clin Proc 1999;74:862-869.

SPARC Study: Aortic atherosclerosis



Overall

Descending

Arch

Ascending

In the ascending aorta, the prevalence was 6.2% (±0.9%) with 48 simple and 1 complex. Within the aortic arch, the prevalence was 25.6% (±1.6%) with 167 simple and 13 complex. In the descending aorta, the prevalence of simple and complex was 34.4% (±1.7%) and 3.8% (±0.7%), respectively. No sex differences were observed, regardless of location .

Meissner, Khandheria et al. Mayo Clin Proc 1999;74:862-869.

SPARC Study: Aortic atherosclerosis

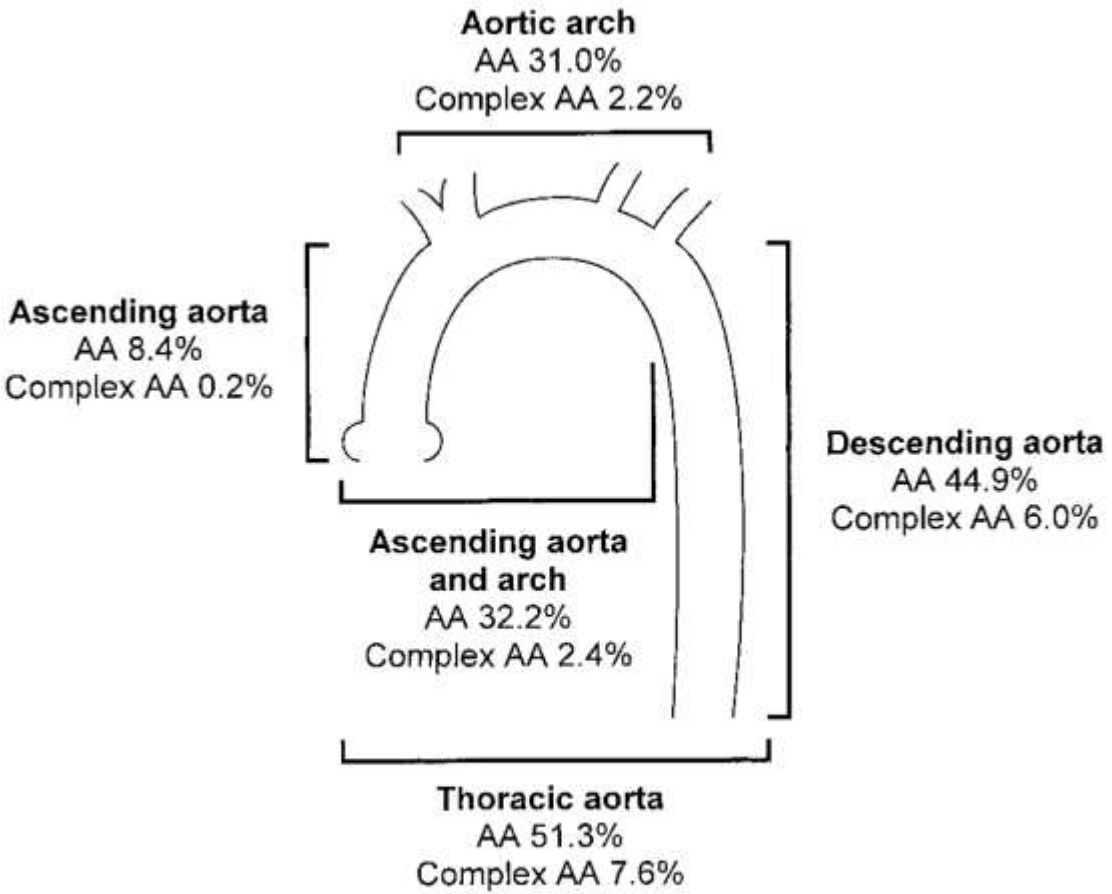


Figure 4. Distribution of atherosclerosis (of any degree) and complex atherosclerosis in various segments of thoracic aorta. AA indicates aortic atherosclerosis.

Agmon Y et al. Circulation. 2000;102:2087.

SPARC Study: Aortic atherosclerosis

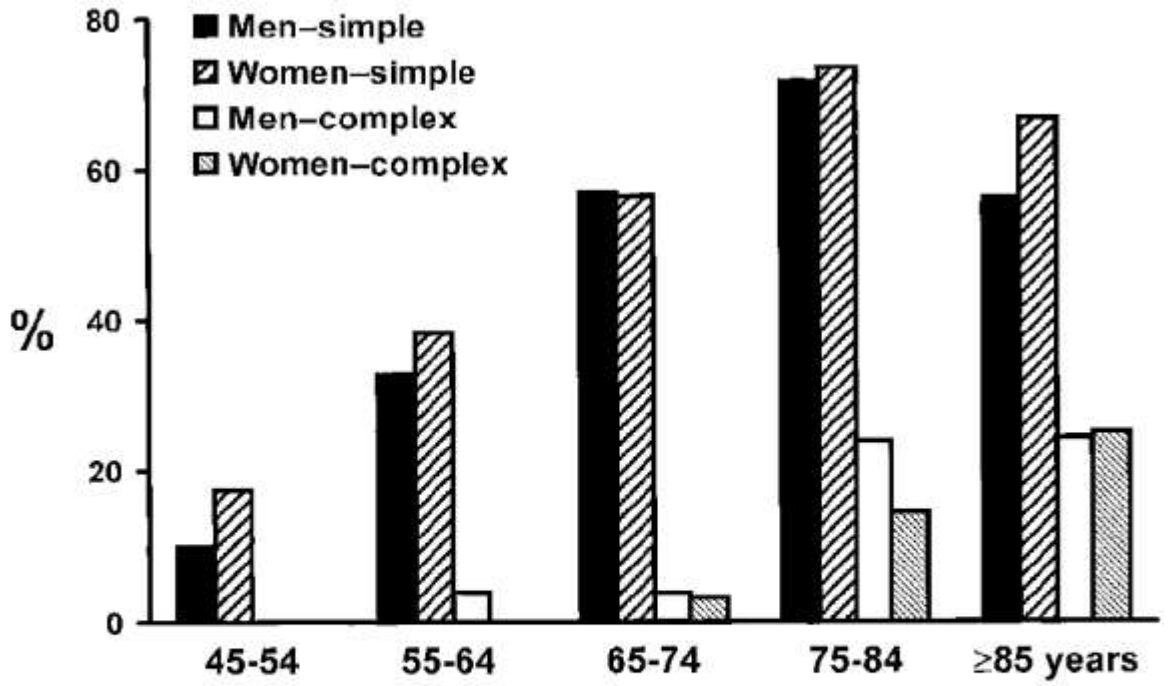
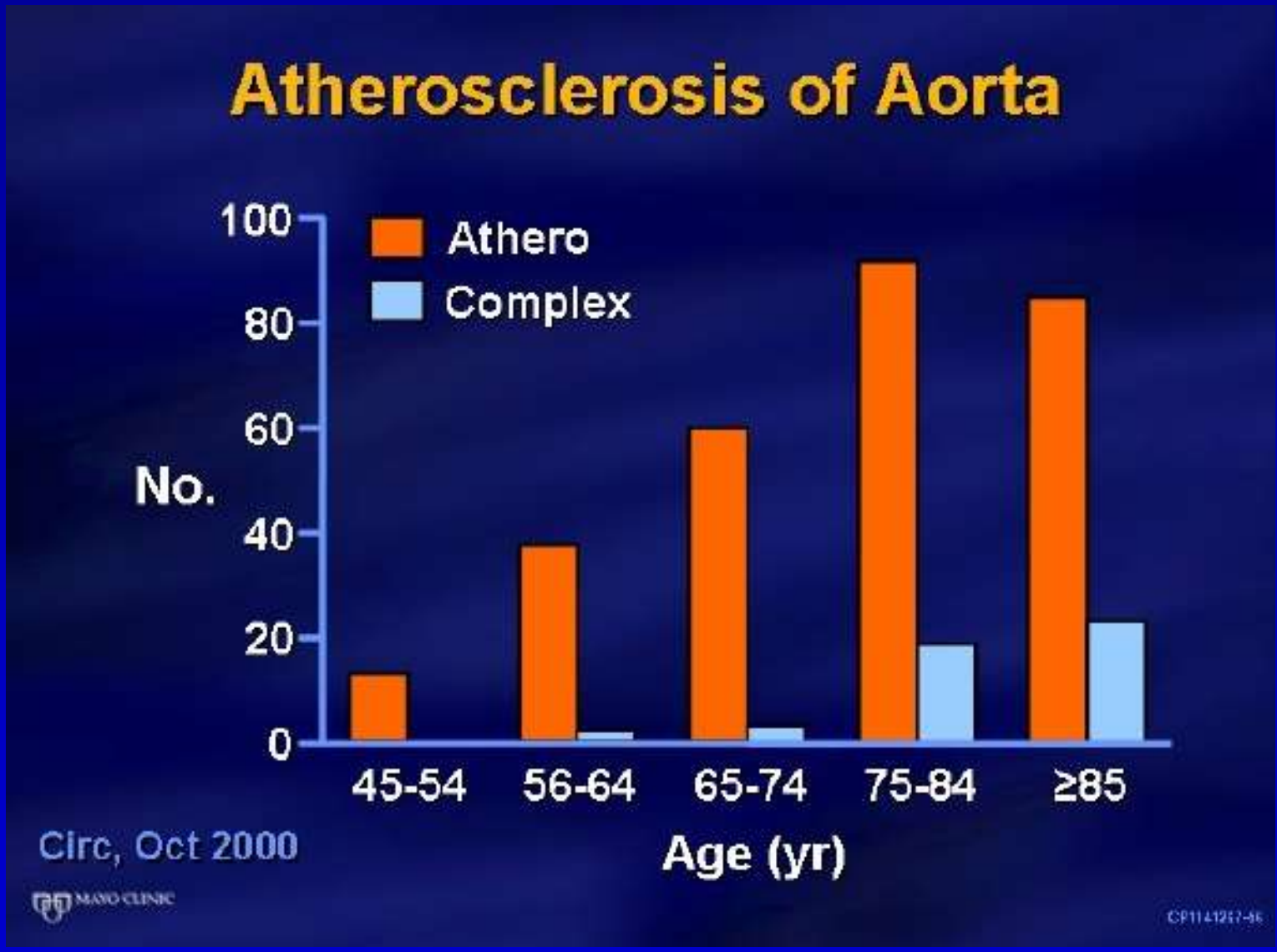


Figure 3. Frequency of simple and complex aortic atherosclerosis within each SPARC age and sex stratum. Increasing age was associated with higher frequency of simple and complex atherosclerosis. There were no major differences in frequencies between sexes.

