Contrast echo and evaluation of cardiac function: basic principles

Y. Yotov

University Hospital "St.Marina"

Varna, Bulgaria

EAE Teaching Corse, 5-7 April 2012, Sofia, Bulgaria

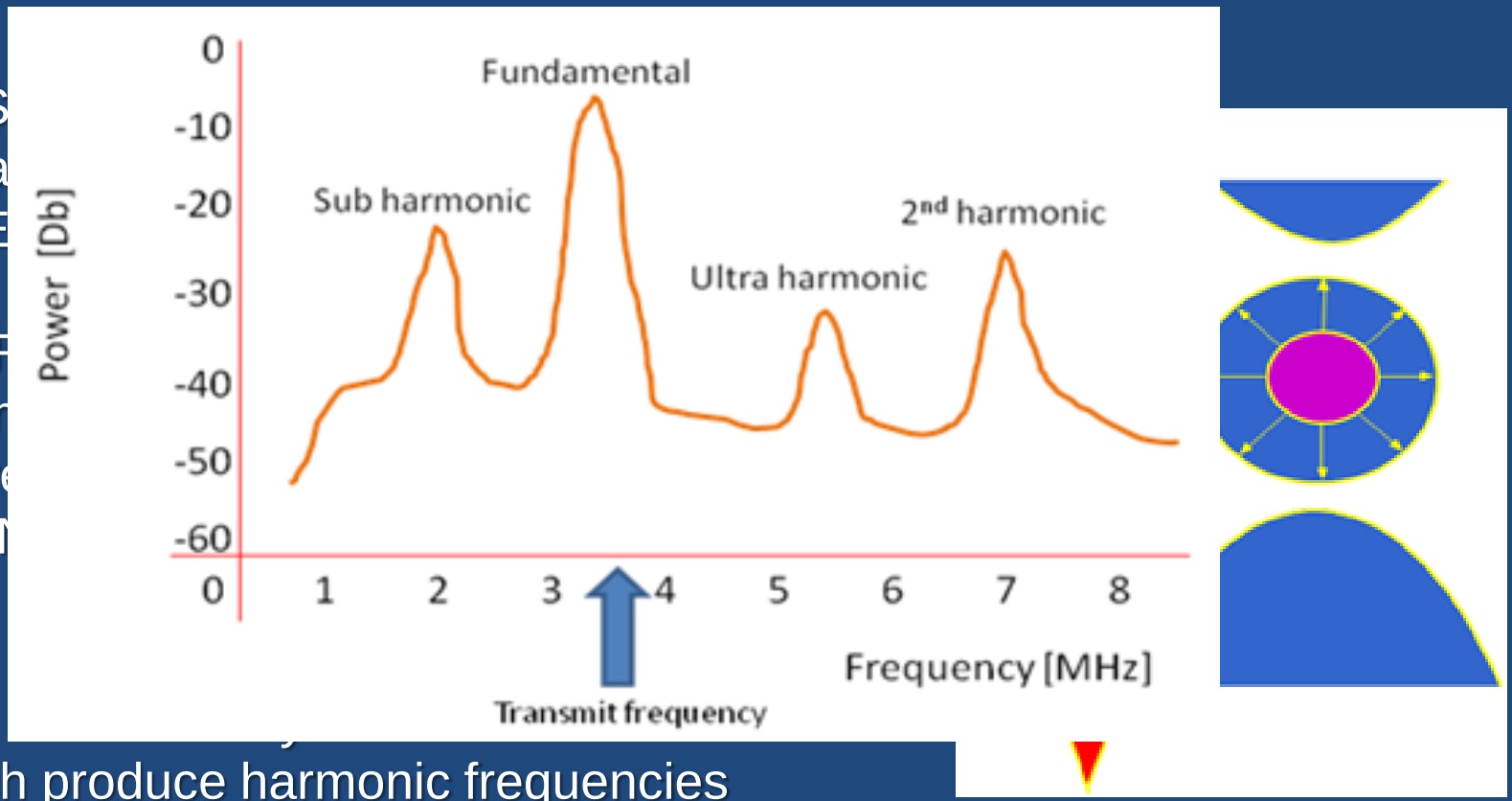
Contrast in echocardiography: Why?

- **To delineate the endocardium by cavity opacification.**
  - for assessment of global and regional systolic function, LV volumes and ejection fraction.
  - LV opacification (LVO) for improved visualisation of structural abnormalities
  - enhanced visualisation of wall thickening during stress echocardiography
- To enhance Doppler flow signals from the cavities and great vessels.
- To determine myocardial ischaemia and viability using myocardial perfusion contrast echocardiography (MCE)
- Quantification of the coronary flow reserve, which has prognostic value in various disease conditions

TISS
equa
LINE

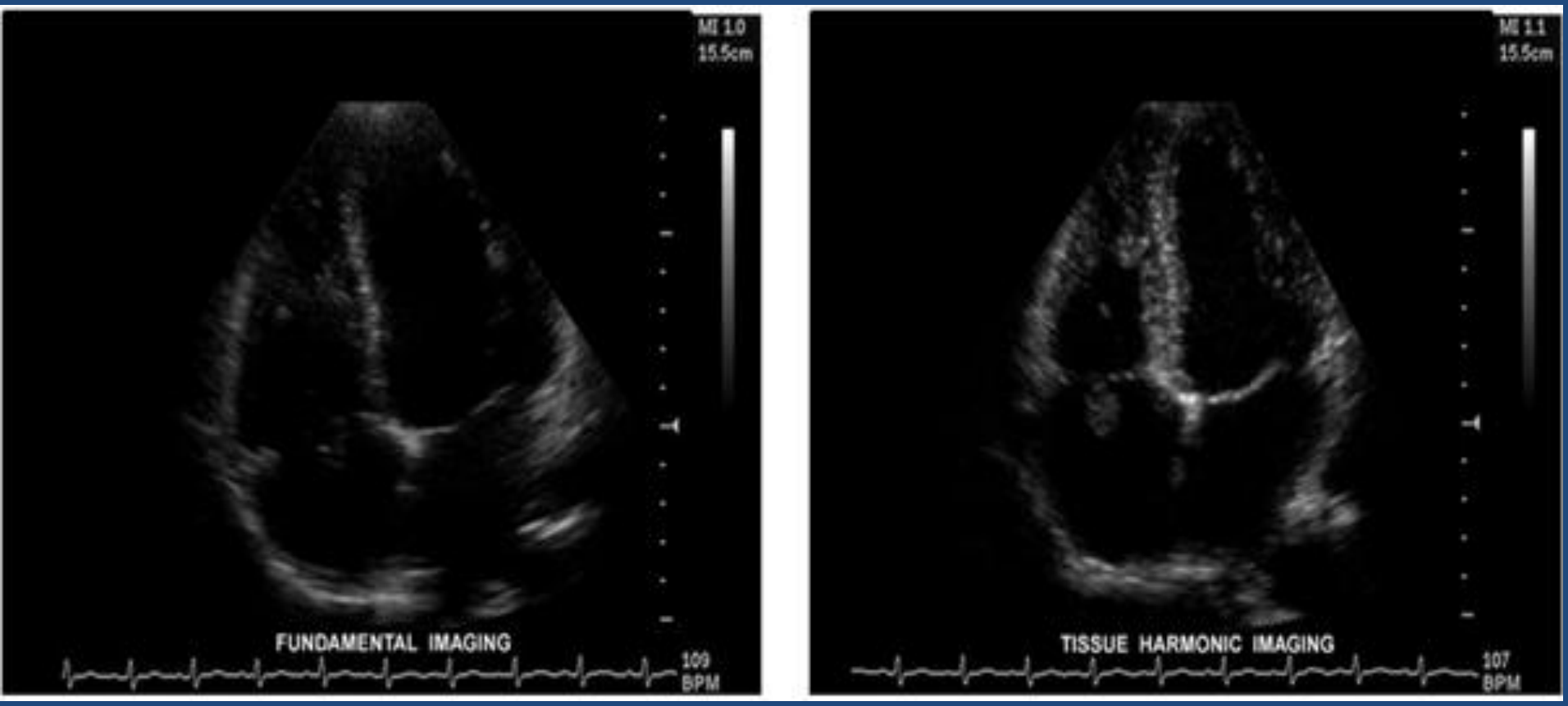
MICR
so sm
degre
(i.e. M

This
which produce harmonic frequencies



http://www.escardio.org/communities/EAE/contrast-echo-box/

TISSUE HARMONIC IMAGING



Principles of Contrast echocardiography

Blood appears black on conventional two dimensional echocardiography, not because blood produces no echo, but because the ultrasound scattered by red blood cells at conventional imaging frequencies is very weak—several thousand times weaker than myocardium—and so lies below the displayed dynamic range.

Stewart MJ. Heart. 2003; 89(3): 342–348.

- It is a remarkable coincidence that gas bubbles of a size required to cross the pulmonary capillary vascular bed (1–5 mm) resonate in a frequency range of 1.5–7 MHz, precisely that used in diagnostic ultrasound.

Stewart MJ. Heart. 2003; 89(3): 342–348.

The properties of the ideal UCA

- High Echogenicity: strong ultrasound reflectors
- Linear relationship between concentration and signal intensity
- Ability to cross the pulmonary capillary bed
- Stability over the duration of the procedure
- Minimal imaging artefacts
- Ability for rapid disruption at higher power outputs
- Safety : Non toxicity
- Additional special properties (e.g. site-specific therapeutic drug delivery)

The ultrasonic characteristics depends on :

a) size of the bubbles

b) composition of the shell

c) the gas in the shell

- In general, the stiffer the shell, the more easily it will crack or break with ultrasonic energy. Conversely, the more elastic the shell, the greater its ability to be compressed or resonated and to produce a nonlinear backscatter signature.

Types of agents

- Blood pool agents
  - Free gas bubbles – Gramiak and Shah first injected saline with air bubbles in the aorta in 1968; agitated fluids: indocyanine green, renografin, etc.
  - Encapsulated air bubbles (first generation agents) – nitrogen in gelatin (Carrol, 1980); human serum albumin (Feinstein, 1984) - Albunex; microcrystalline galactose microparticles with palmitic acid – Levovist
  - Low solubility gas bubbles – 2nd generation - perflurocarbons – Optison, Echogen, SonoVue, Definity
- Selective uptake agents – 3rd generation agents in the cell metabolism – colloidal suspensions of liquids as perfluorocarbons or durable shell

