30 GIORNATE CARDIOLOGICHE TORINESI

TURIN,
October
25th-27th
2018

PRESIDENT
MAURO RINALDI

CO-PRESIDENTS
SEBASTIANO MARRA
FIORENZO GAITA

UNIVERSITÁ DEGLI STUDI DI TORINO

AZIENDA OSPEDALIERO UNIVERSITARIA
Città della Salute e della Scienza di Torino

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Sala ELEONORA

Friday
October
26th
Morning

CONTROVERSIES IN CARDIOLOGY

8:30 WORKSHOP OPENING
Chairpersons: CARLA GIUSTETTO, MAURO RINALDI

8:45 20 years of Cardiology: what have we learned? What are the challenges ahead?
MAURO GIORGI

BESIDES EJECTION FRACTION: THE ROLE OF ECHOCARDIOGRAPHY

ANTONELLA FAVA

10:00 Biomarkers vs echocardiography. How can we monitor cardiotoxicity?
- Biomarkers as early cardiotoxicity markers
- Besides ejection fraction: the role of echocardiography
MAURO GIORGI

10:30 Target therapy and cardiotoxicity
- How the survival curve has changed over the years PATRIZIA PREGNO
- Management of the peripheral

TURIN,
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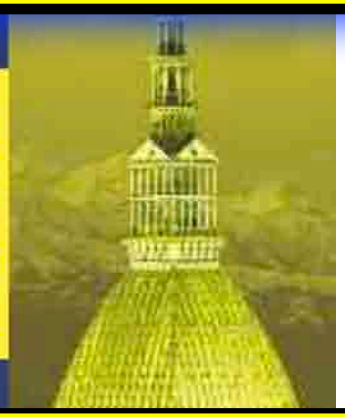
2018
Starhotels Majestic



PRELIMINARY PROGRAM

GIORNATE CARDIOLOGICHE TORINESI

Mauro GIORGI
S.C. CARDIOLOGIA U - OSP. MOLINETTE
CITTA' della SALUTE e della SCIENZA di TORINO

In general, the cardiovascular complications of cancer therapy can be divided into nine main categories, which are discussed in this document:

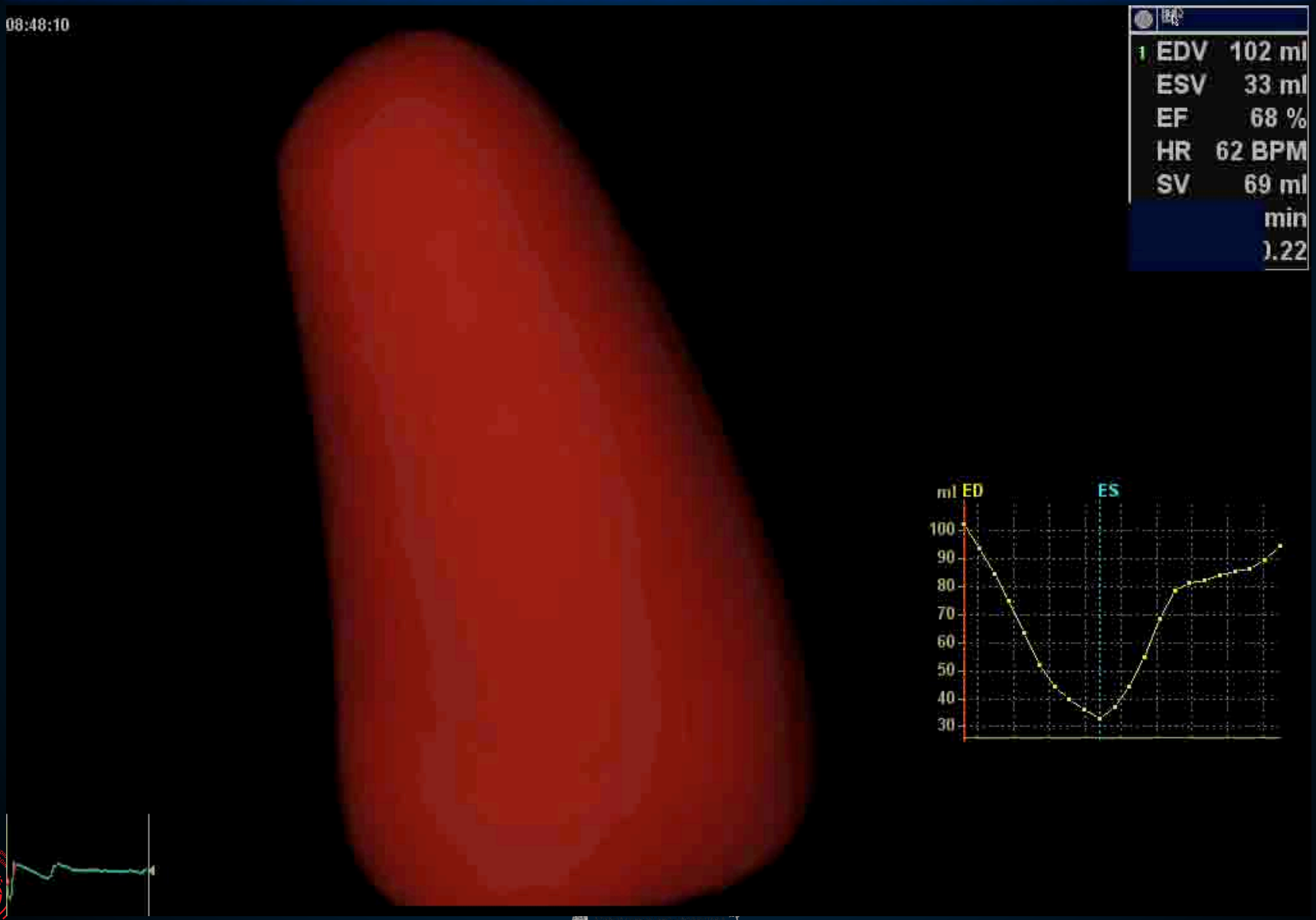
- myocardial dysfunction and heart failure (HF);
- coronary artery disease (CAD);
- valvular disease;
- arrhythmias, especially those induced by QT-prolonging drugs;
- arterial hypertension;
- thromboembolic disease;
- peripheral vascular disease and stroke;
- pulmonary hypertension and
- pericardial complications.