Agmon Y et al. Circulation. 2000;102:2087.

SPARC Study: Aortic atherosclerosis



Agmon Y et al. Circulation. 2000;102:2087.

SPARC Study Abnormality Summary

Condition	Prevalence (±SE) (%)	
	Unadjusted	Adjusted*
Valvular strands	46.4 (±2.2)	46.9 (±2.2)
Aortic atherosclerosis	44.3 (±1.8)	44.7 (±1.8)
Patent foramen ovale	25.6 (±1.9)	25.5 (±1.9)
Atrial septal aneurysm	2.2 (±0.6)	2.2 (±0.7)
Carotid stenosis		
Plaque analysis		
Moderate	13.4 (±1.3)	13.3 (±1.3)
Severe	1.5 (±0.5)	1.4 (±0.5)
Velocity analysis		
Moderate	7.7 (±1.1)	7.7 (±1.1)
Severe	0.3 (±0.2)	0.2 (±0.2)

*Olmsted County prevalence adjusted to the 1990 white US population aged 45 years or older.

Estimated Prevalence of Transesophageal Echocardiography- and Carotid Ultrasonography-Defined Cardiovascular Variables in Olmsted County

Meissner, Khandheria et al. Mayo Clin Proc 1999;74:862-869.

Cardiovascular Source of Emboli: Where Do We Stand? - 1

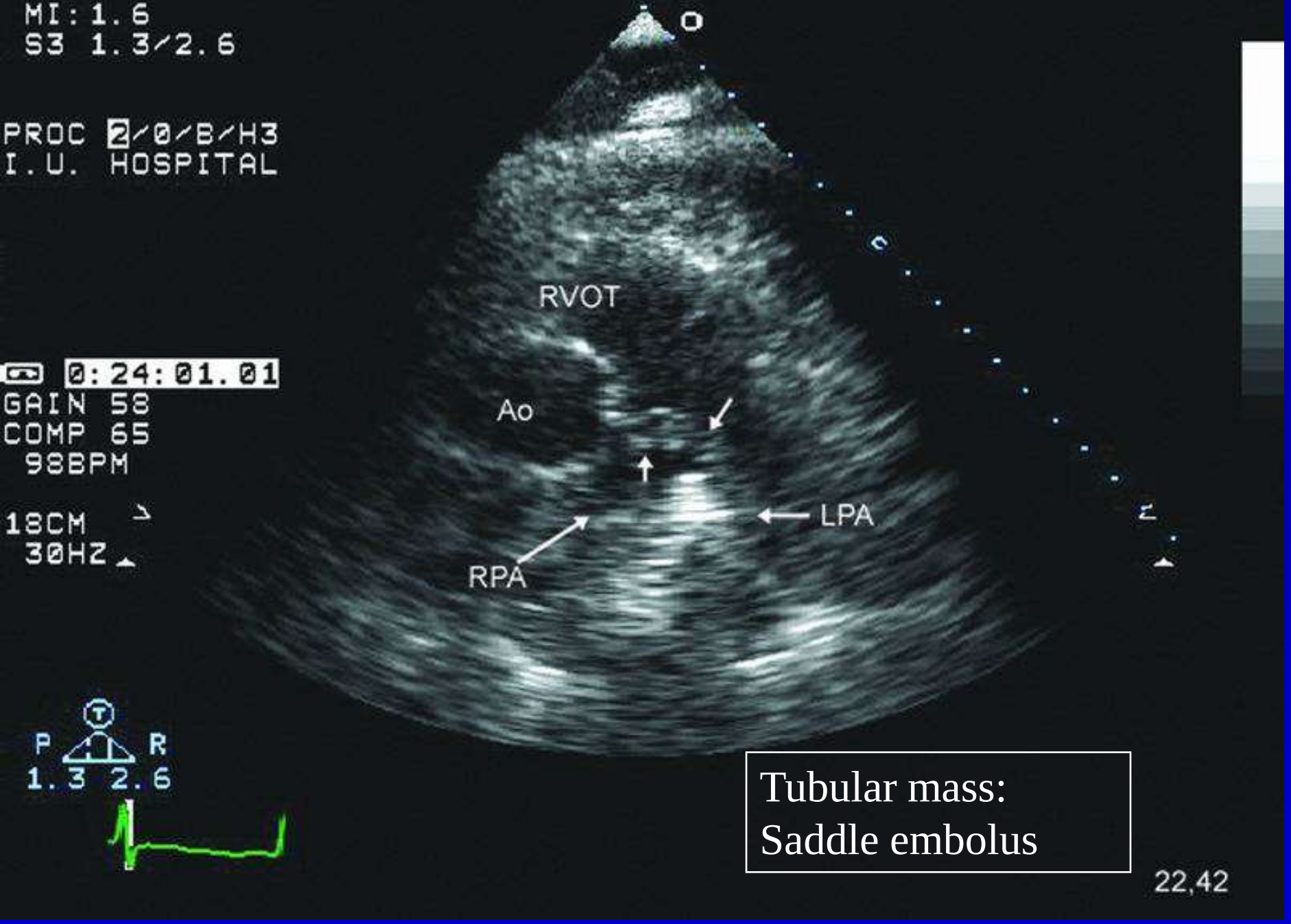
- PFO: "One cannot derive conclusions regarding superiority of interventional versus medical treatment. Ongoing randomized trials are attempting to determine which approach is better."
- Anticoagulation
  - LV Post MI Aneurysm with thrombus – warfarin for ≥3 months (also patients with marked LV dysfunction)
  - AFib ≥60 yo and DM or CAD; ≥75 yo (esp women); htn, HF, EF≤35%, RHD, prosthetic valves, thyrotoxicosis, or prior embolic events ("SEC is an independent predictor of TE risk leading to a 3%-12%/yr increase in embolic rate")
  - "Clots can form on the surface of tumors such as myxomas; therefore, anticoagulation is recommended if surgery is not indicated"

Block, P. ACC Cardiosource Review Journal. January 2007, pp 55-60

Cardiovascular Source of Emboli: Where Do We Stand? - 2

- Aortic atheroma and thrombus: aggressive treatment of risk factors for atherosclerosis, including ASA, statins, strict BP and glucose control – warfarin debatable; aortic arch endarterectomy is adverse in preventing future strokes – debatable (ongoing study in Europe and Australia - ARCH - of ASA clopidogrel and warfarin in patients with complex aortic atheroma)
- Imaging emboli: TTE for initial screening (better apical thrombus vis and better Valsalva results); TEE better for LAA clots, aortic atheroma, prosthetic valve vegetations and clots and right-sided catheter vegetations and clots and better for PFO and ASA and ASD, only do it if it will affect treatment

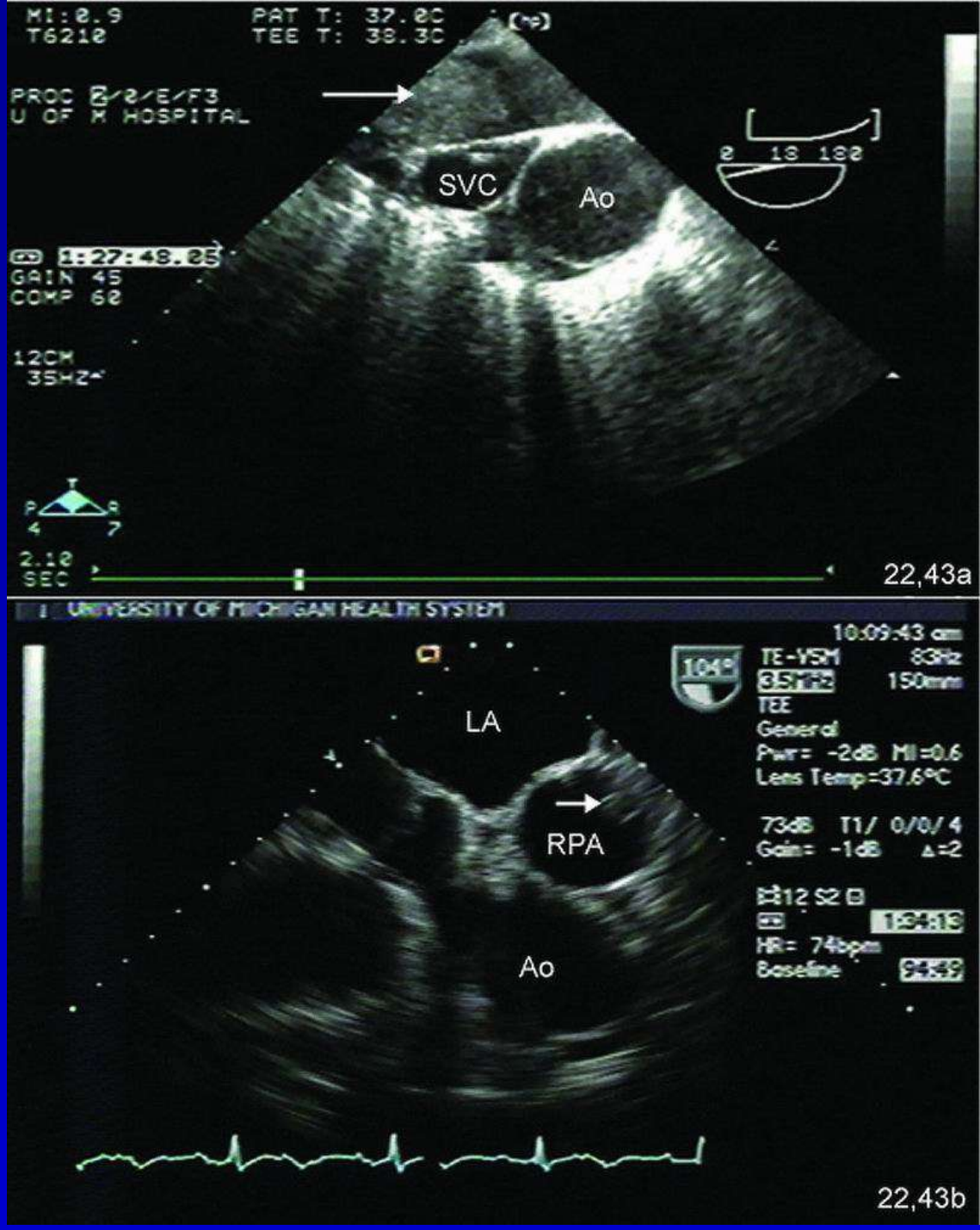
Block, P. ACC Cardiosource Review Journal. January 2007, pp 55-60