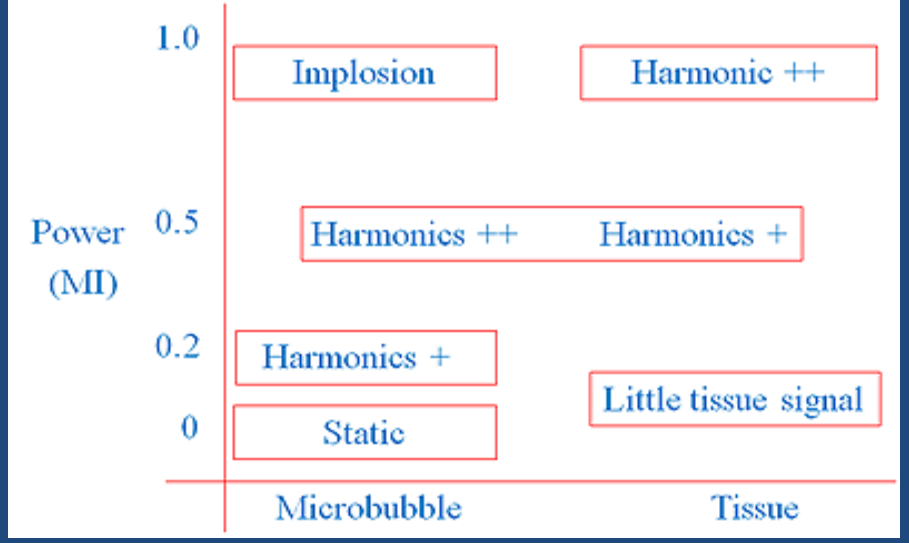
2nd generation contrast agents

Table 1 Characteristic of currently available contrast agents in UK and Europe

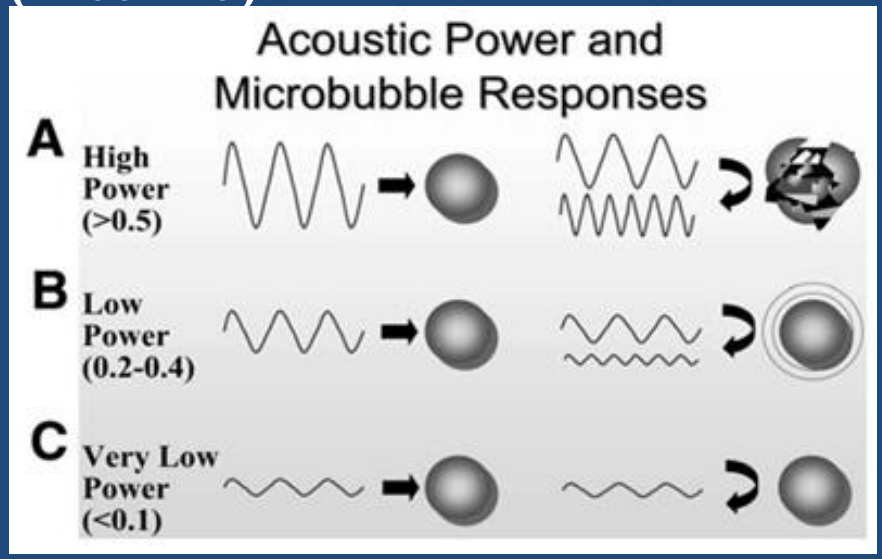
	SonoVue[6]	Optison[7]	Luminity[8]
Gas	Sulphur hexafluoride	Perfluoropropane	Perfluoropropane
Bubble size	2–8 μm	3.0–4.5 μm	1.1–2.5 μm
Surface coating	Surfactant/powder	Human albumin	Naturally occurring lipids
Contraindications and precautions			
Patients experiencing side effects in clinical trials (%)	11	17	8
Most frequent side effects in clinical trials	Headache (2.1%), nausea (1.3%), chest pain (1.3%), taste perversion (0.9%), hyperglycaemia (0.6%), injection site reaction 0.6%), paresthesia (0.6%), vasodilation (0.6%), injection site pain (0.5%).	Headache (5.4%), nausea and/or vomiting (4.3%), warm sensation or flushing (3.6%), dizziness (2.5%).	Headache (2.0%), flushing (1.0%), back pain (0.9%). rash/urticaria, wheezing/,allergic/anaphylaxis
Manufacturer	Bracco Diagnostics	GE Healthcare	Lantheus Medical Imaging (formerly Bristol-Myers Squibb)

Senior R, et al. Eur J Echocard 2009; 10:194:212

- At low poweroutput (PO) settings, there is mostly a linear response (fundamental enhancement) with some generation of harmonic frequencies.
- As the PO is increased, the bubbles generate more nonlinear resonance and thus generate greater harmonic frequencies.
- At a high power setting, fracture and destruction of the microbubble occur, allowing the air or gas inside to be released.



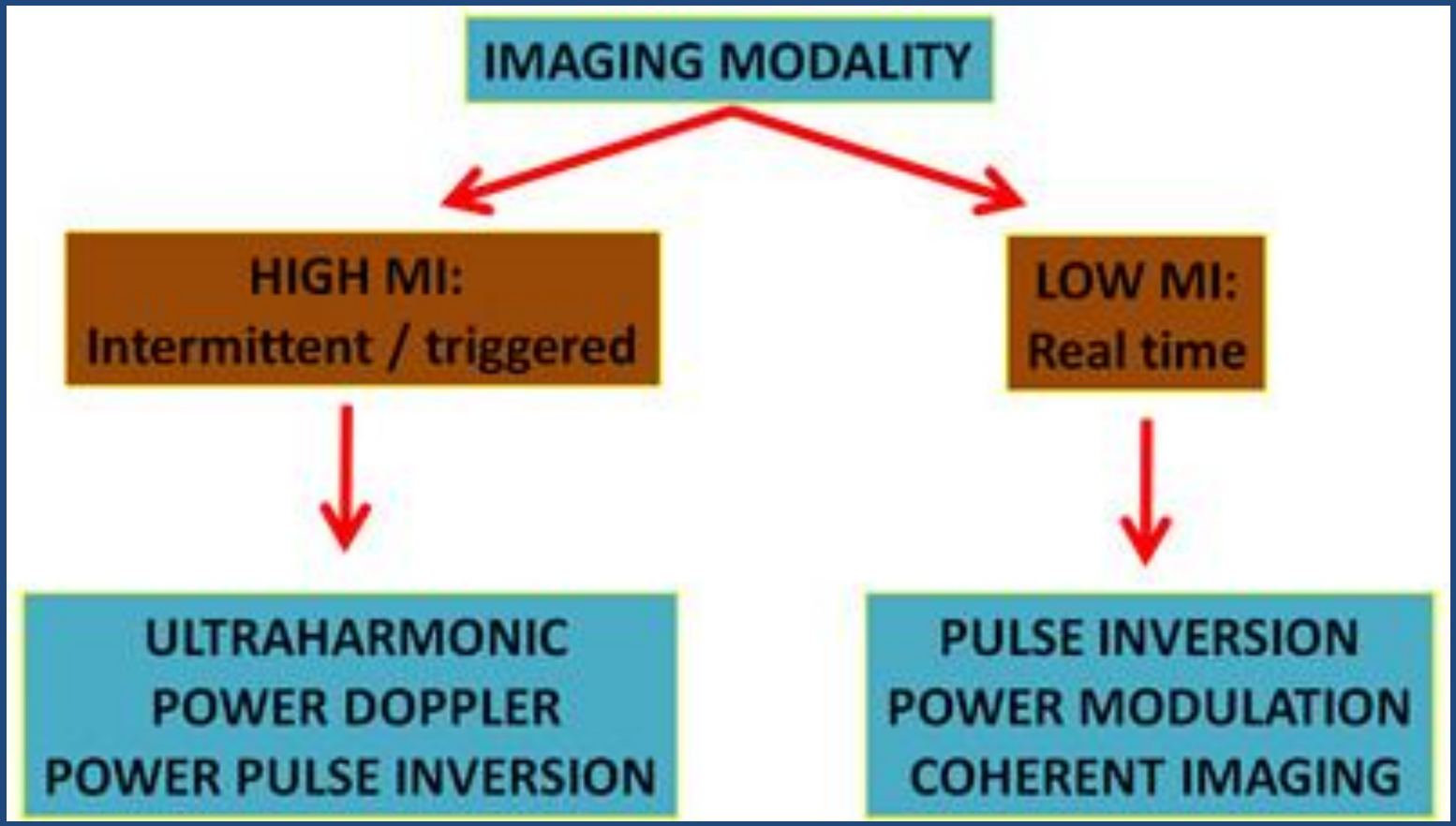
(<100 kPa)



(100 kPa–1 Mpa)

- Power output is usually measured with the mechanical index (MI)
- MI = Pneg/$\sqrt{f}$ where Pneg – peak negative pressure of ultrasound ; f – ultrasound frequency
- Different behavior in various MI

CE modalities



http://www.escardio.org/communities/EAE/contrast-echo-box/

Patients most likely to benefit from contrast echocardiography

- With obesity
- With chronic obstructive pulmonary disease
- In intensive care settings
- Mechanically ventilated
- With chest deformities
- With oncology diseases on chemotherapy

LEFT VENTRICULAR OPACIFICATION

- **Assessment of left ventricular (LV) systolic function.**
- **Accurate assessment and quantification is dependent on visualising the entire endocardium.**
- **Contrast opacification enhances endocardial border definition.**
- **PV Doppler signal is also enhanced for diastolic LV function.**

Machine settings for LVO

Scanhead frequency	**2.5-3.5 MHz**
Transmit power	**Mechanical index (MI) < 0.6**
Dynamic range	**Low-medium**
Line density	**Medium or high**
Compression	**Medium-high**
Persistence	**Disabled**
Focus	**Bellow mitral valve (apical views), bellow posterior wall (parasternal view)**
Receive gain	**Slightly reduced to decrease the grey levels in the myocardium before contrast injection**