LA DIAGNOSI DI CARDIOTOSSICITÀ

La cardiotox può interessare tutte le strutture cardiache
(miocardio, pericardio, coronarie, tessuto di conduzione, valvole)

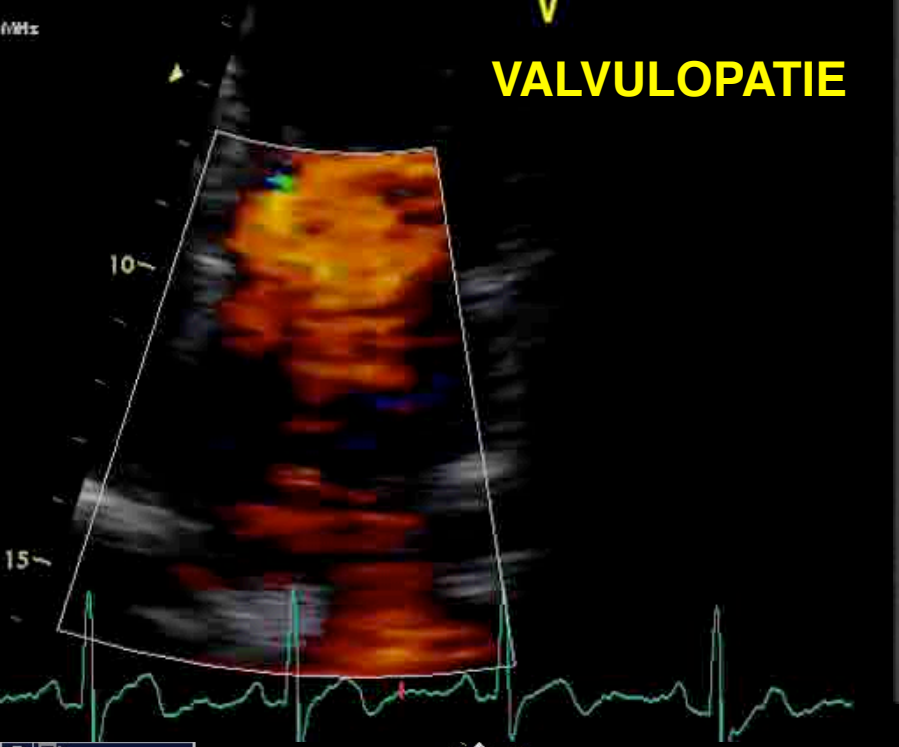
- ECG basale
- ECG HOLTER - LOOP RECORDER
- TEST ERGOMETRICO
- SCINTIGRAFIA MIOCARDICA BASALE e SFORZO
- CORONAROGRAFIA
- RMN / MRI
- MARKERS BIOCHIMICI (TnI – BNP)
- ECOCARDIOGRAFIA