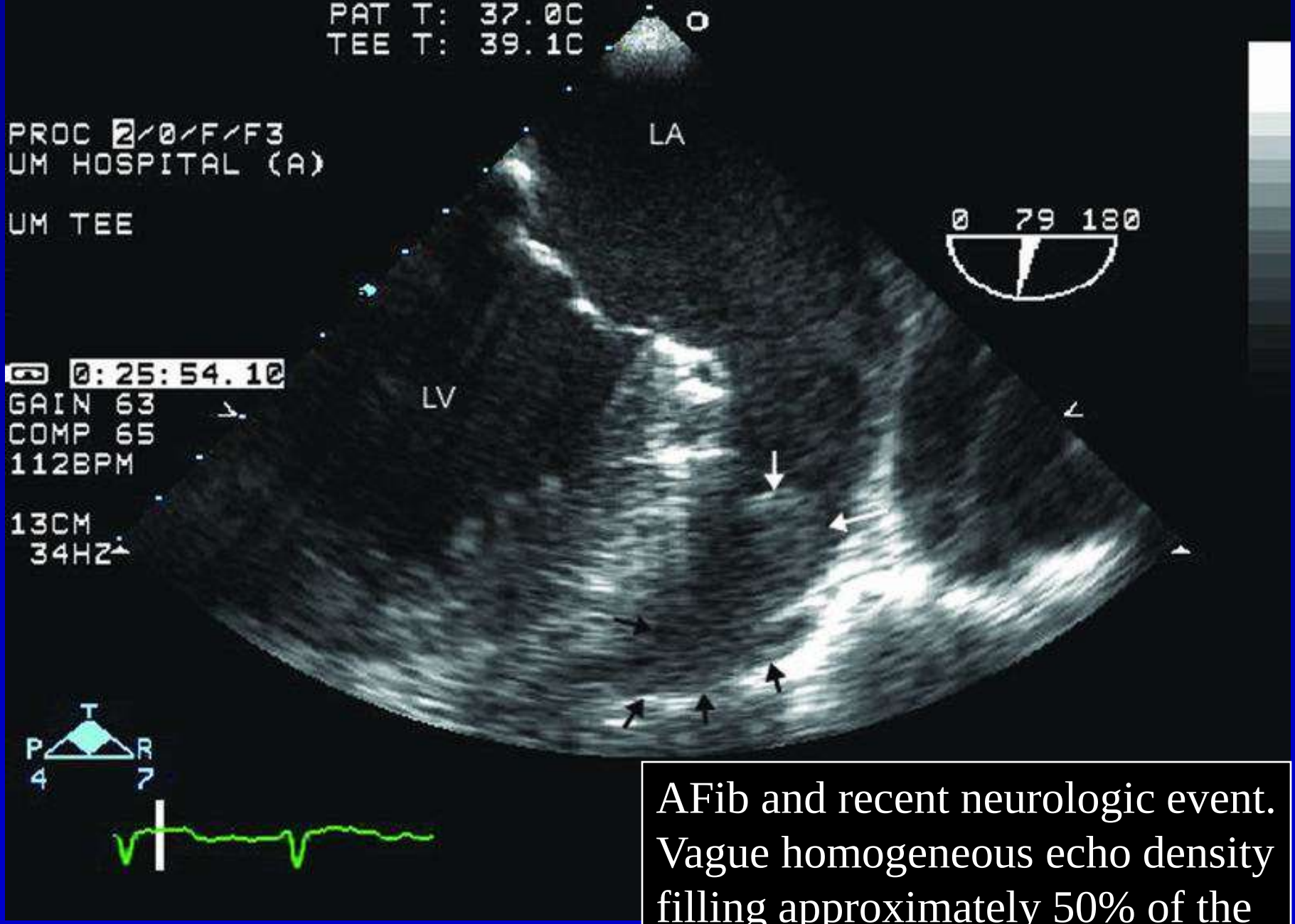
Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

Top: Mass occluding a significant portion of the proximal RPA

Bottom: Circular density in RPA

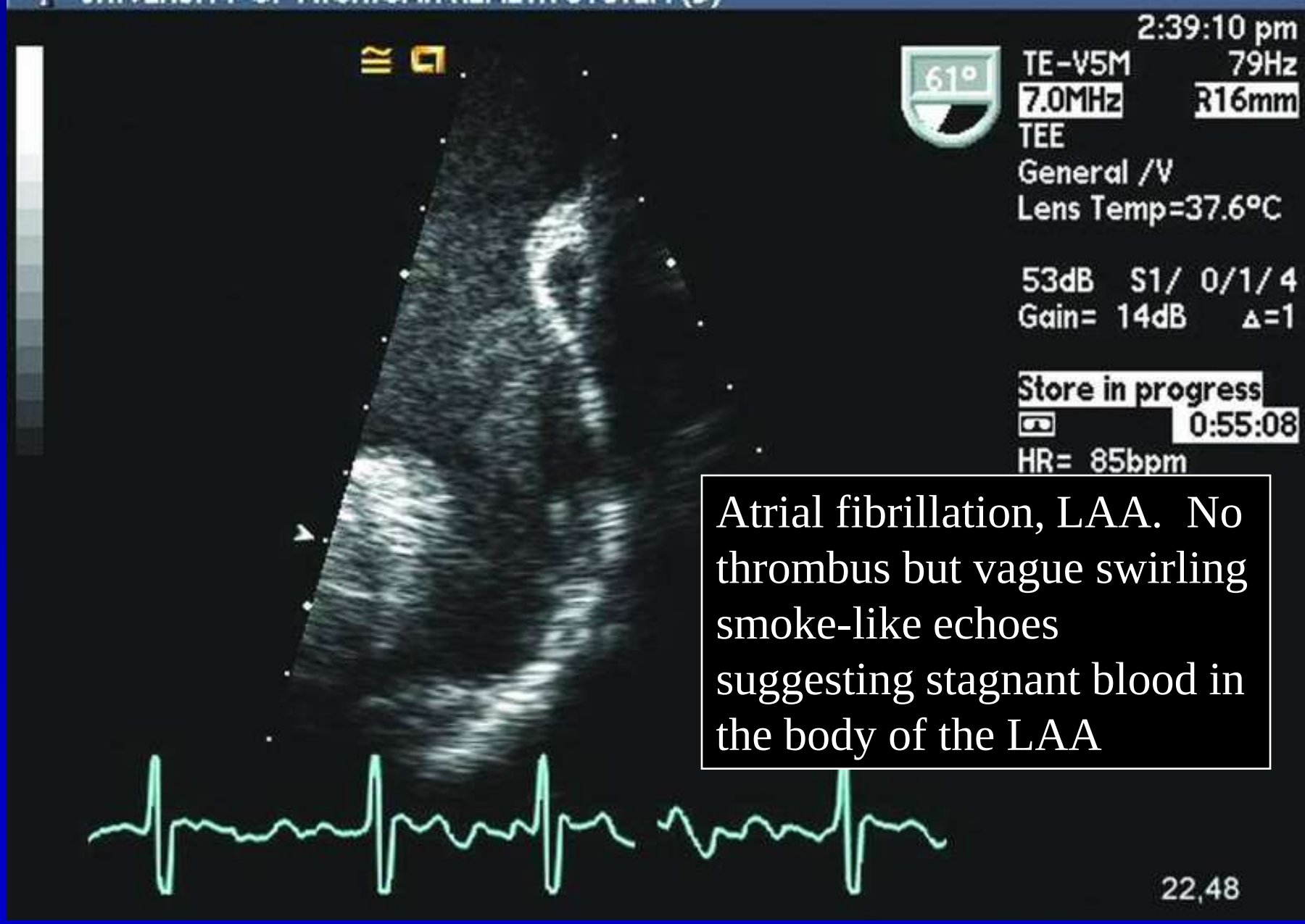


Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.



AFib and recent neurologic event. Vague homogeneous echo density filling approximately 50% of the LAA

Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.