LEFT VENTRICULAR OPACIFICATION

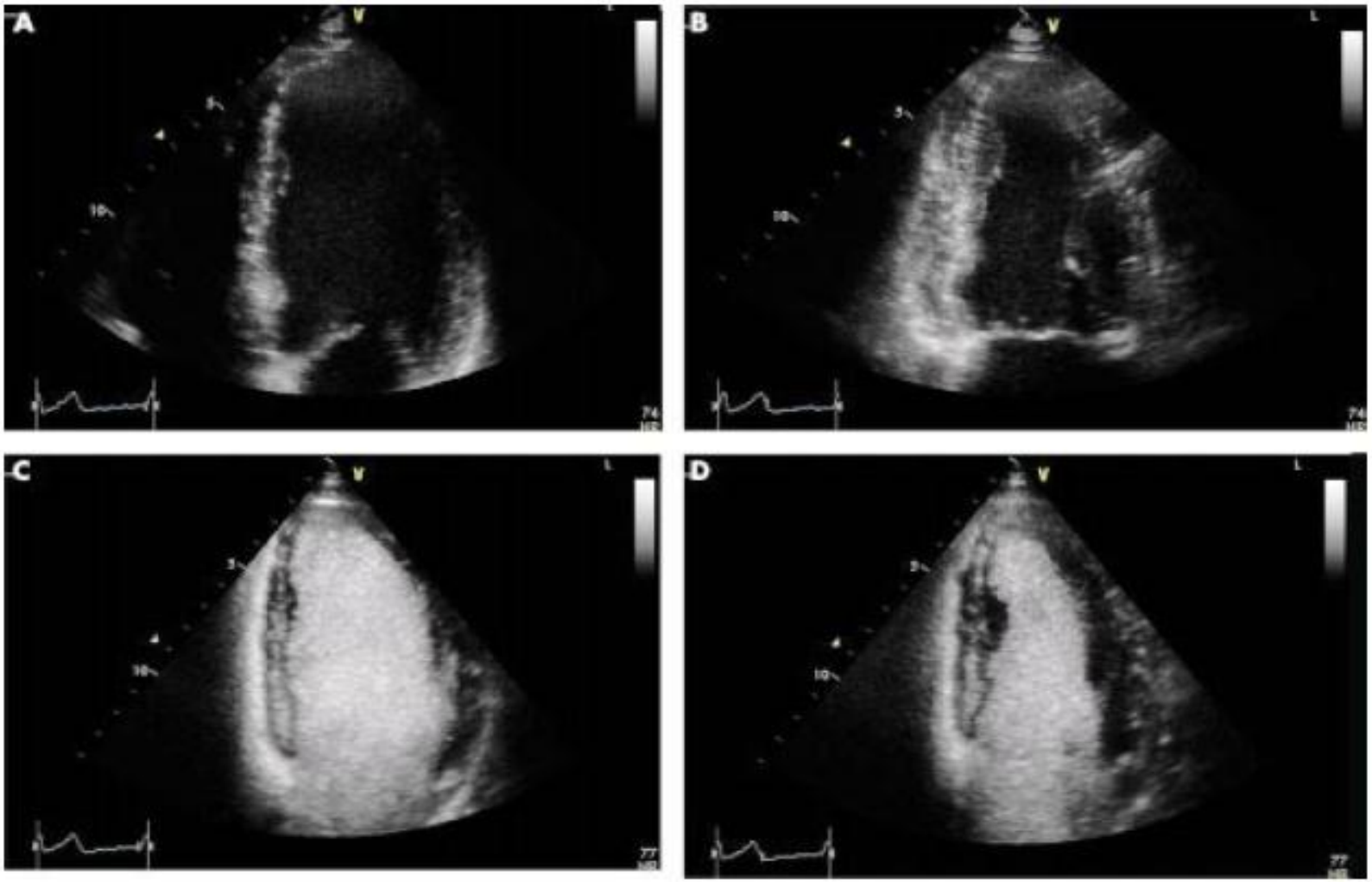
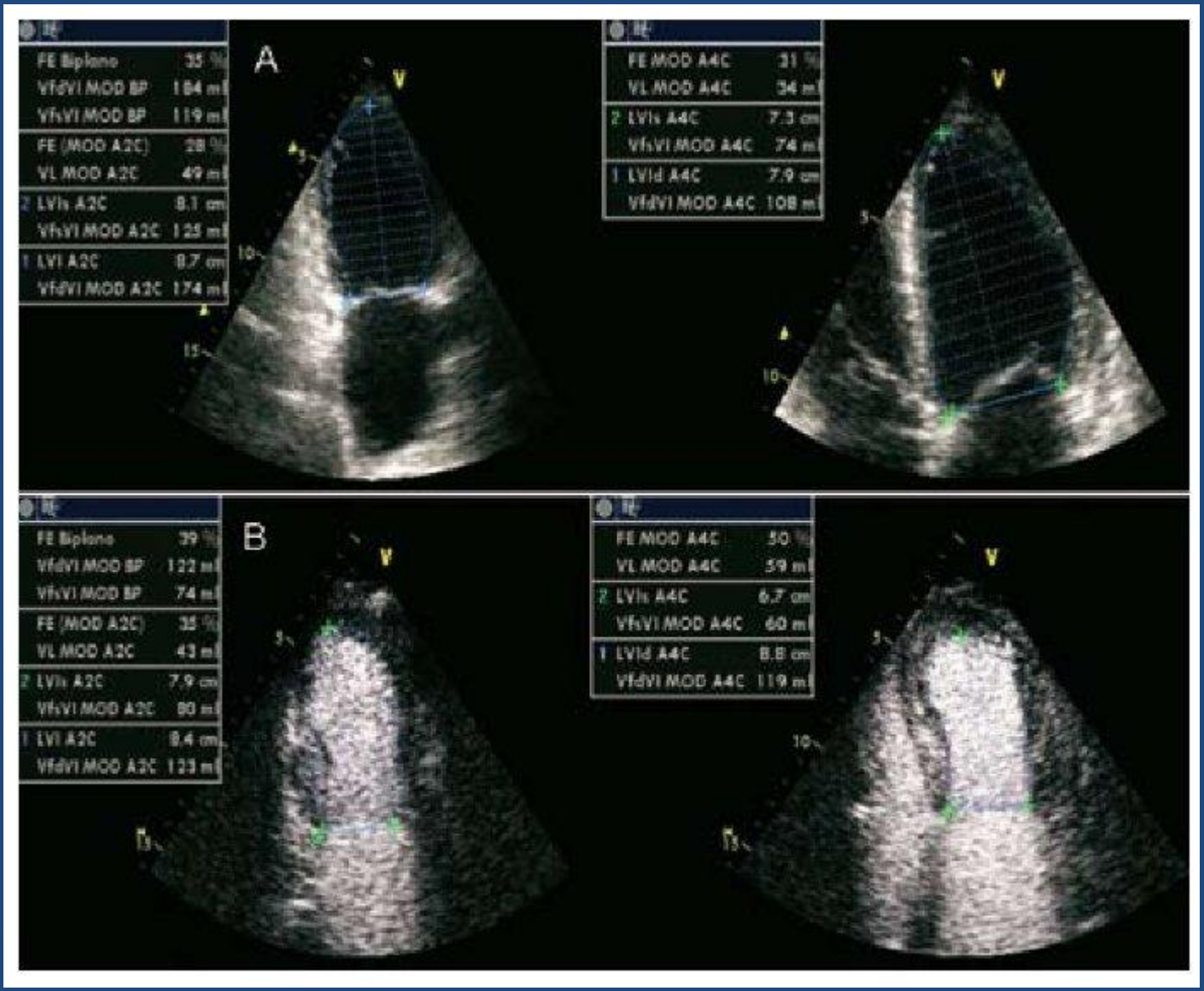


Figure 2 Left ventricular opacification. Apical four chamber view, end diastolic (A) and end systolic (B) frames, in a patient with recent myocardial infarction referred for assessment of left ventricular systolic function. Images acquired utilising tissue harmonic imaging at frequency of 3.8/1.9 MHz and a mechanical index of 1.0. Lateral wall endocardium was not clearly defined making accurate measurement of left ventricular volumes difficult. Apical four chamber view, end diastolic (C) and end systolic (D) frames, imaged after intravenous bolus injection of 0.5 ml of SonoVue. The mechanical index has been reduced to 0.5 but all other parameters are unchanged. The entire endocardial border is now clearly defined and systolic thickening of entire lateral wall appreciated.

Becher H, Burns PN. 2000



Rev Esp Cardiol.2009; 62(05) :535-51

Efficacy of CE in assessment of LV EF volumes and wall motion abnormalities

	Cont-	Contr+
Mean correlation coefficient [95% CI]	0.85 (EF)[0.82-0.88]	0.94 (EF)[0.91-0.97]
	0.81 (EDV)[0.6-1.02]	0.94 (EDV)[0.92-0.96]
	0.92 (ESV)[0.87-0.97]	0.97 (ESV)
Mean % agreement with gold standard	77% (EF)	94% (EF)
	61% (RWMA)	83% (RWMA)

Senior R, et al. Eur J Echocard 2009; 10:194:212

Apical Thrombus in AMI

Becher H, Burns PN. 2000

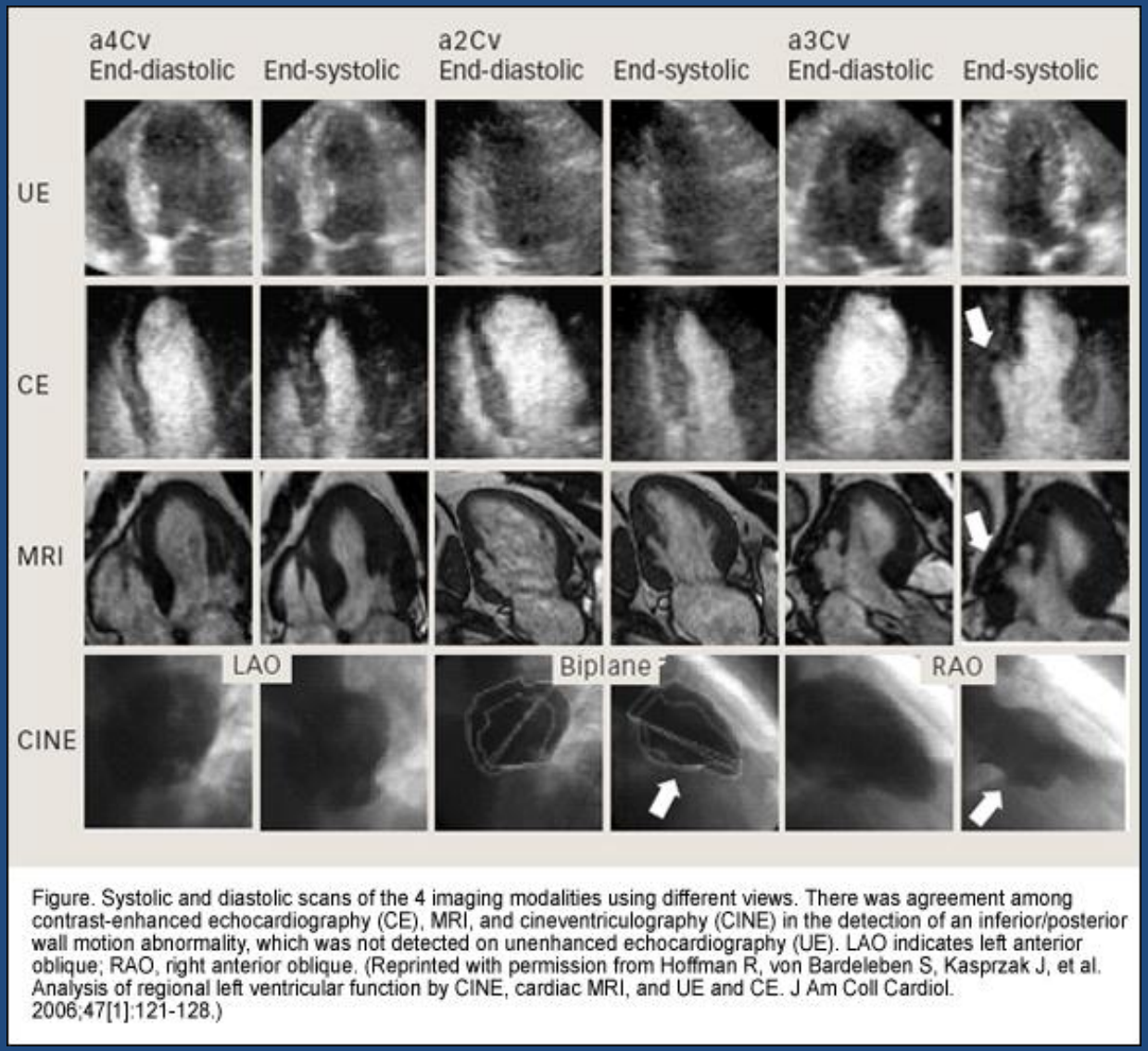
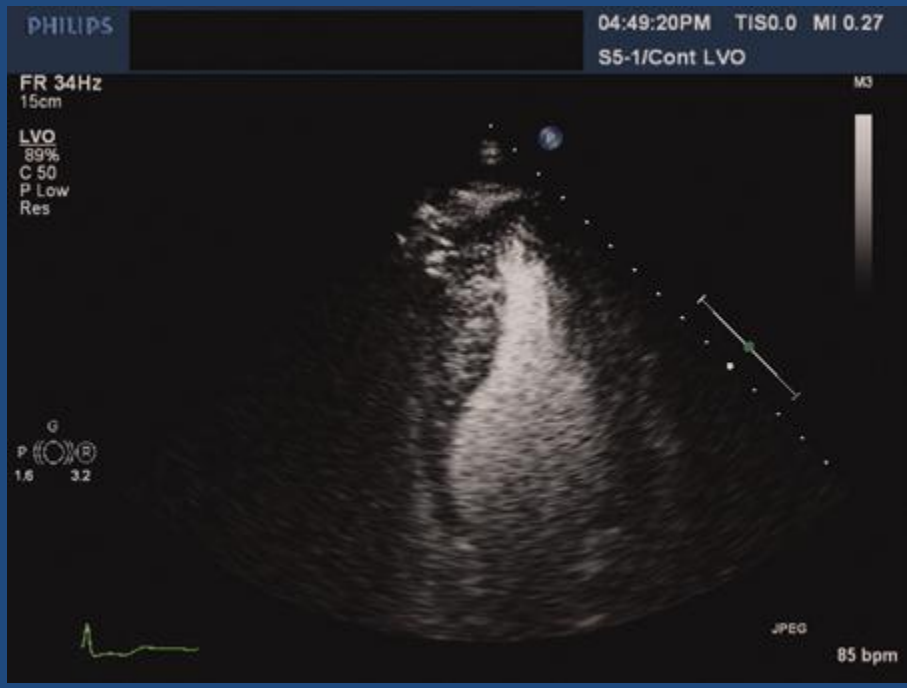