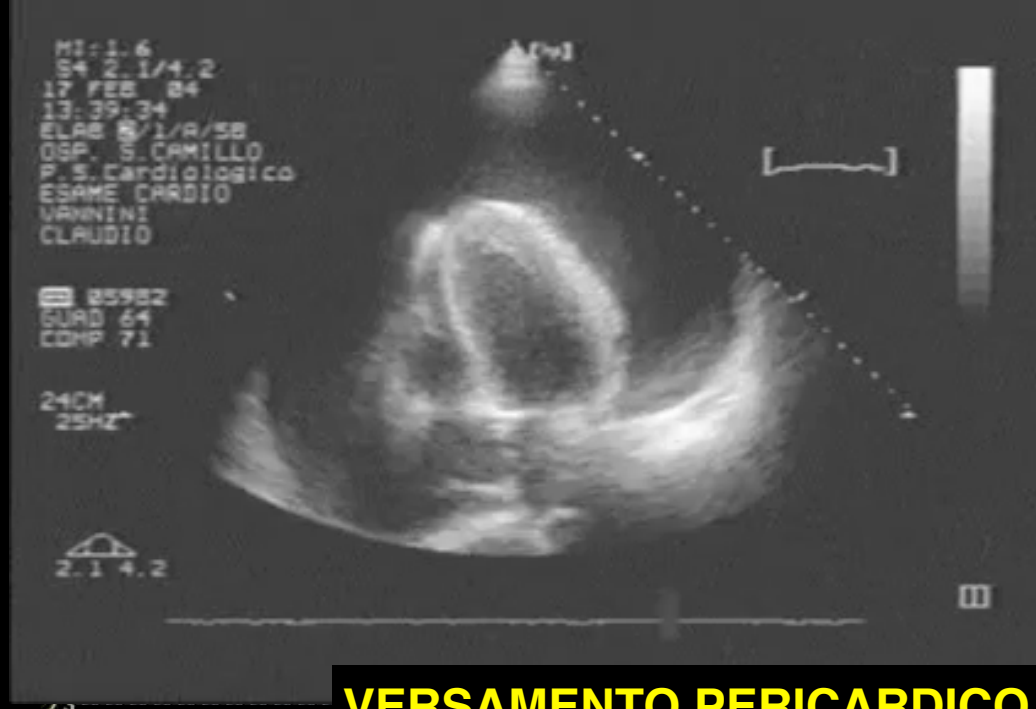
ECOCARDIOGRAFIA

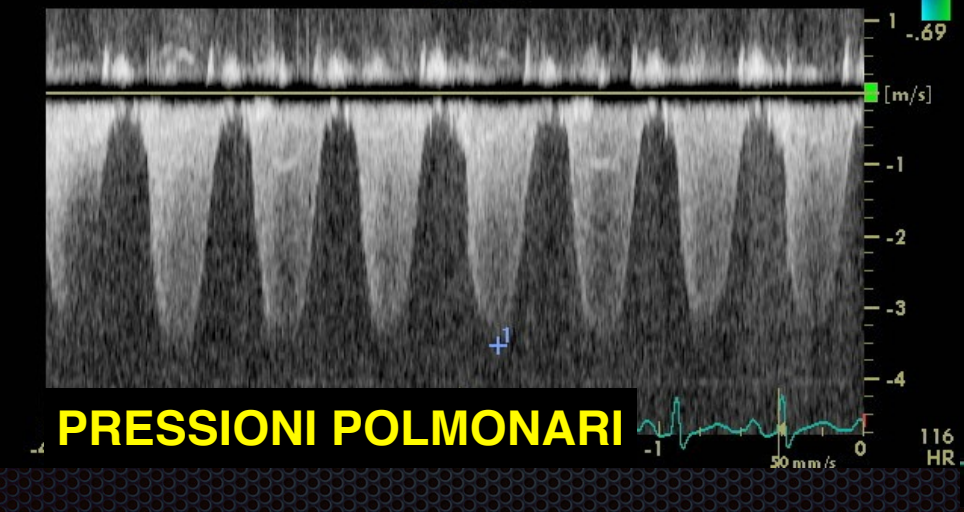


RUOLO dell'ECOCARDIOGRAFIA

- Al giorno d'oggi è quasi inimmaginabile fare una diagnosi di una cardiopatia senza ricorrere all'echo
- Capacità di misurare parametri strutturali e funzionali del cuore
- L'Echo è l'**esame cardine** nella valutazione dei Pts **pre, durante e dopo terapie antitumorali**
- **Ampia disponibilità, versatilità, facile ripetibilità, trasportabilità, sicurezza** (assenza di radiazioni, IRC)