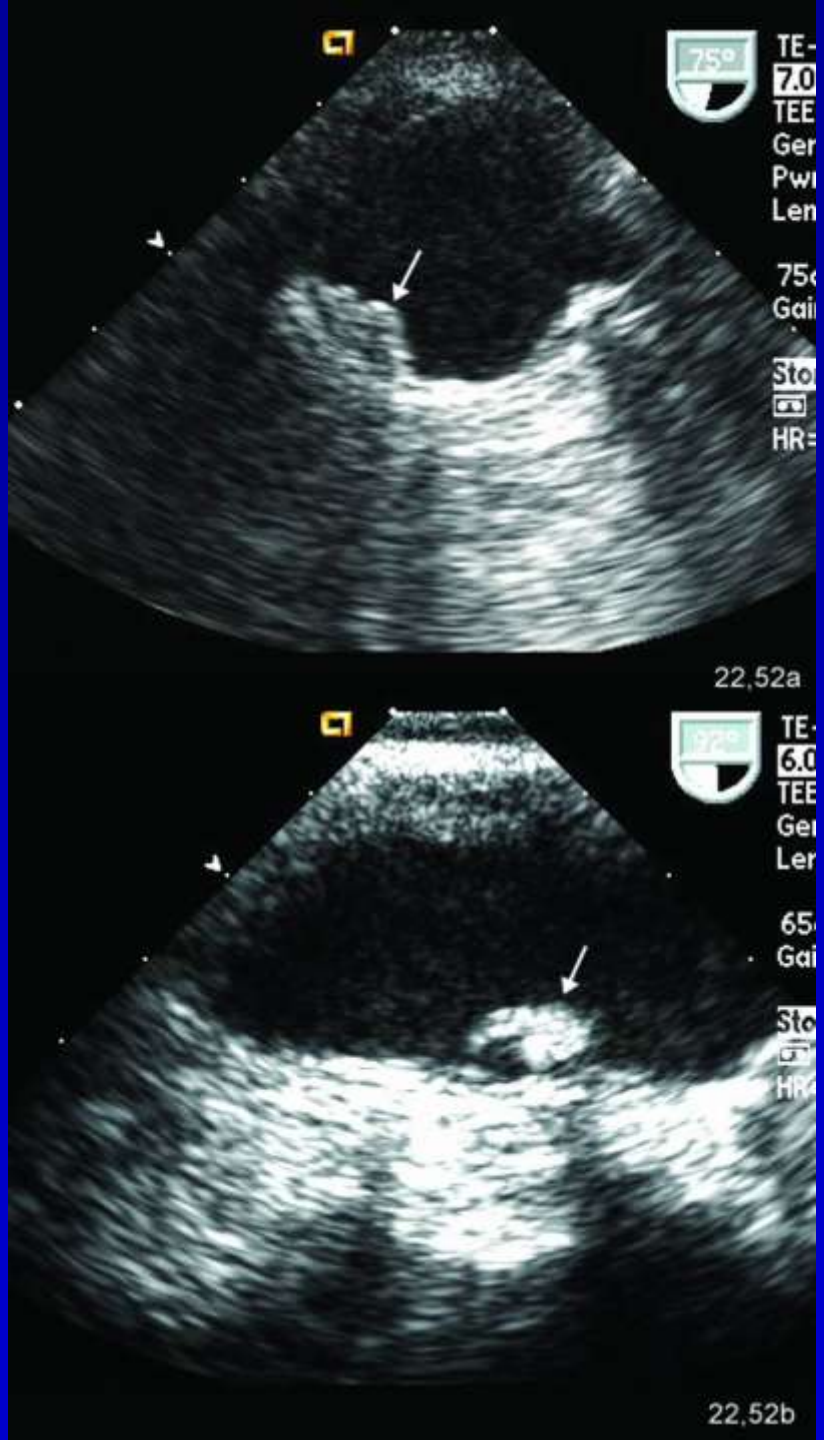
Atrial fibrillation, LAA. No thrombus but vague swirling smoke-like echoes suggesting stagnant blood in the body of the LAA

Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

TEE in 2 patients with cryptogenic stroke – significant aortic atheroma:

Top: broad-based but pedunculated atheroma in proximal descending aorta with thickness exceeding 4 mm

Bottom: Mobile atheroma (on real time clip)