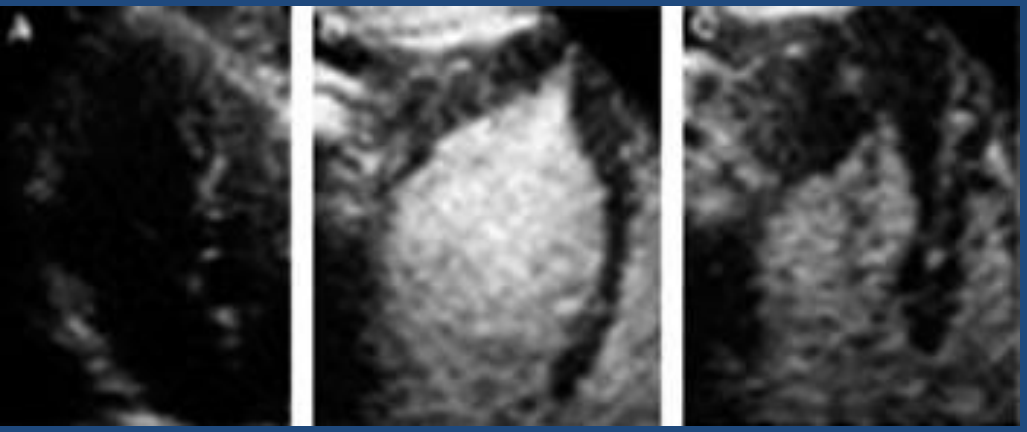
Figure. Systolic and diastolic scans of the 4 imaging modalities using different views. There was agreement among contrast-enhanced echocardiography (CE), MRI, and cineventriculography (CINE) in the detection of an inferior/posterior wall motion abnormality, which was not detected on unenhanced echocardiography (UE). LAO indicates left anterior oblique; RAO, right anterior oblique. (Reprinted with permission from Hoffman R, von Bardeleben S, Kasprzak J, et al. Analysis of regional left ventricular function by CINE, cardiac MRI, and UE and CE. J Am Coll Cardiol. 2006;47[1]:121-128.)

Becher H, Burns PN. 2000

Apical HCM

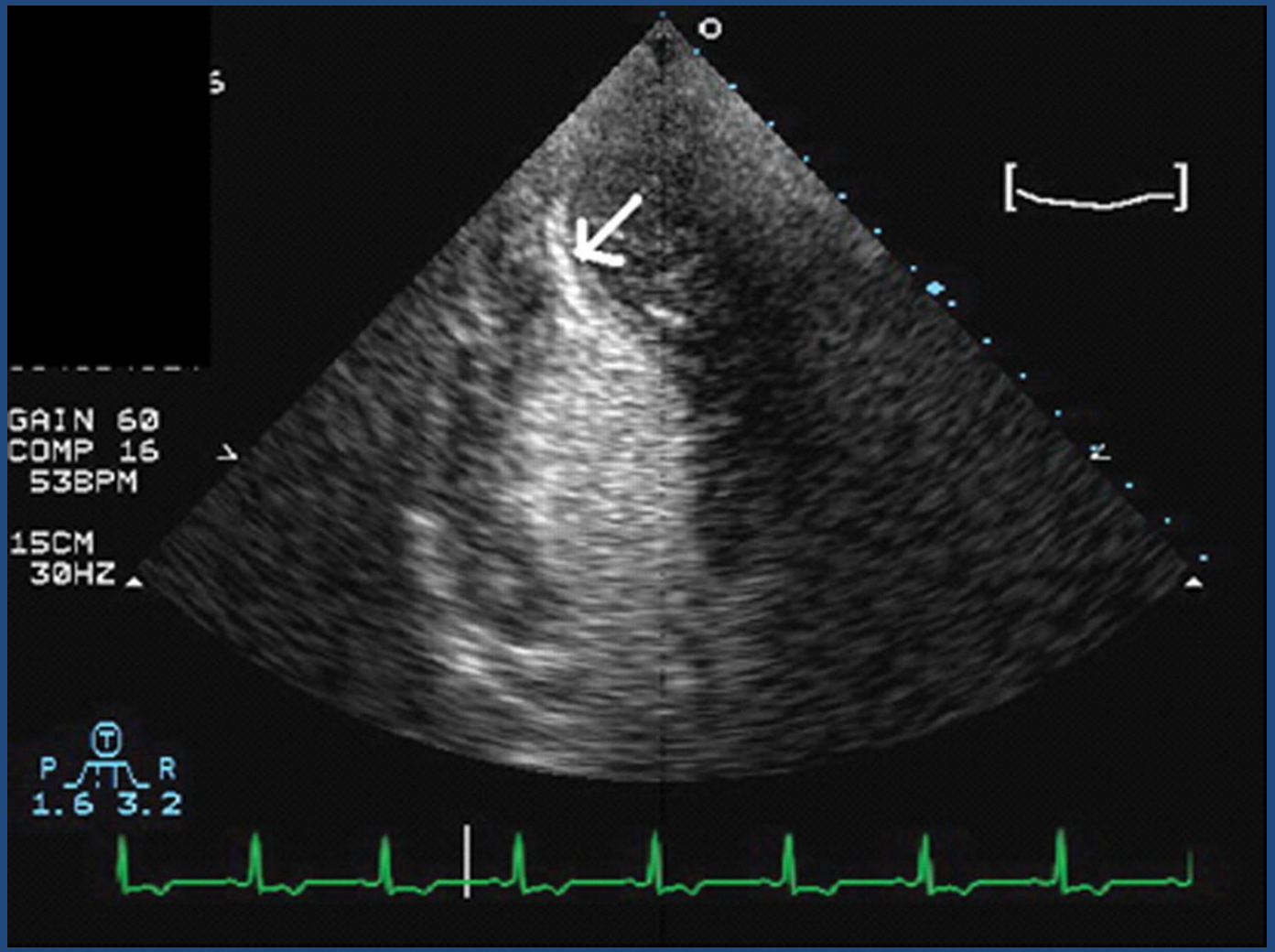


The EAE Textbook of Echocardiography.



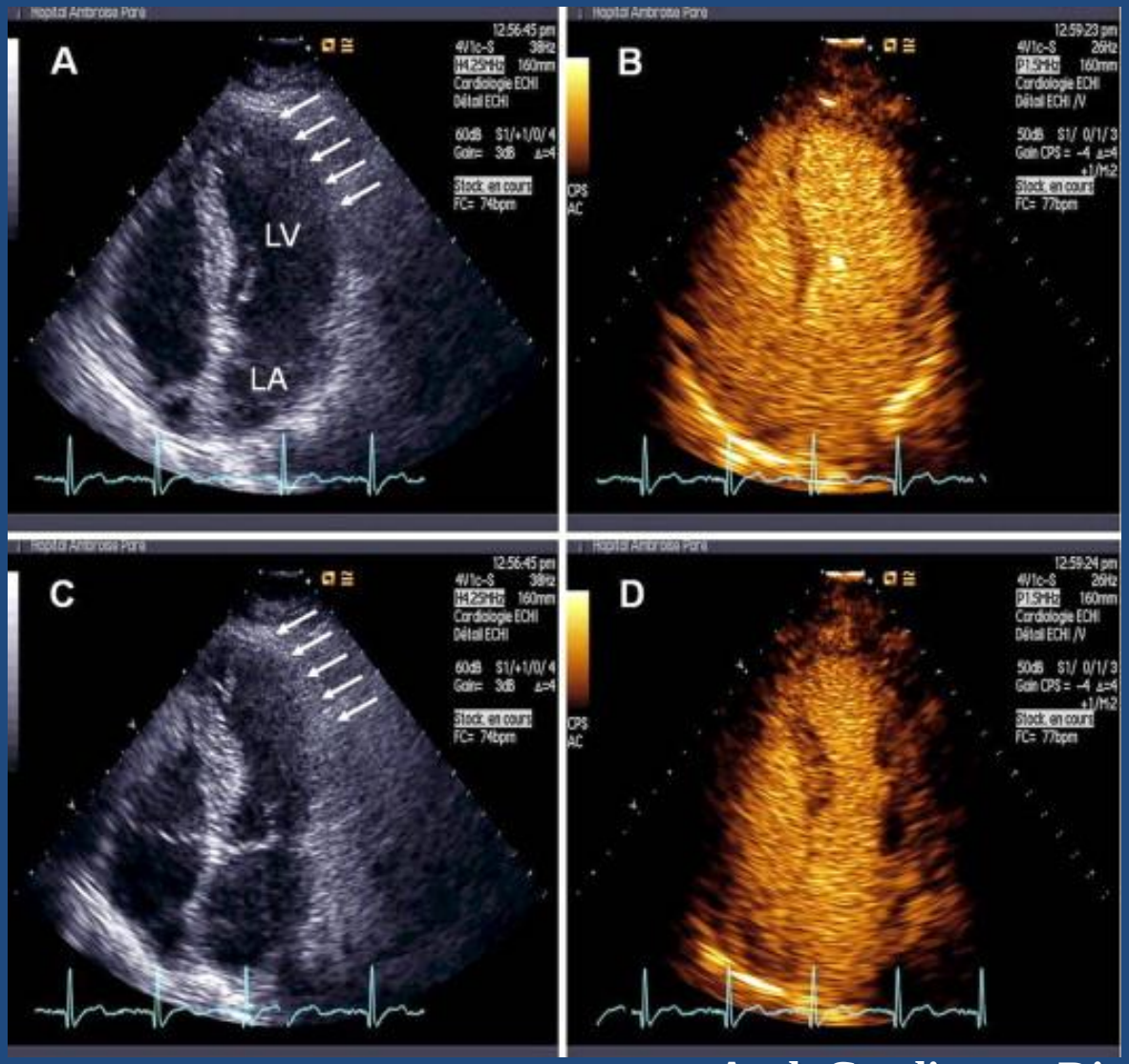
BMJ Case Reports. 2009;doi:10.1136/bcr.04.2009.17