VALVULOPATIE
10
15
1 v 3.56 m/s
p 50.61 mmHg
Frq 9.12 kHz


MI:1.6
S4 2.1/4.2
17 FEB 04
13:39:34
OSP. S.CAMILLO
P.S.Cardiologico
ESAME CARDIO
VANNINI
CLAUDIO
QUAD 64
COMP 71
24CM
25HZ
2.1 4.2


PRESSIONI POLMONARI
1
[m/s]
-1
-2
-3
-4
50 mm/s


VERSAMENTO PERICARDICO
HR11:47:51
.69
-.69
116
HR
1:117

TIPO II

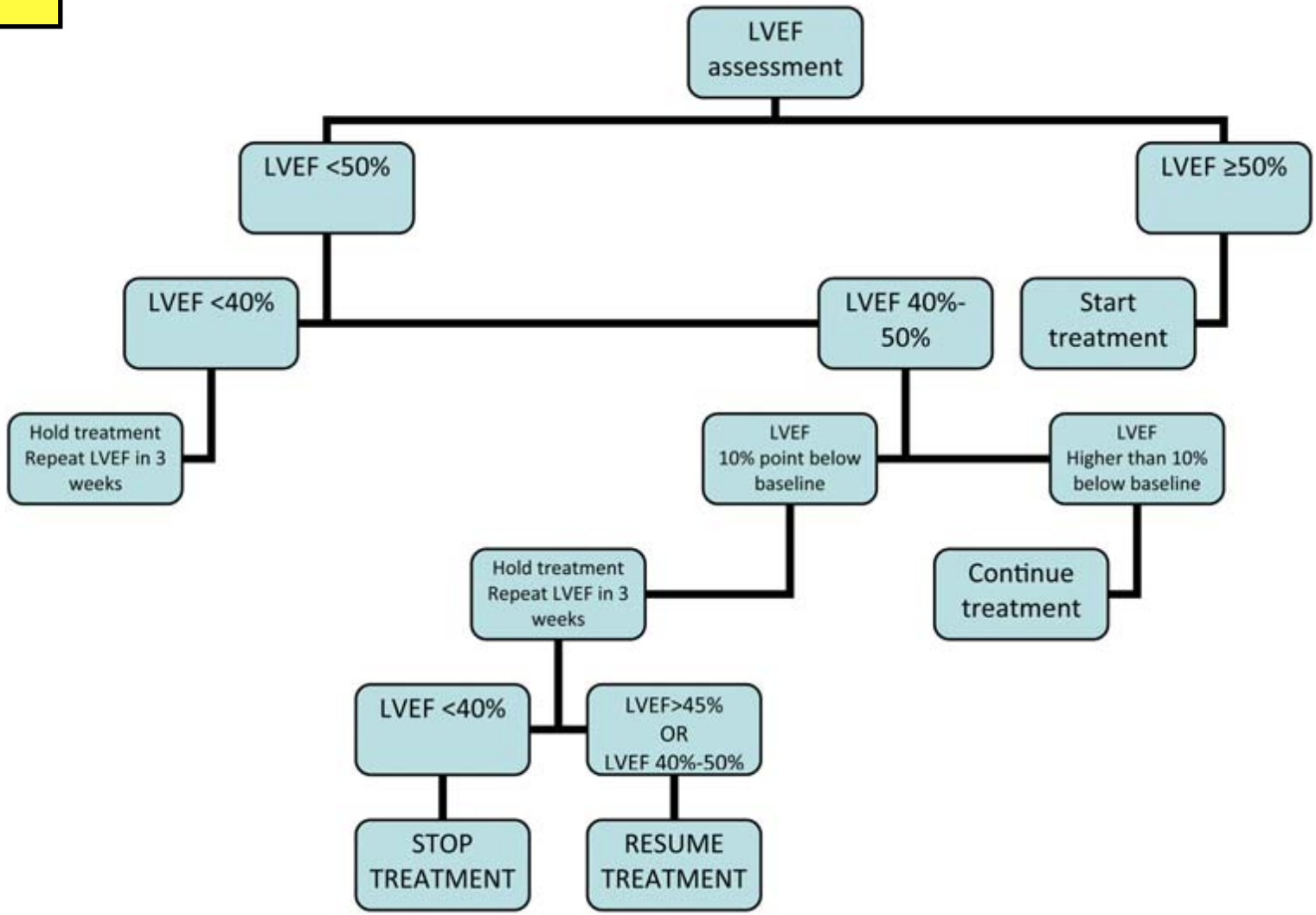


Figure 2. Algorithm for continuation and discontinuation of trastuzumab based on LVEF assessments.