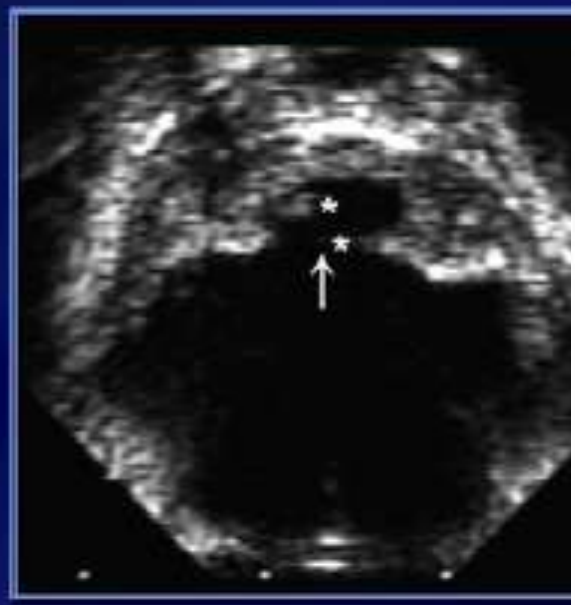


Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

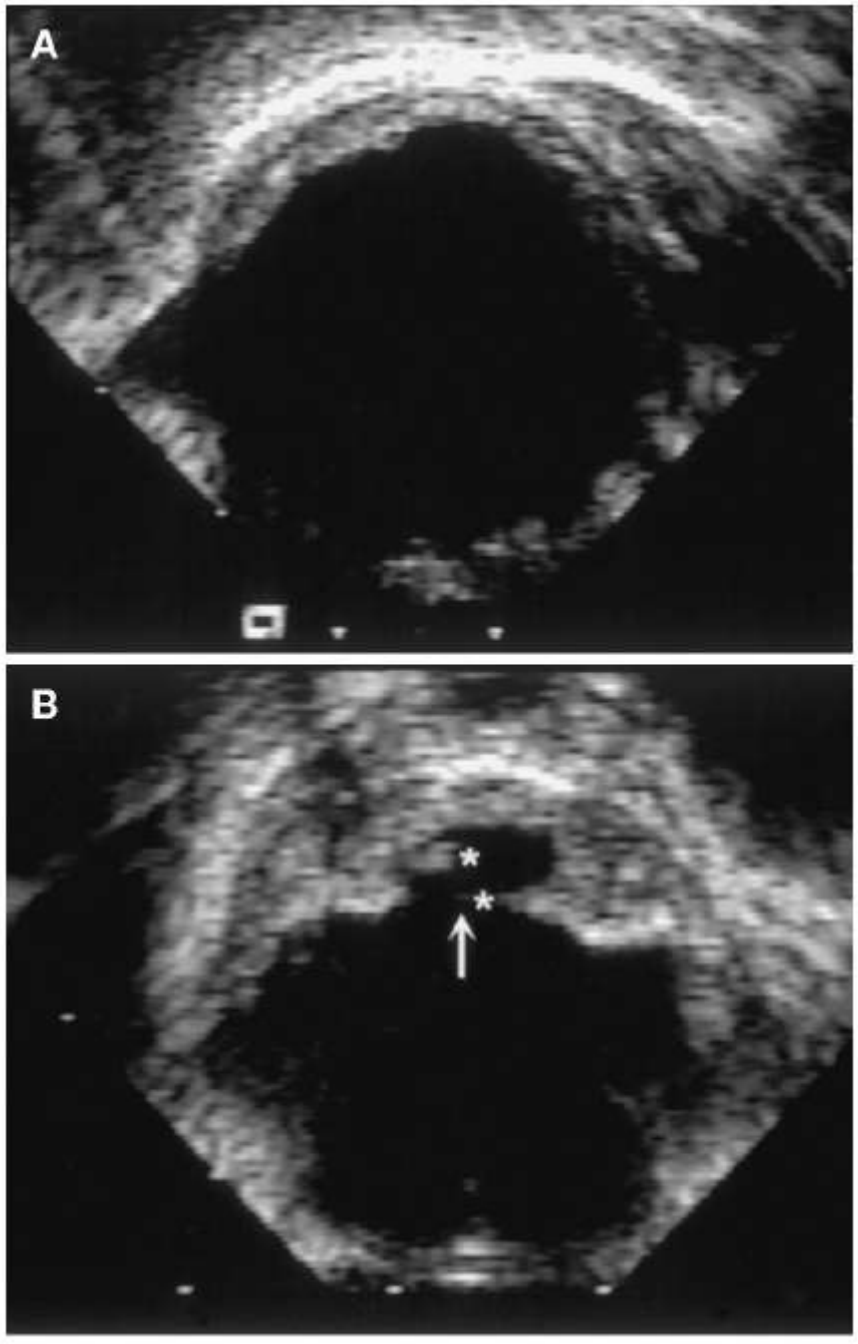
Aortic Atherosclerotic Plaques

Simp
plaqu

Complex plaques

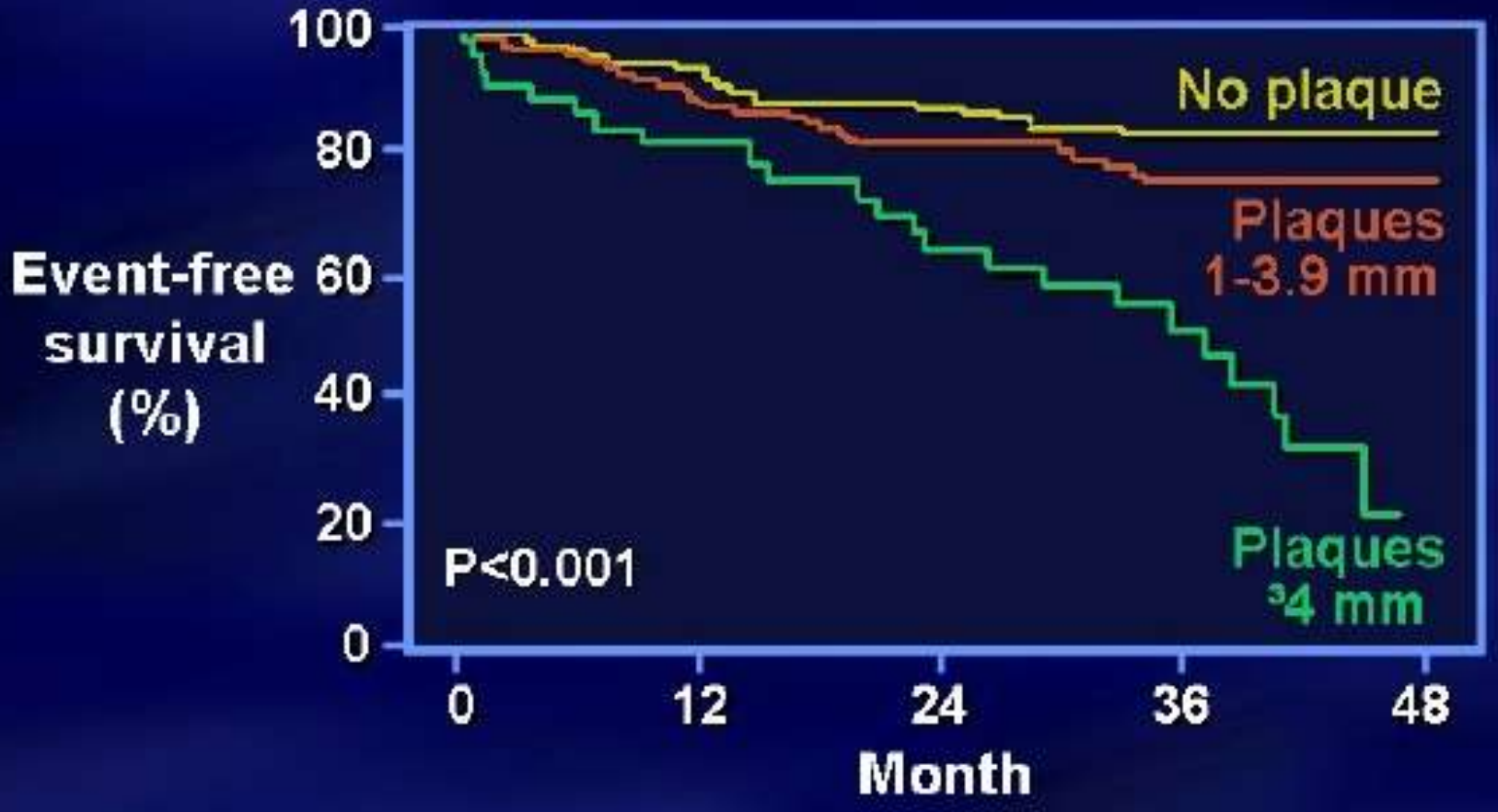


MAYO CLINIC



Khandheria BK. “Cardioembolic Disease.” AHA Scientific Sessions 11/06

Atheromatous Plaque in the Arch
Risk of Emboli



MAYO CLINIC

NEJM, May 1966

Khandheria BK. "Cardioembolic Disease." AHA Scientific Sessions 11/06

Atherosclerosis and CAD and CVD Endpoints

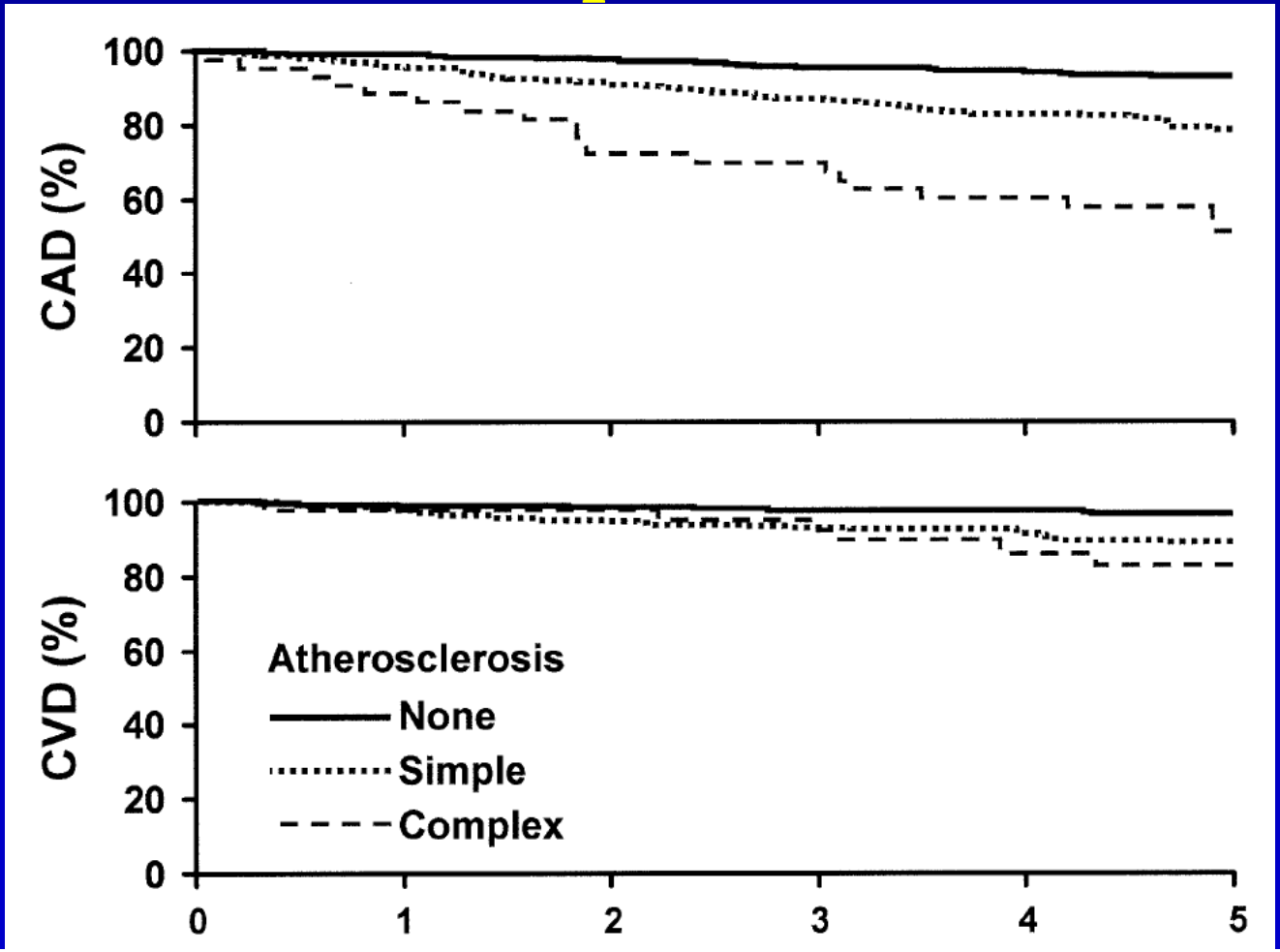


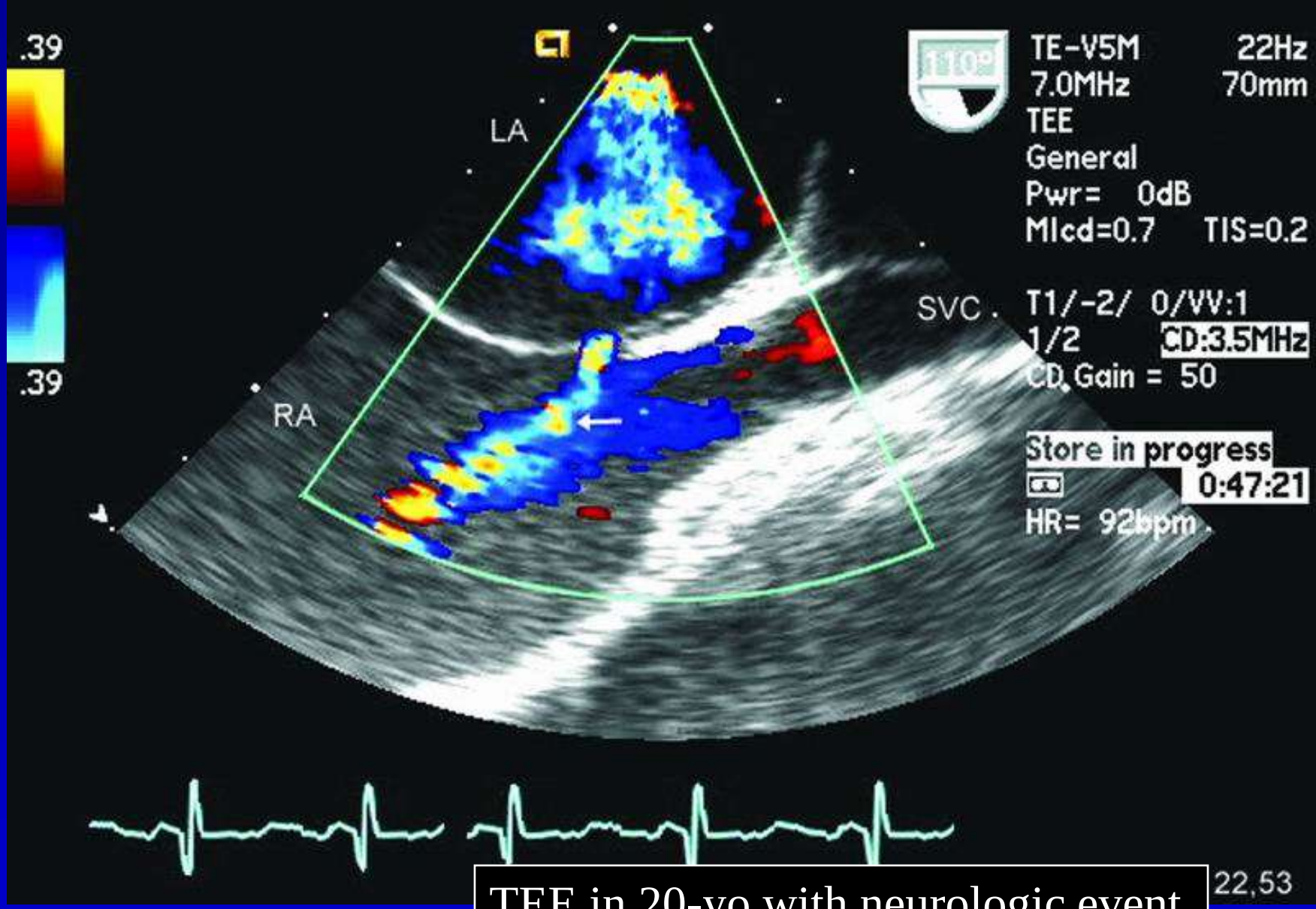
Figure 2. Kaplan-Meier curves for cardiac events (CAD) and cerebrovascular events (CVD) by type of atherosclerosis (stacked).