Contrast-enhanced echo: apical HCM



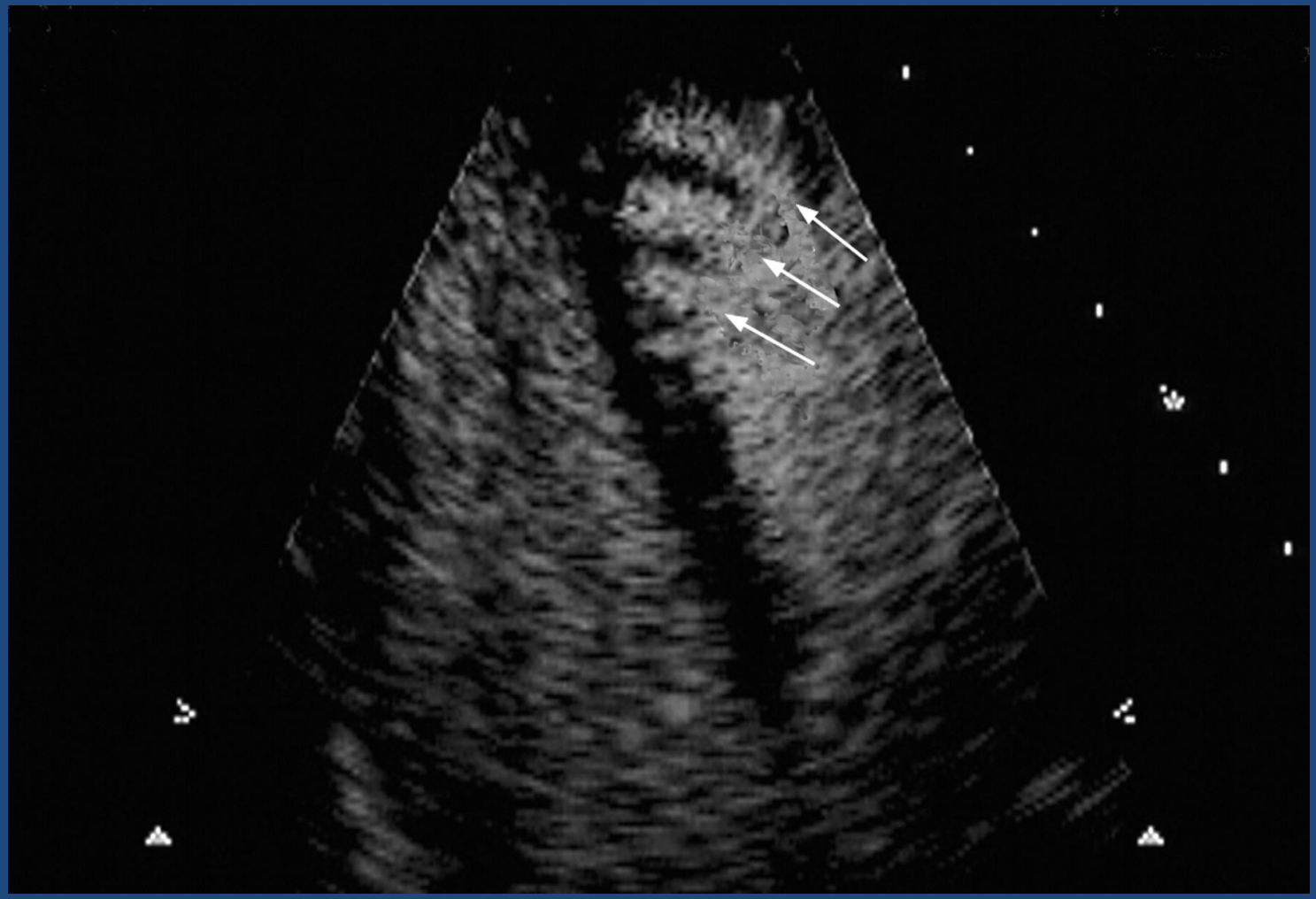
Reddy M et al. Eur J Echocardiogr 2008;9:560-562

Tako-Tsubo cardiomyopathy



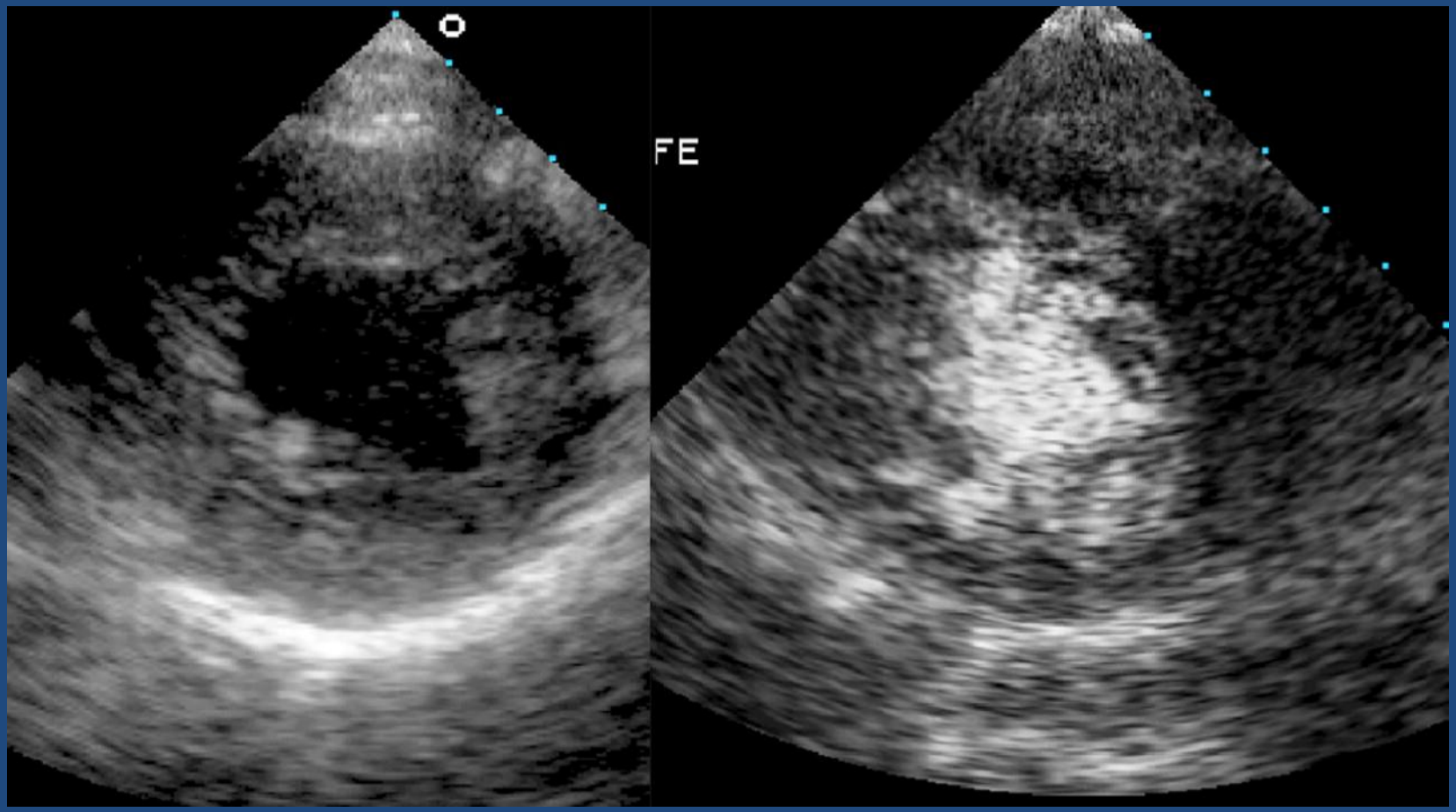
Arch Cardiovasc Dis 2010; 103: 447-453

Non-compaction LV



Postgrad Med J 2009;85:202-207

Non-compaction LV



Olszewski R et al. Eur J Echocardiogr 2007;8:s13-s23

Indications for LV contrast imaging

Indications for resting left ventricular opacification contrast echo[2]

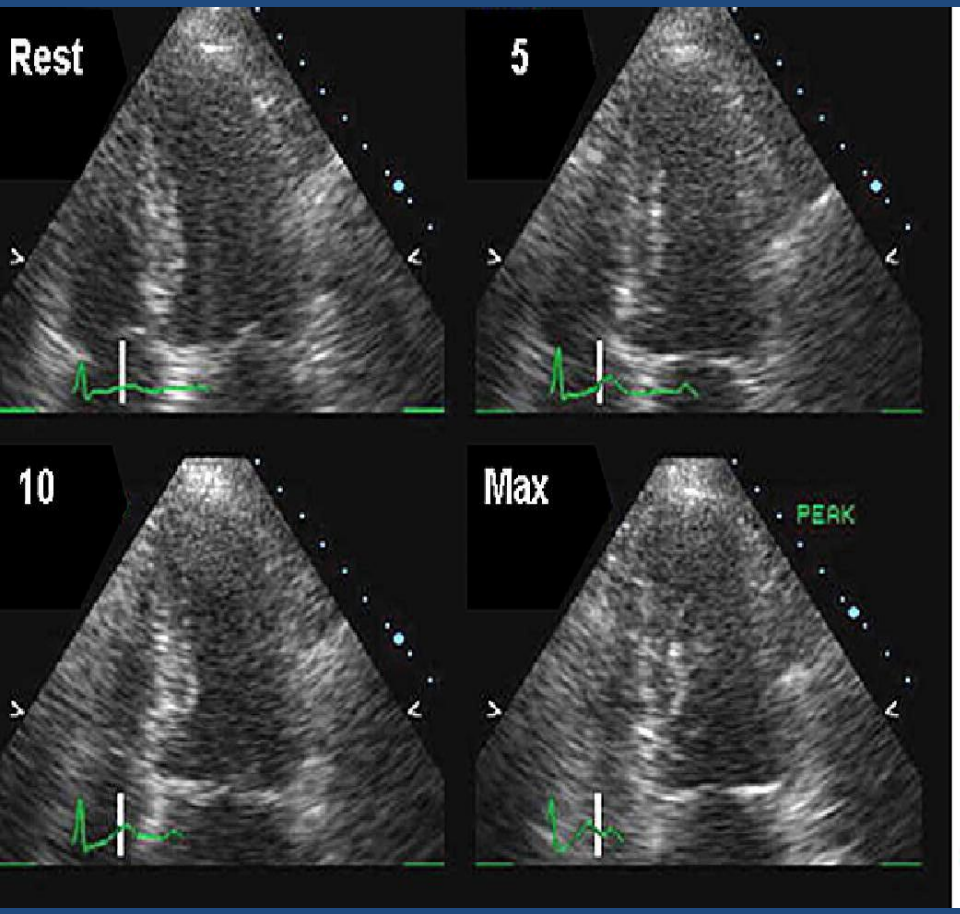
In patients with suboptimal images:

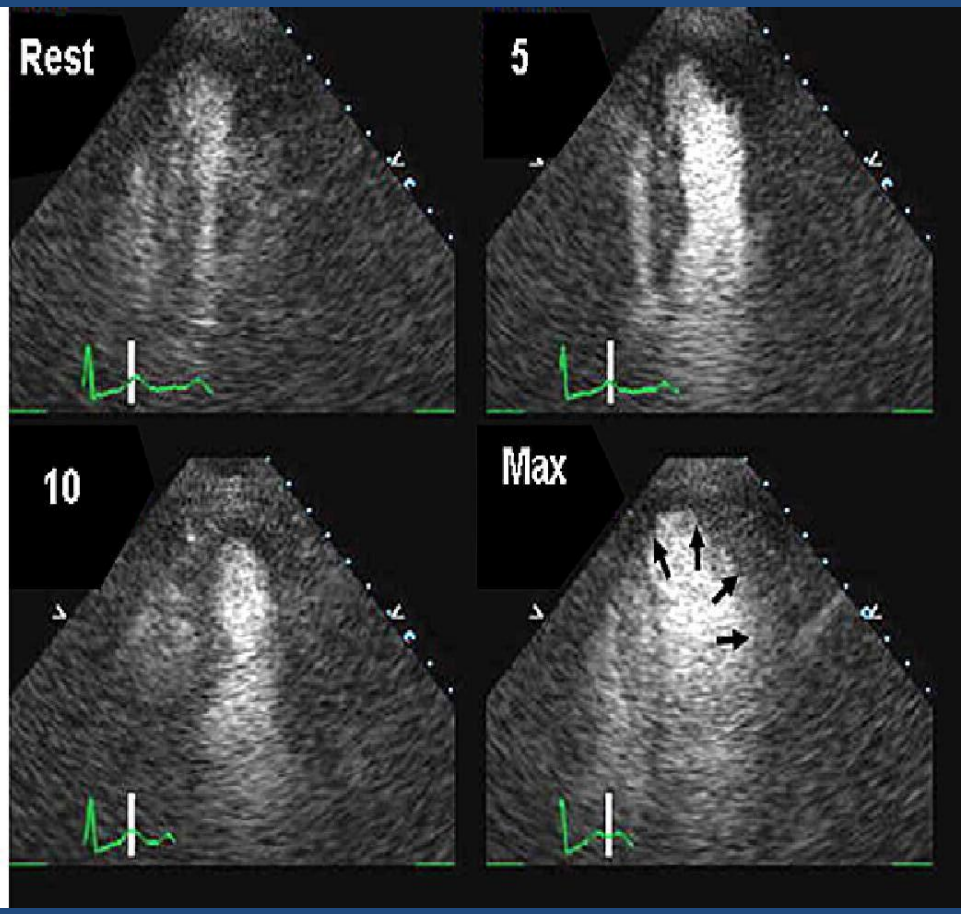
(1) To enable improved endocardial visualization and assessment of LV structure and function when two or more contiguous segments are NOT seen on non-contrast images
(2) To have accurate and repeatable measurements of LV volumes, and ejection fraction by 2D Echo
(3) To increase confidence of the interpreting physician in the LV function, structure and volume assessments
(4) To confirm or exclude the echocardiographic diagnosis of the following LV structural abnormalities, when non-enhanced images are suboptimal for definitive diagnosis:

- apical hypertrophic cardiomyopathy
- ventricular non-compaction
- apical thrombus
- ventricular pseudoaneurysm

Senior R, et al. Eur J Echocard 2009; 10:194:212

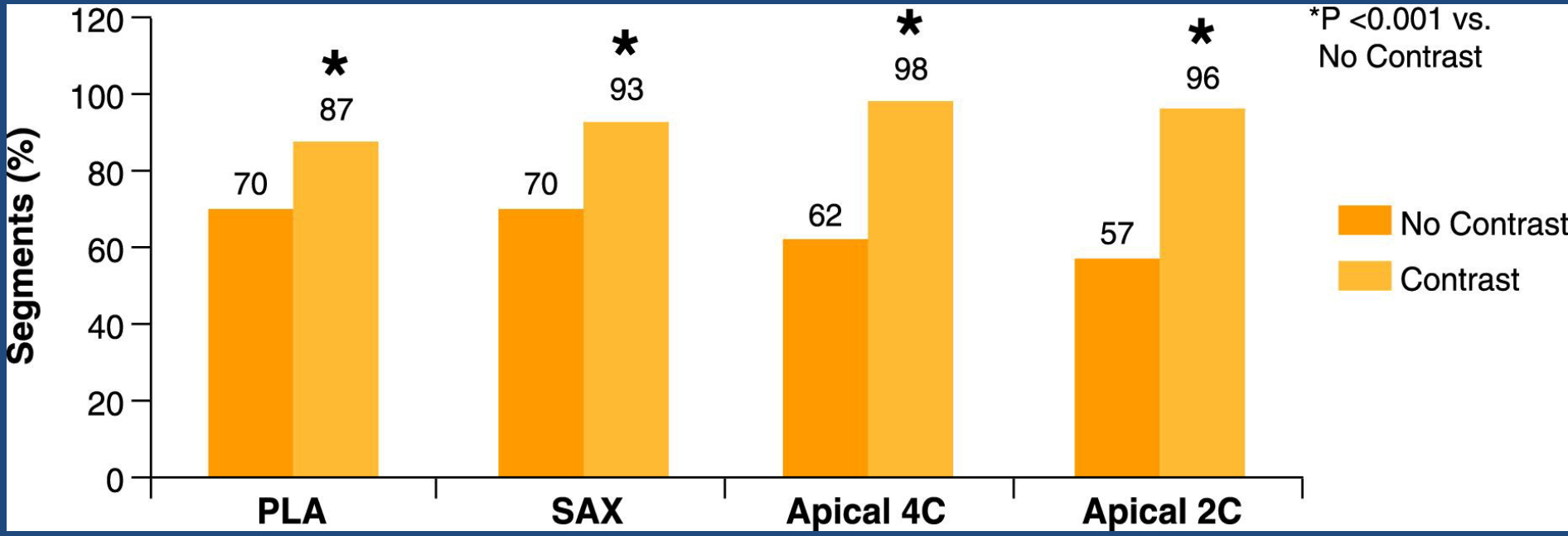
CE in stress testing





JACC Cardiovasc Imaging. 2008 ;1(2):145-52.

Improvement in quality assessment with CE: OPTIMIZE



JACC Cardiovasc Imaging. 2008 ;1(2):145-52.

Contrast application in stress echocardiography

Indications for use of contrast in stress echocardiography

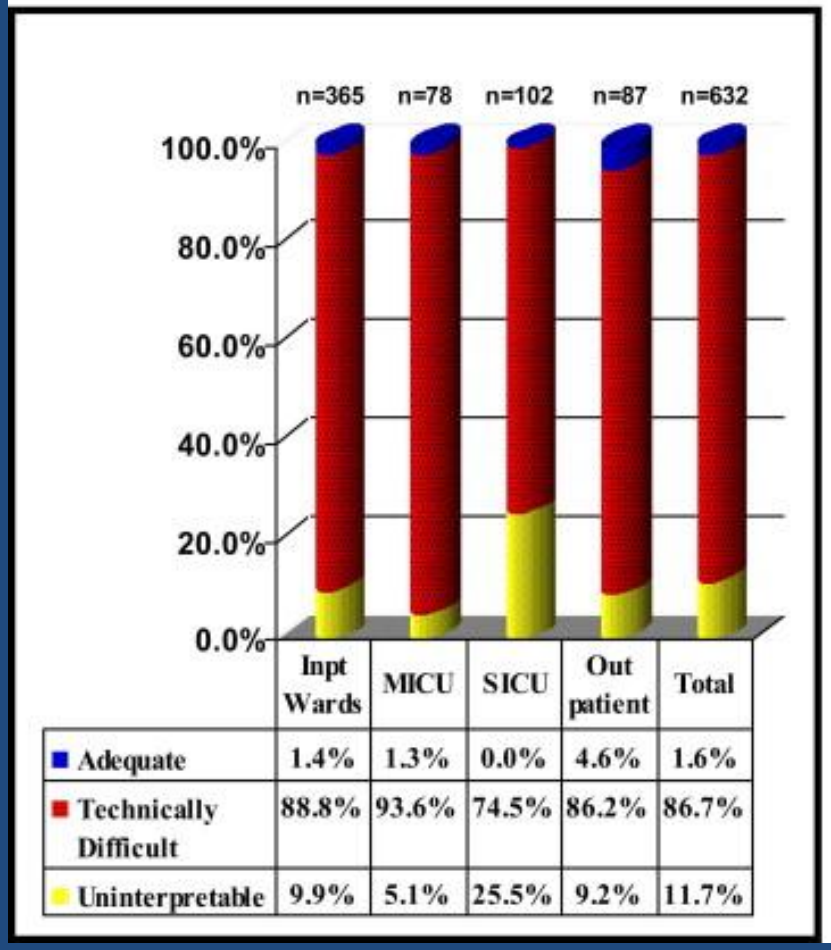
When two or more endocardial border contiguous segments of LV are not well visualized in order to:

- To obtain diagnostic assessment of segmental wall motion and thickening at rest and stress
- To increase the proportion of diagnostic studies
- To increase reader confidence in interpretation

Senior R, et al. Eur J Echocard 2009; 10:194:212

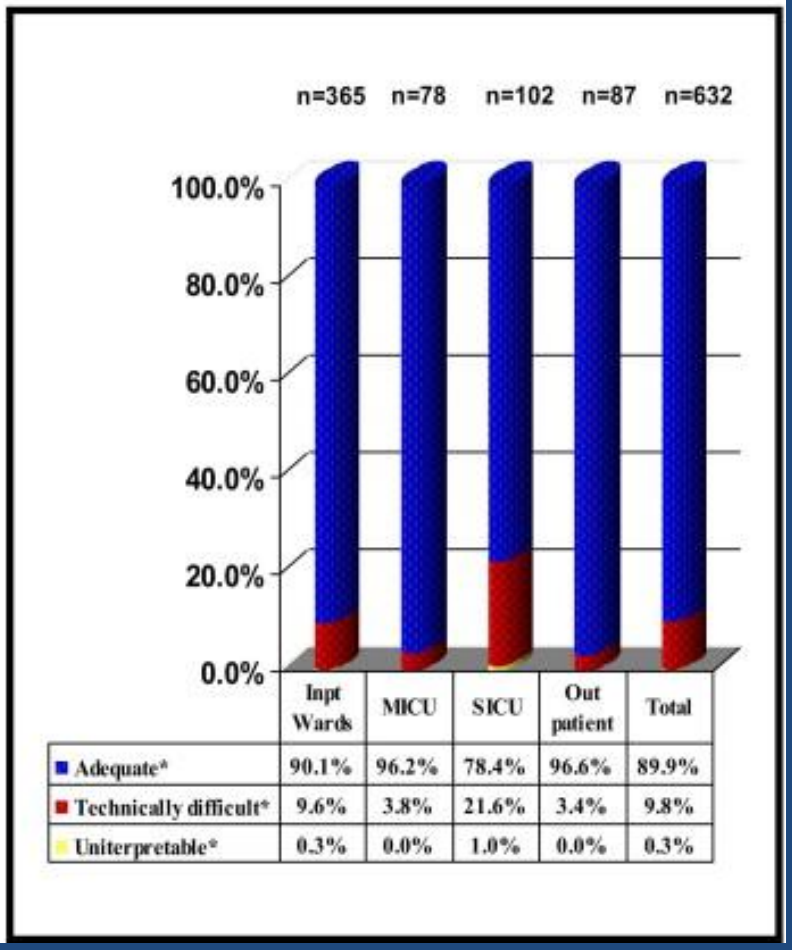
Improvement in quality of image after CE in 632 difficult cases

Before Contrast



	Inpt Wards	MICU	SICU	Out patient	Total
Adequate	1.4%	1.3%	0.0%	4.6%	1.6%
Technically Difficult	88.8%	93.6%	74.5%	86.2%	86.7%
Uninterpretable	9.9%	5.1%	25.5%	9.2%	11.7%