TIPO I

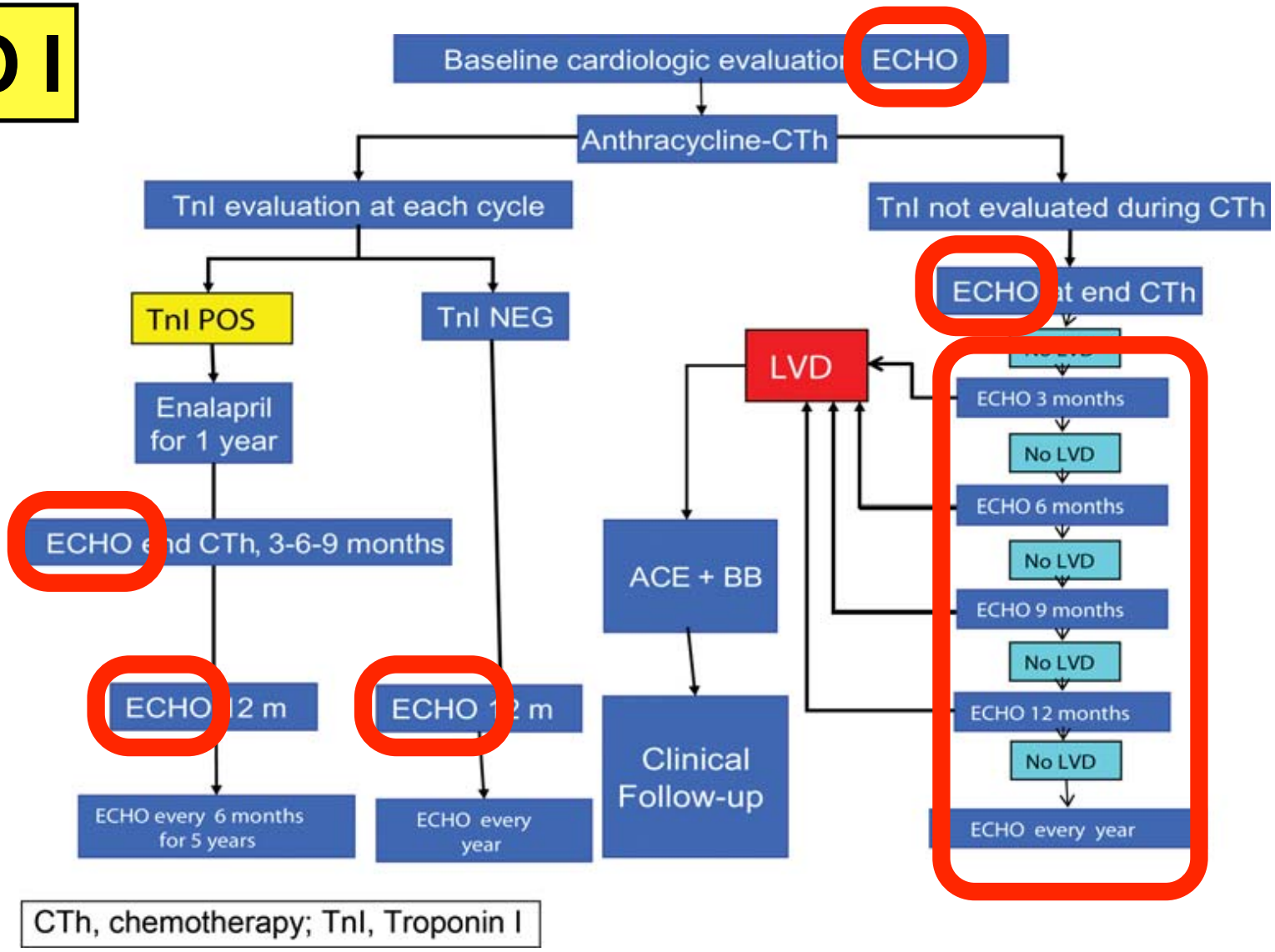
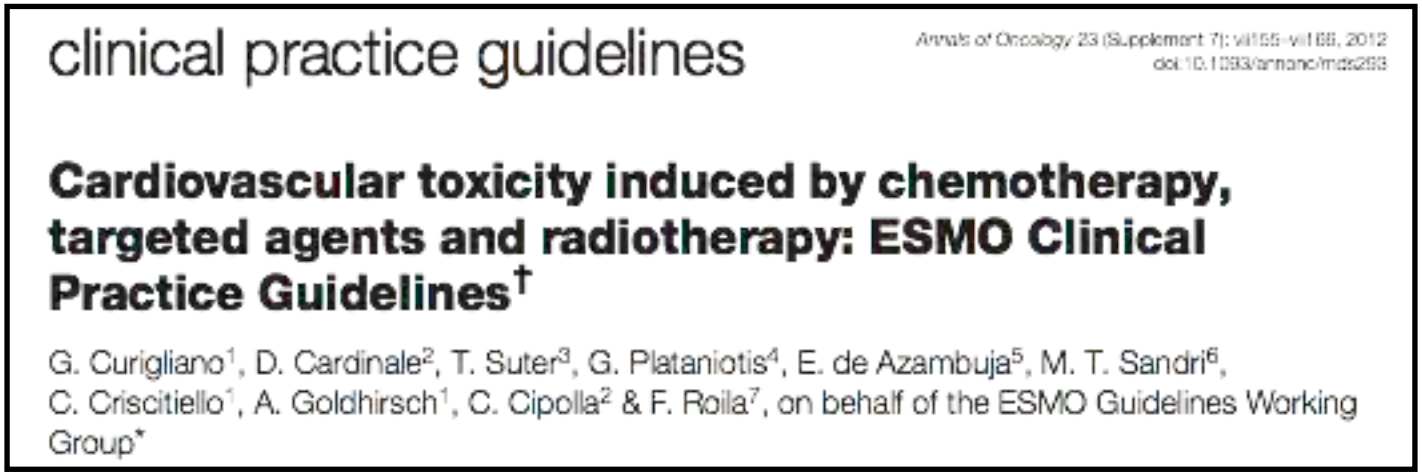