Meissner I et al. J Am Coll Cardiol. 2004;44:1018.

Atherosclerosis and CAD and CVD Endpoints

- Although highly significant in the univariate analysis, aortic atherosclerosis of any severity, after adjustment for age and other risk factors, was not an independent predictor of cardiac events or stroke.
- Several atherosclerotic risk factors (age, male gender, higher pulse pressure, and diabetes) are significant independent predictors of cardiac events.
- Age, prior myocardial infarction, and atrial fibrillation are predictive of cerebrovascular events.

Meissner I et al. J Am Coll Cardiol. 2004;44:1018.



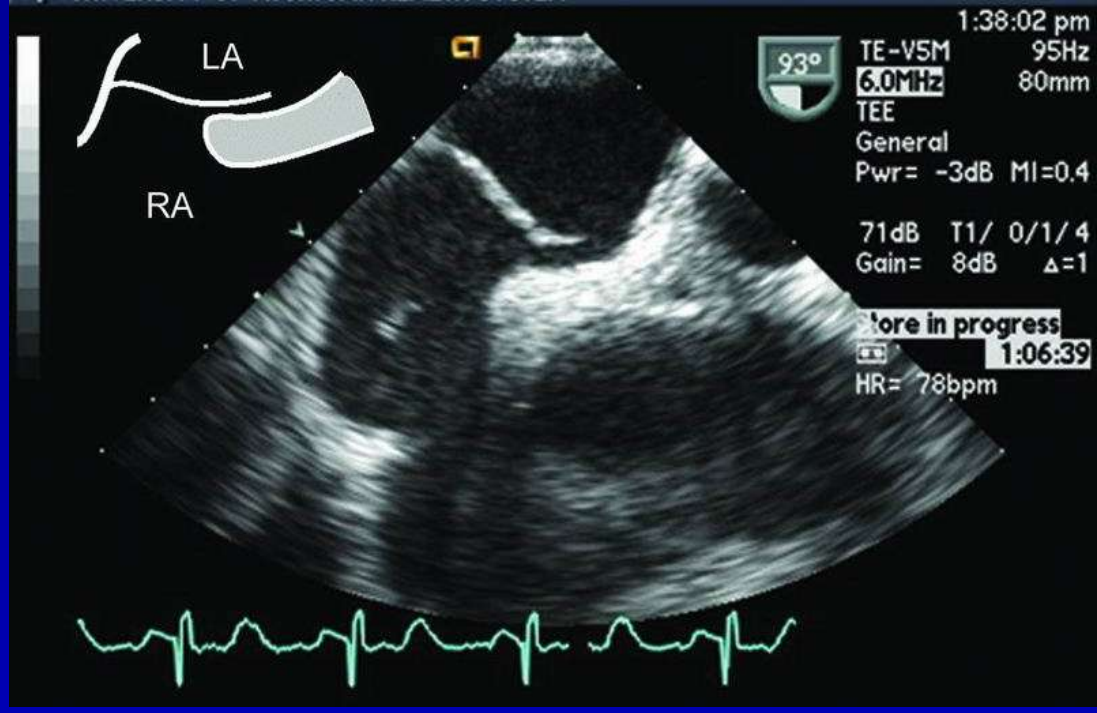
TEE in 20-yo with neurologic event showing PFO vs very small ASD documented by color flow

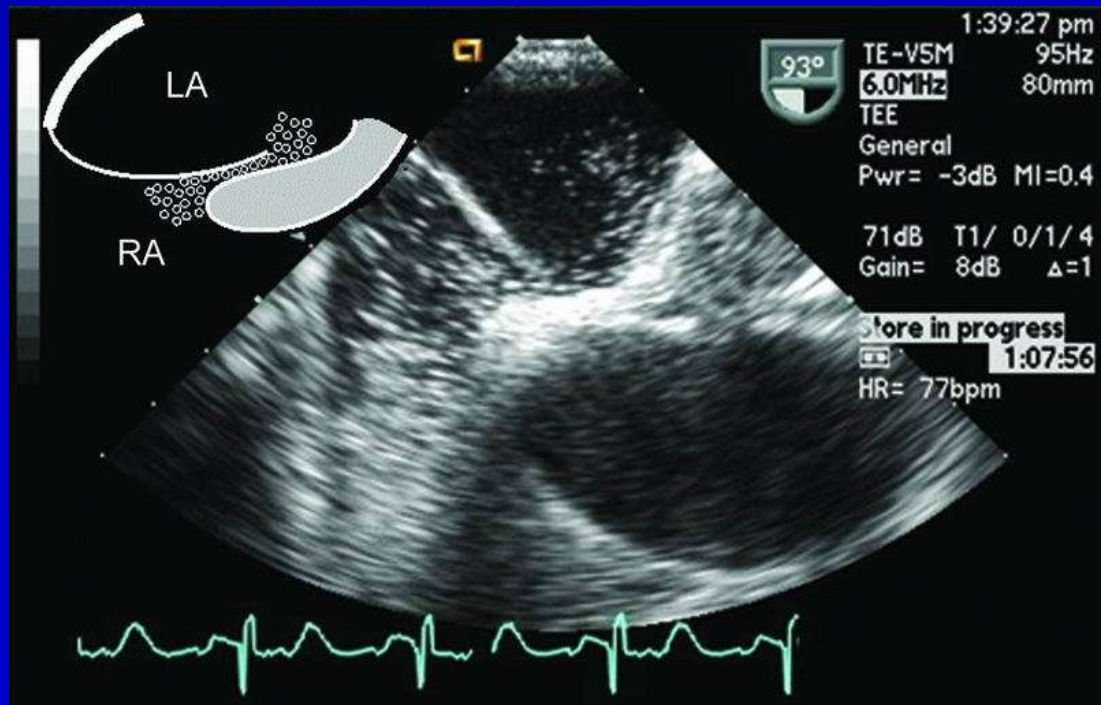
Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

TEE in young patient with cryptogenic stroke and PFO

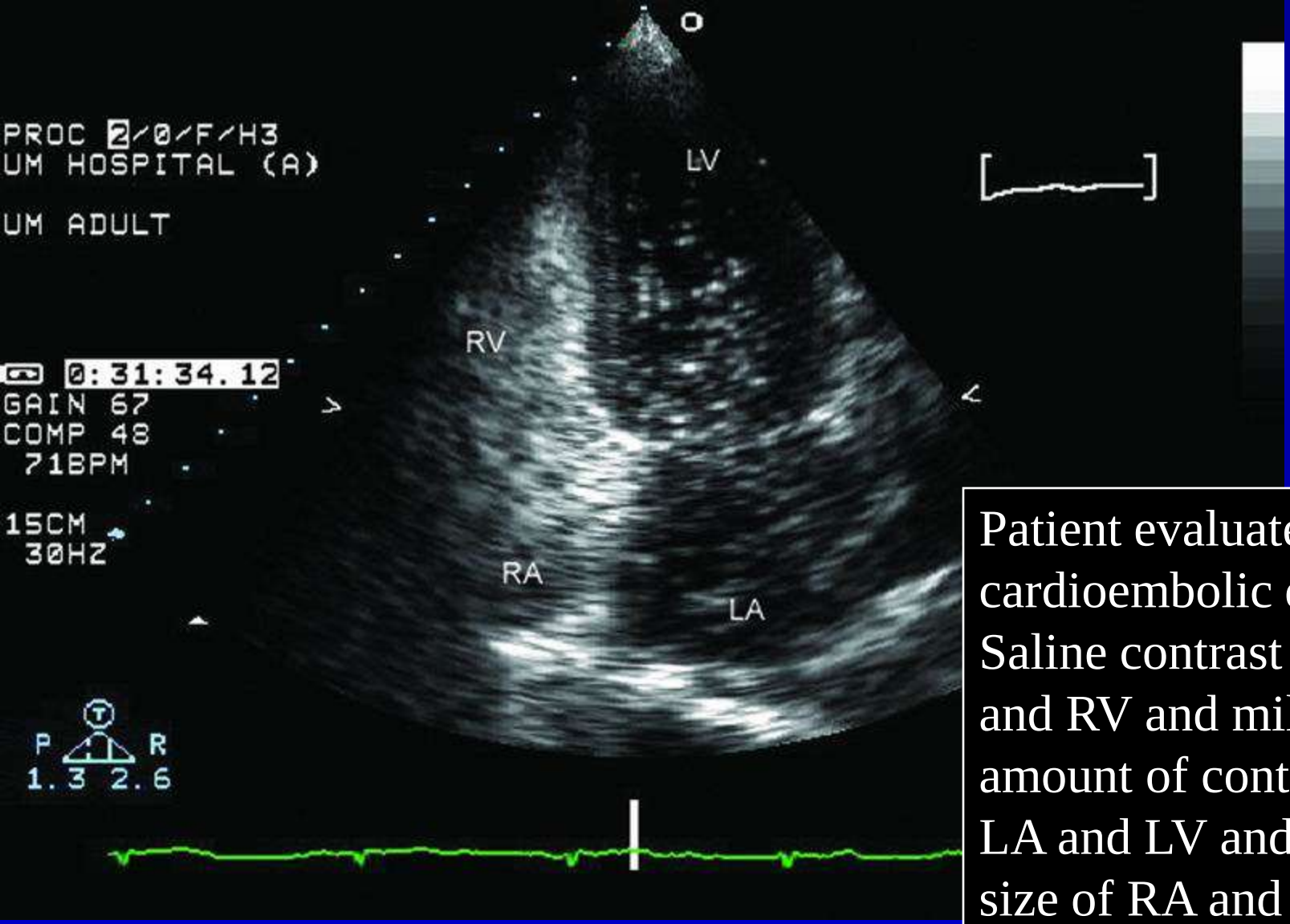
Top: redundancy of foraminal tissue and the "liftoff" of the tissue from the primum portion of the septum of approximately 3-4 mm

Bottom: R to L shunting of saline through PFO





Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.