After Contrast

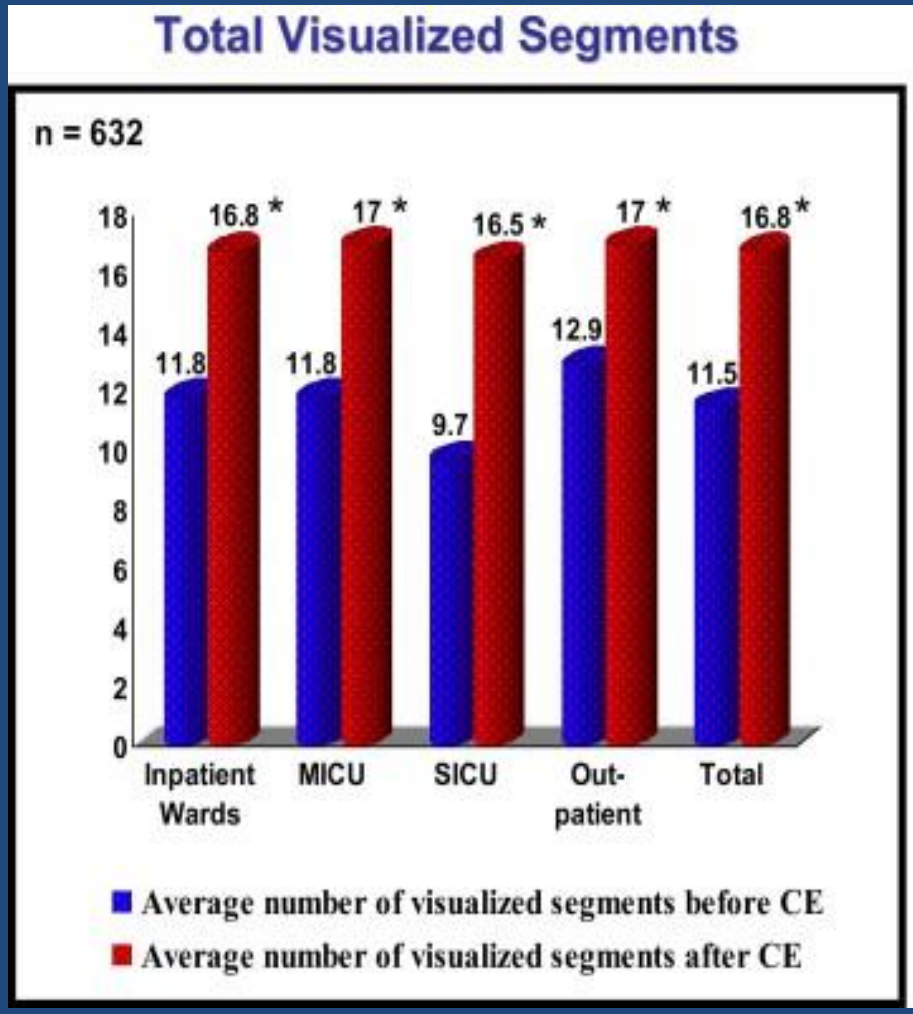


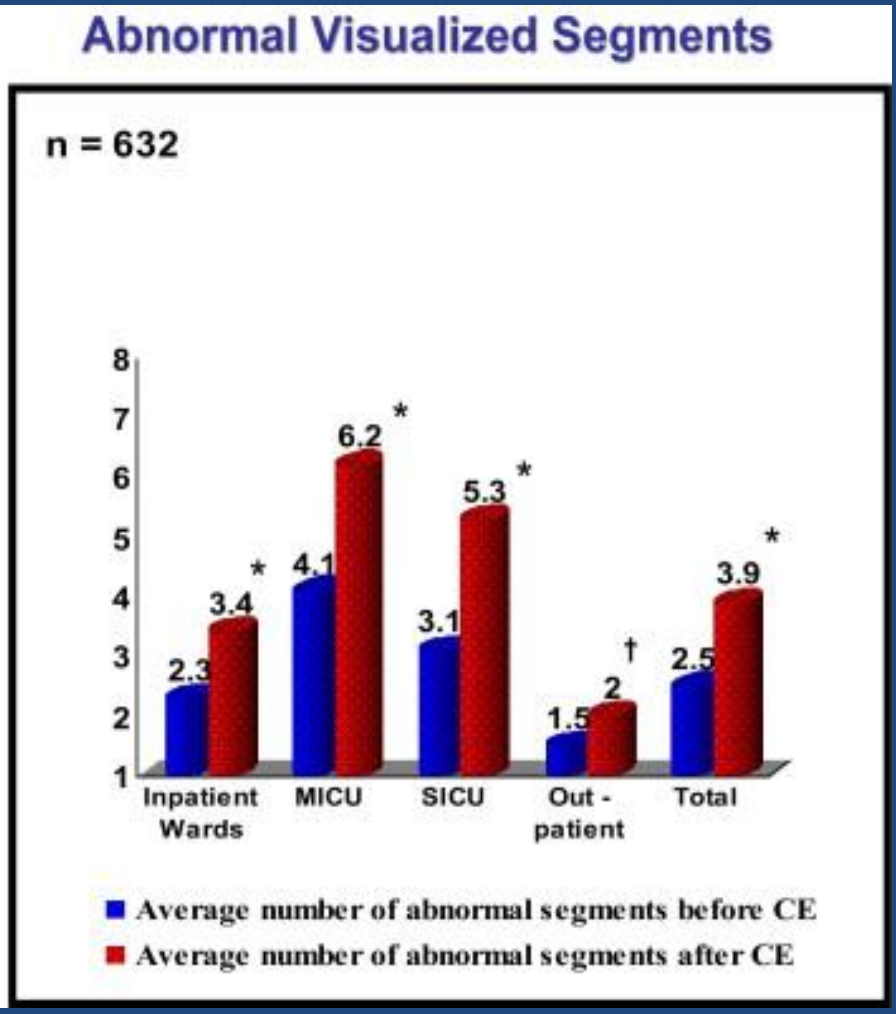
	Inpt Wards	MICU	SICU	Out patient	Total
Adequate*	90.1%	96.2%	78.4%	96.6%	89.9%
Technically difficult*	9.6%	3.8%	21.6%	3.4%	9.8%
Uniterpretable*	0.3%	0.0%	1.0%	0.0%	0.3%

p<0.0001

Kurt M, et al. J Am Coll Cardiol 2009 53(9):802-10.