Figure 1. Algorithm for the management of cardiotoxicity in patients receiving anthracyclines.



clinical practice guidelines

Annals of Oncology 23 (Supplement 7): vii155–vii166, 2012
doi:10.1093/annonc/mds293

Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines†

G. Curigliano[1], D. Cardinale[2], T. Suter[3], G. Plataniotis[4], E. de Azambuja[5], M. T. Sandri[6], C. Criscitiello[1], A. Goldhirsch[1], C. Cipolla[2] & F. Roila[7], on behalf of the ESMO Guidelines Working Group*

La cardiotossicità è caratterizzata da almeno uno tra:

-sintomi di scompenso cardiaco

-segni clinici di scompenso cardiaco (es. T3 o tachicardia)

-Riduzione di EF di almeno 5% sotto i 55% con sintomi o segni di scompenso

-Riduzione di EF del 10% sotto i 55% senza segni o sintomi associati

Come deve essere valutata la frazione d'eiezione?

BMJ Journals

Heart

Home / Archive / Volume 94, Issue 4

Editorial

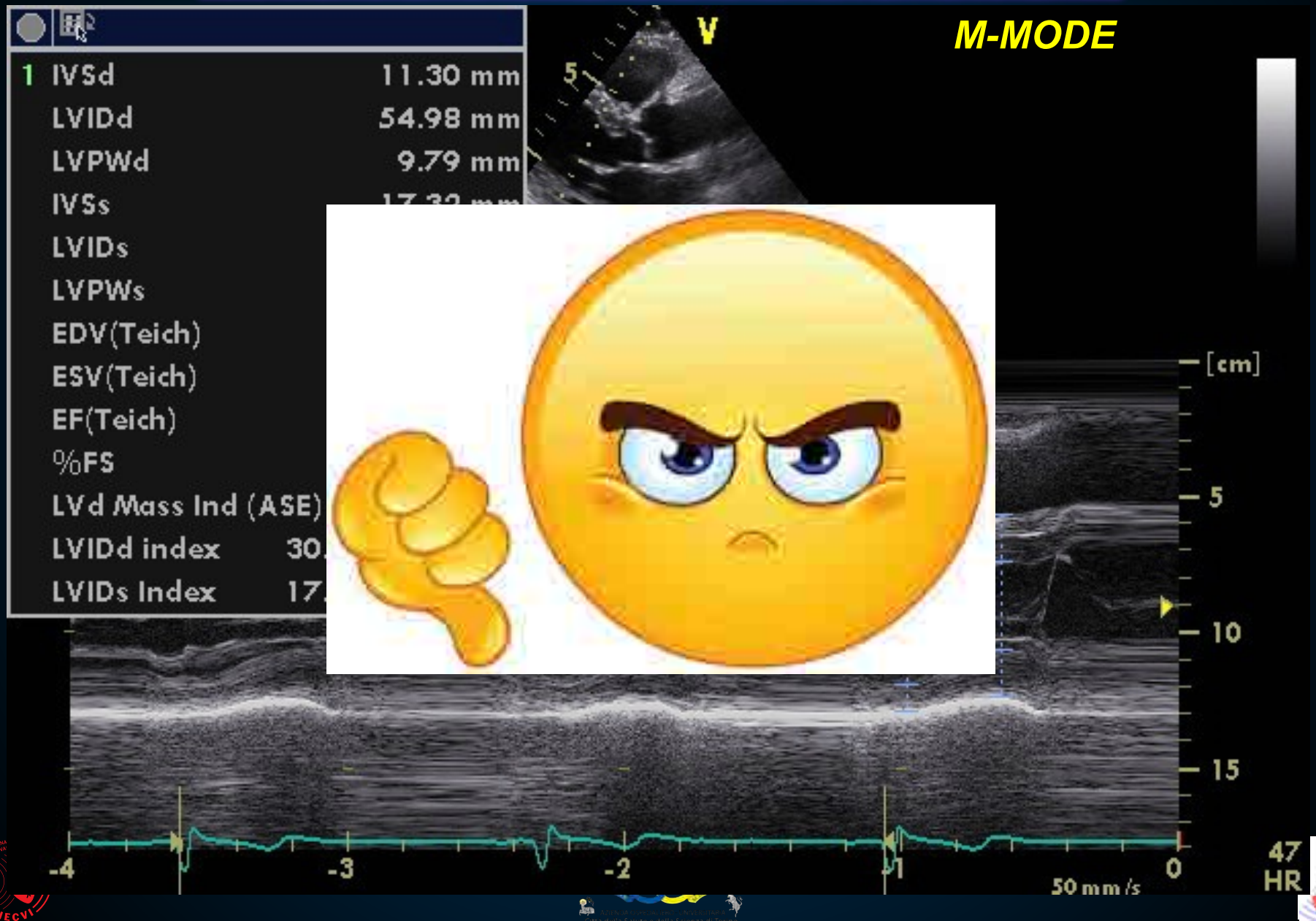
Ejection fraction: a measure of desperation?