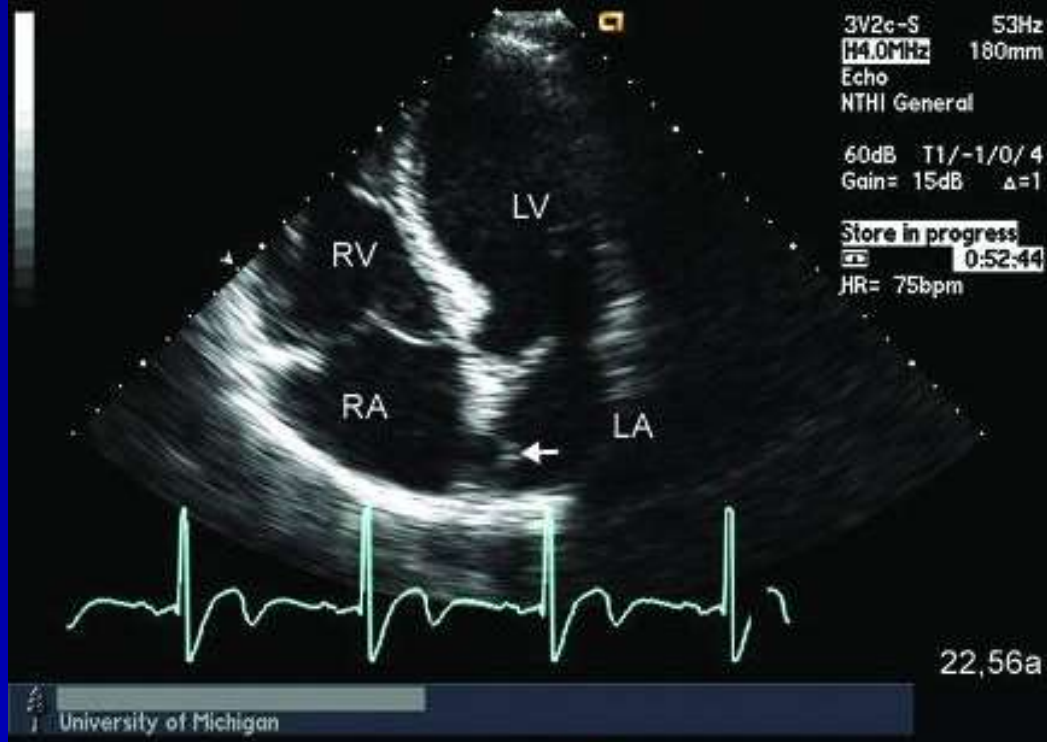
Patient evaluated for cardioembolic disease. Saline contrast fills RA and RV and mild amount of contrast in LA and LV and normal size of RA and RV leading to presumptive diagnosis of PFO and R to L shunting

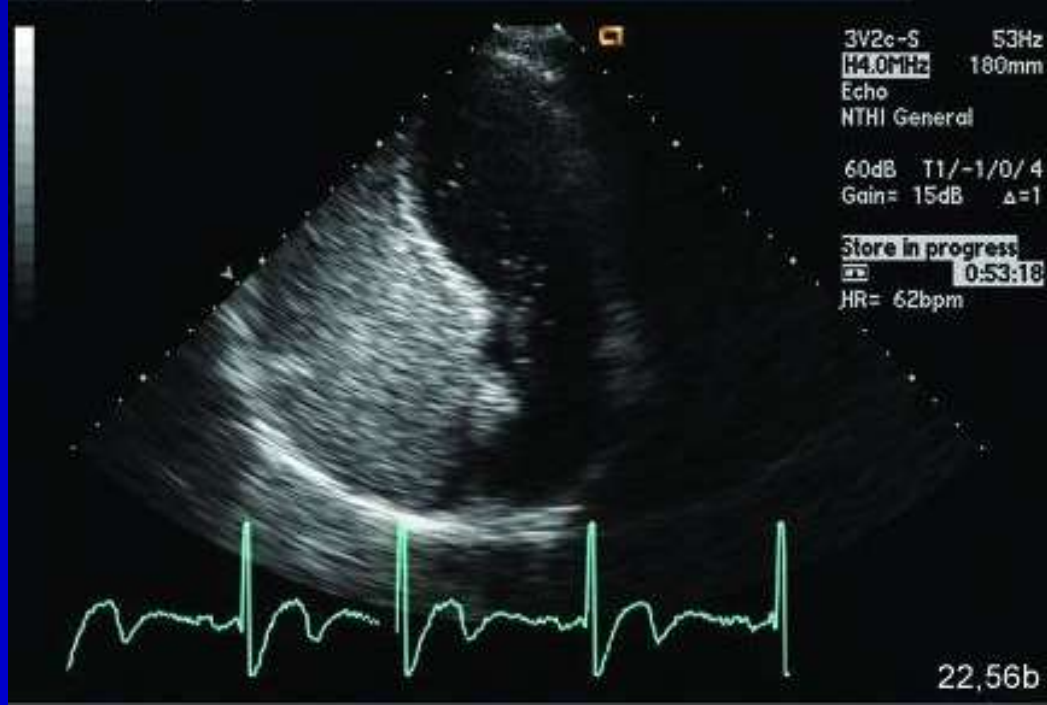
Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

Patient with ASA

Top: Discrete bulging of a portion of the atrial septum into the left atrium

Bottom: Small amount of shunting consistent with a PFO associated with the ASA

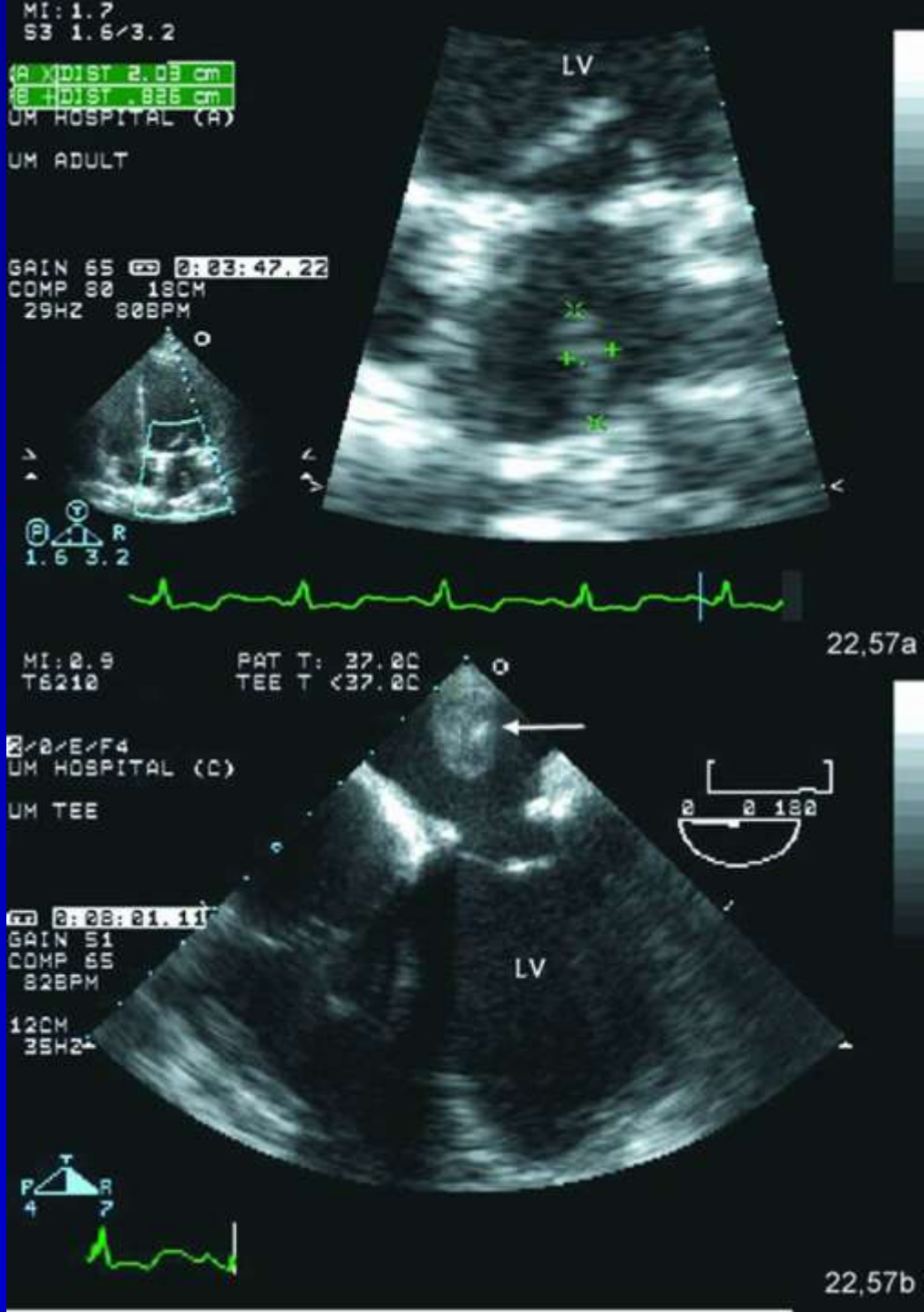




Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

Top: Expanded view of A4C in patient with prior mitral annular ring for MR. Vague pedunculated mass arising from the back wall of LA