Improvement in number of segments visualized after CE

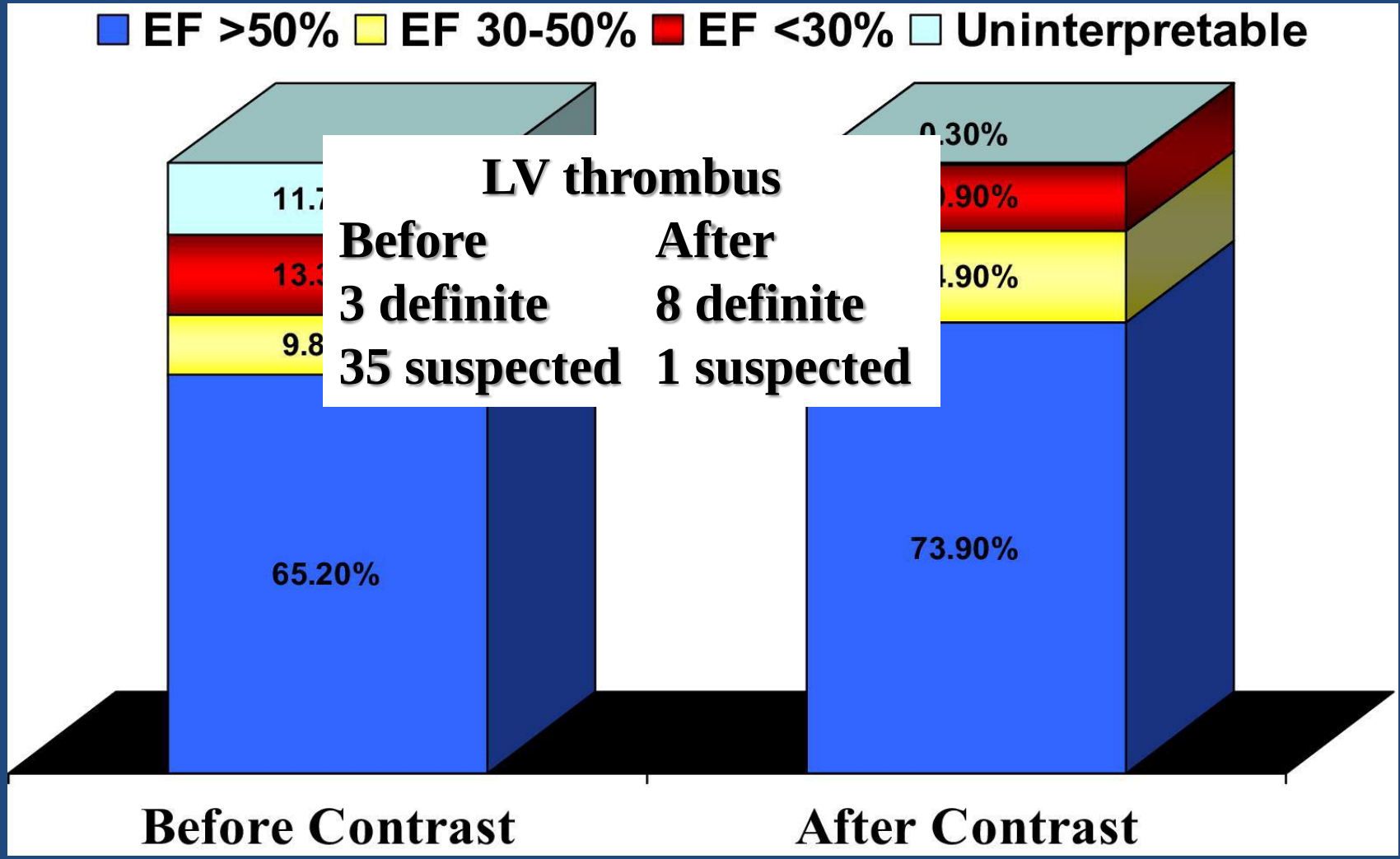




* p < 0.0001; † p=0.0016

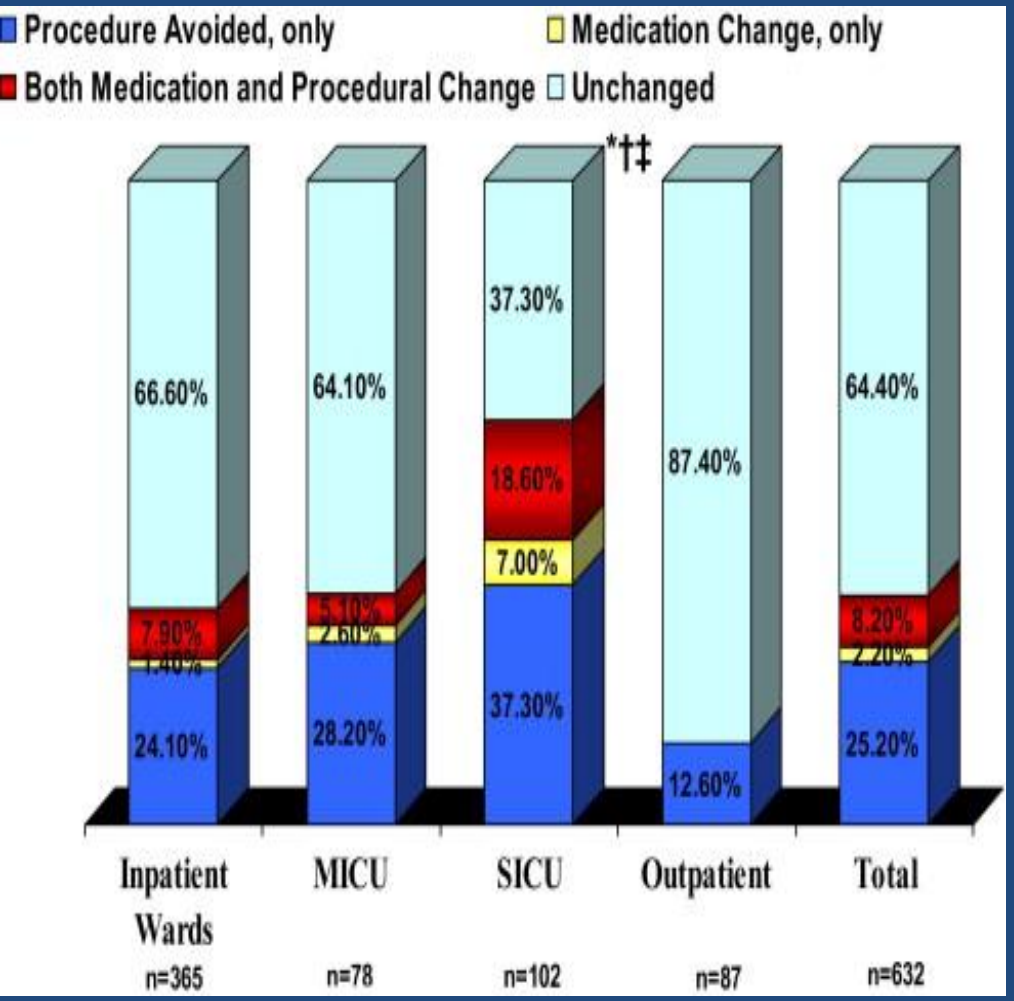
Kurt M, et al. J Am Coll Cardiol 2009 53(9):802-10.

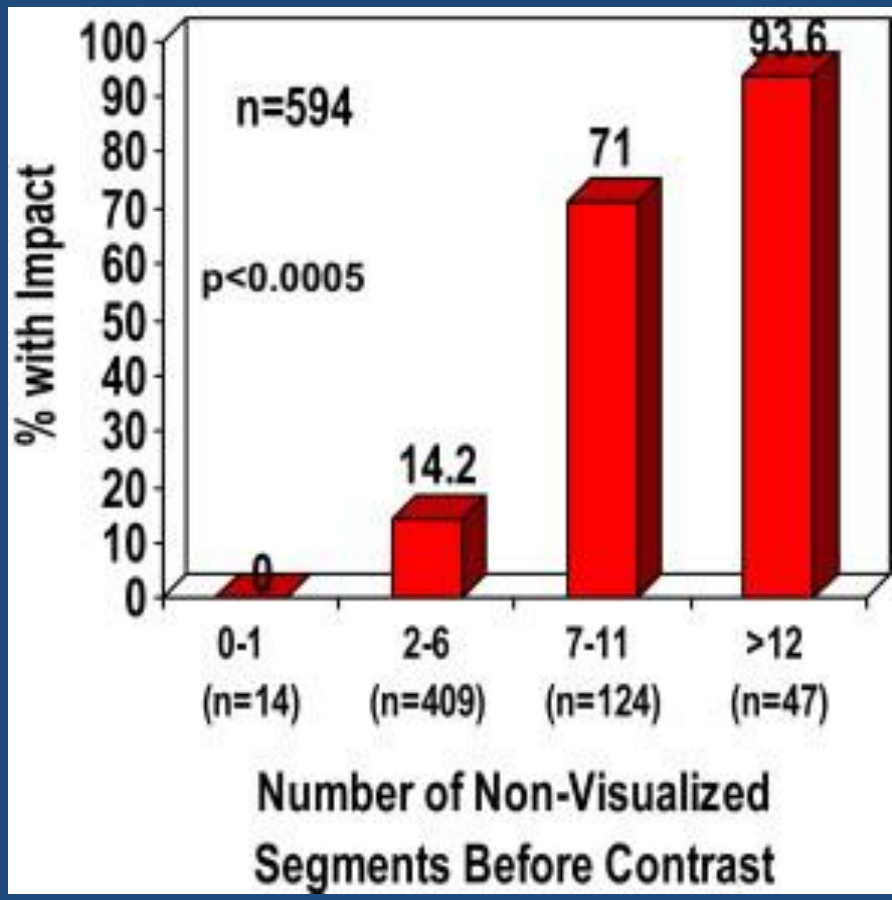
LV assessment before and after CE



Kurt M, et al. J Am Coll Cardiol 2009 53(9):802-10.

Total Impact of Contrast on Patient Management





Kurt M, et al. J Am Coll Cardiol 2009 53(9):802-10.

Contrast in echocardiography:

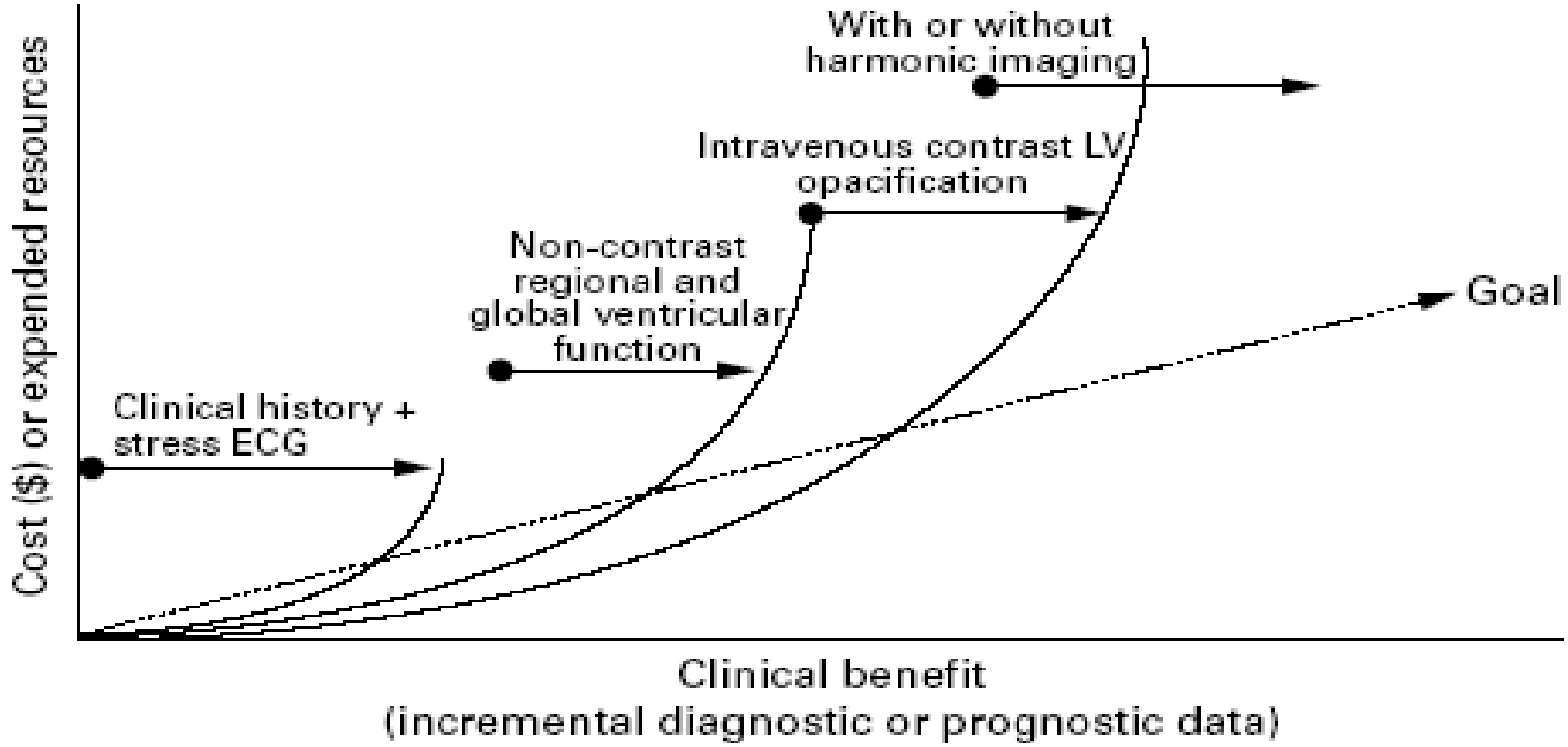


Figure 1 Interaction of cost quality with new advances in echocardiography. ECG, electrocardiography; LV, left ventricular.

Clinical and economic outcomes assessment with myocardial contrast echocardiography

Leslee J Shaw, Mark J Monaghan and Petros Nihoyannopolous

Heart 1999;82;16-21

SAFETY:

- A multicenter registry of 4 300 966 hospitalized patients with and without CE echo – 24-h death rate 1.08% vs. 1.06%; HR for contrast agent vs. no contrast 0.76, 95%CI 0.70-0.82

Am J Cardiol. 2008;102(12):1742-6.

- Study of 14 500 critically ill patients – contrast vs no contrast OR for same-day mortality 1.18, 95%CI 0.82-1.71 (p=0.37)

JACC Cardiovasc Imaging. 2010;3(6):578-85.

- Retrospection of 18,671 consecutive echo studies – 24-h death rate was 0.42% in the contrast group vs. 0.37% in the non-contrast group (p=0.6)

J Am Coll Cardiol 2008;51(17):1704-6.

- A meta-analysis of 8 studies in more than 5.2 mil pts – all-cause mortality 0.34% in contrast group vs. 0.9% in the non-contrast one, pooled OR =0.57, 95%CI 0.32-1.01 (p=0.05) and MI incidence 0.15% vs. 0.2%, OR=0.85, 0.35-2.05 (p=0.72)

Am J Cardiol 2010;106(5):742-7

- A retrospective analysis of 78,383 administered contrast doses between 2001 and 2007 – severe reaction probably related to contrast agent Definity in 0.01% of out=patient pts, anaphylactoid reactions in 0.006%, no deaths, no reactions in in-hospital pts.

J Am Soc Echocardiogr 2008;21(11):1202-6.

SAFETY:

Table 5 Comparative mortality in selected cardiac procedures

Procedures	Mortality
Contrast Echo	1:145 000 (SonoVue), 1:500 000 (Definity)
Myocardial Scintigraphy	1:10 000
Exercise ECG	1:2500 (or AMI)
Coronary arteriography	1:1000

Modified from Main *et al.*[41]

Senior R, et al. Eur J Echocard 2009; 10:194:212

WHEN CONTRAST SHOULD NOT BE USED

- Unstable angina or acute coronary syndrome in past 7 days

for SonoVue only

- Unstable (NYHA Class IV) heart failure
- Right-to-left intra-cardiac shunt
- Significant pulmonary hypertension

CONCLUSIONS:

- CE is an effective way to improve the opacification of LV for function assessment in difficult cases
- It may help in the diagnosis of additional findings, such as thrombi, apical HCMP, pseudoaneutysms, etc.
- CE enhances the segment delineation in sress testing
- The cost-effect ratio seems beneficial at a relatively low cost increment
- CE is relatively safe with no more additional adverse reactions than other contrast procedures or other diagnostic procedures in cardiology
- It may be used for assessment of myocardial perfusion and future target for treatment procedures