Charlotte H Manisty, Darrel P Francis

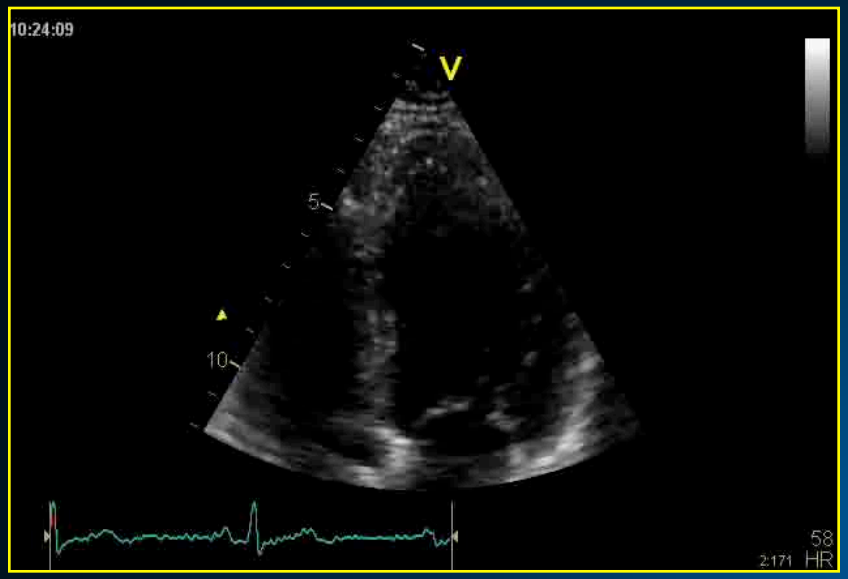
Author affiliations +

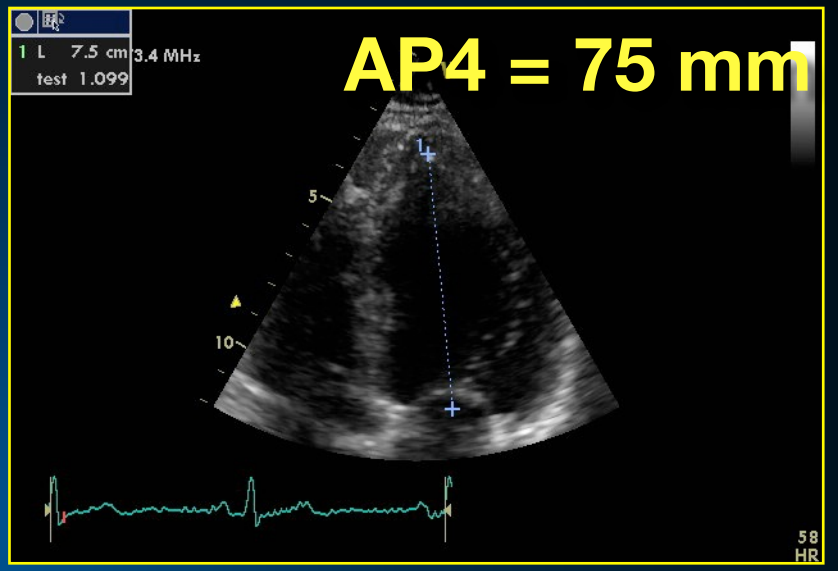