Bottom: TEE confirming large thrombus in body of LA



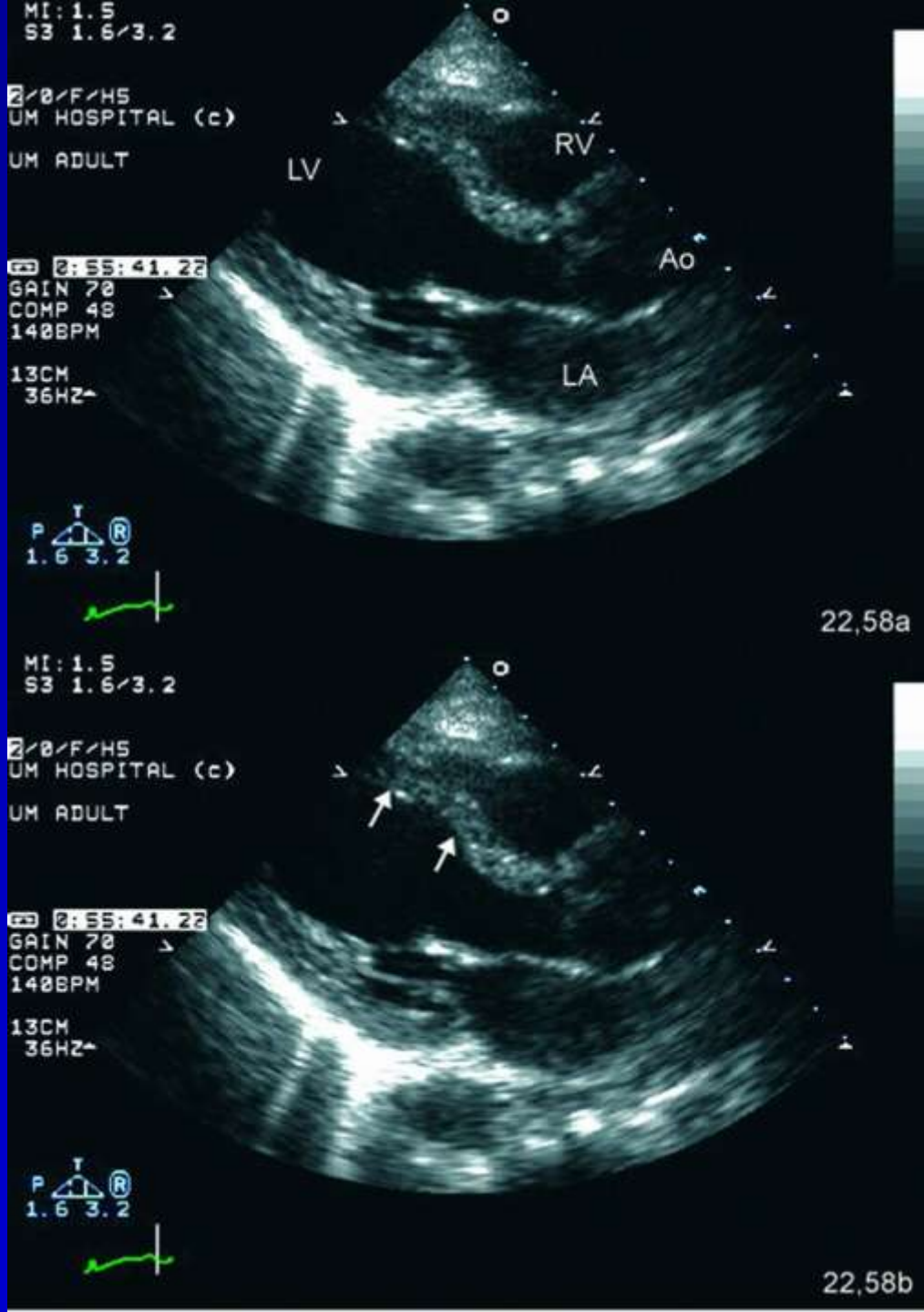
Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

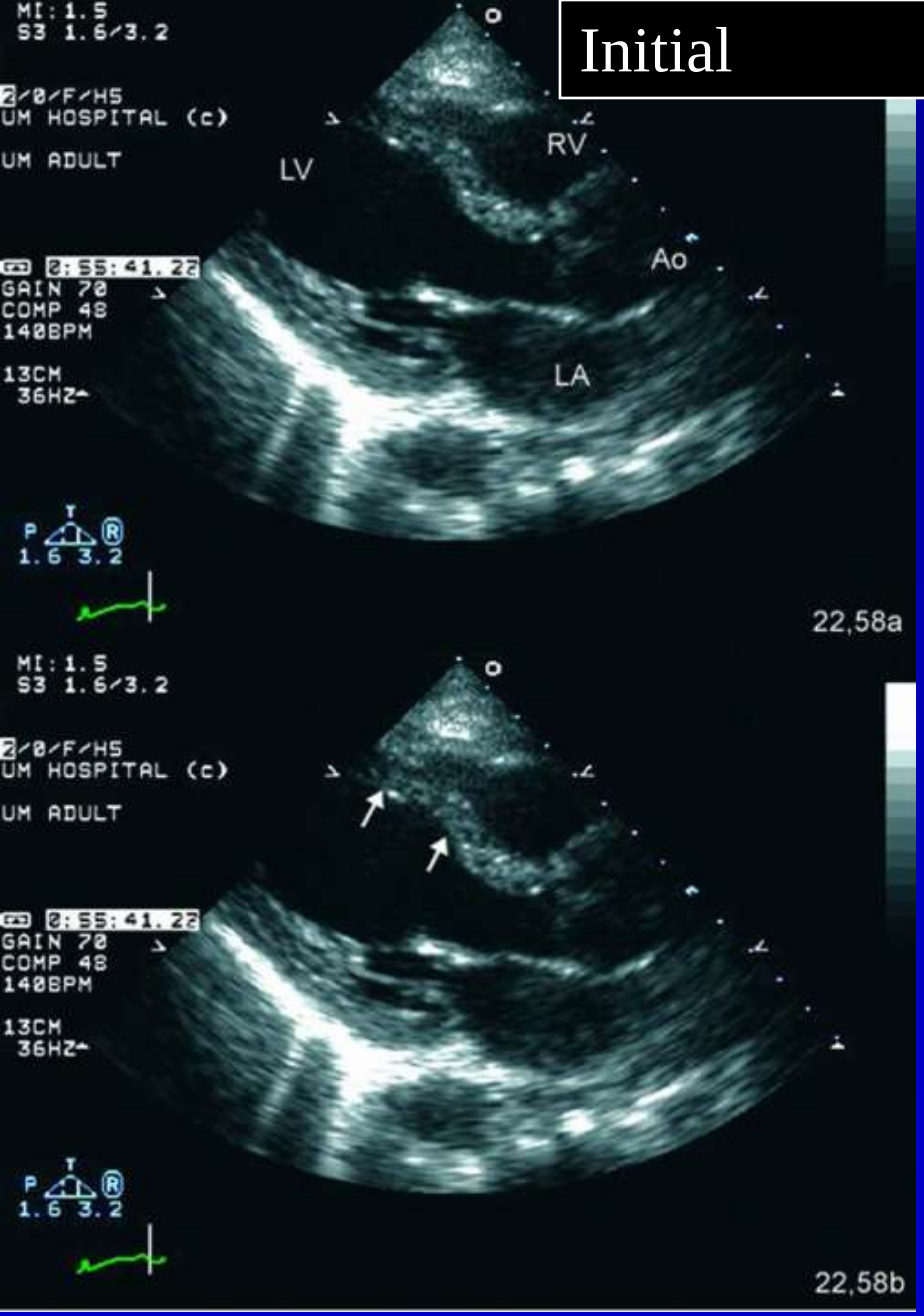
PSLA in 58-yo pt after intracranial hemorrhage. Dyskinesis of distal ¾ anteroseptum, hypokinesis of other walls. ECG deep symmetric T inversion. Enzymes negative. Cath – no obstructive CAD. Neurogenic myocardial stunning, typically reverts to normal over 3 to 14 days

Top: Diastole

Bottom: Systole

Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.





Feigenbaum's Echocardiography, 6th ed. Ch. 22, 2005.

Indications for TEE

- Endocarditis and valvular disease
- Dyspnea, edema, and cardiomegaly
- Cardioembolic source
- Pre cardioversion
- Critically ill patients
- Imaging coronary ostia in congenital heart disease

ACC/AHA Practice Guideline, Echo 2003.

Class I Indications for TEE in Anticipation of Cardioversion

- Urgent cardioversion where extended precardioversion anticoagulation is undesirable
- Prior cardioembolic events related to intra-atrial thrombus
- Anticoagulation is contraindicated and decision about cardioversion will be affected by TEE results
- Intra-atrial thrombus by prior TEE
- AFib of <48 hr but other heart disease (IIa)
- AFib of <48 hr and no other heart disease (IIb)

ACC/AHA Practice Guideline, Echo 2003; p. 49, 51.