http://dx.doi.org/10.1136/hrt.2007.118976

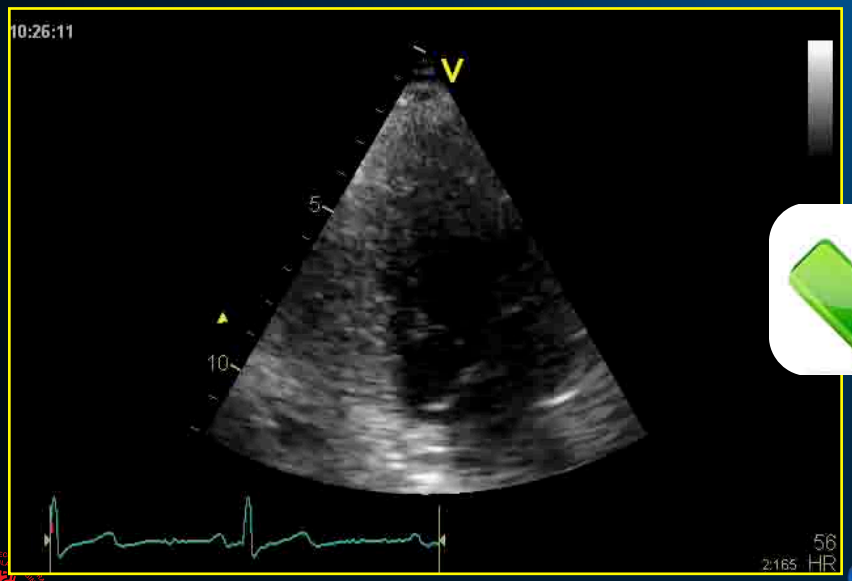
EF - m-MODE: TEICHOLZ

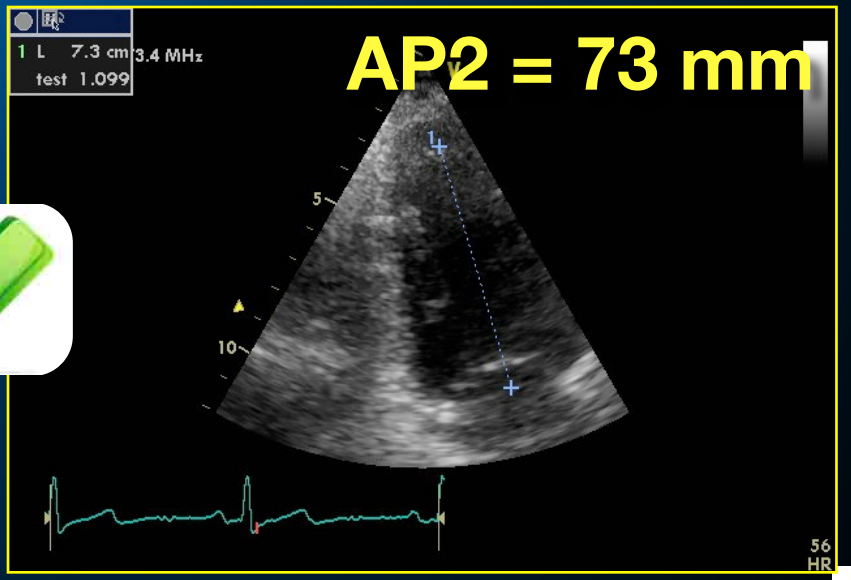


2D SIMPSON RULE

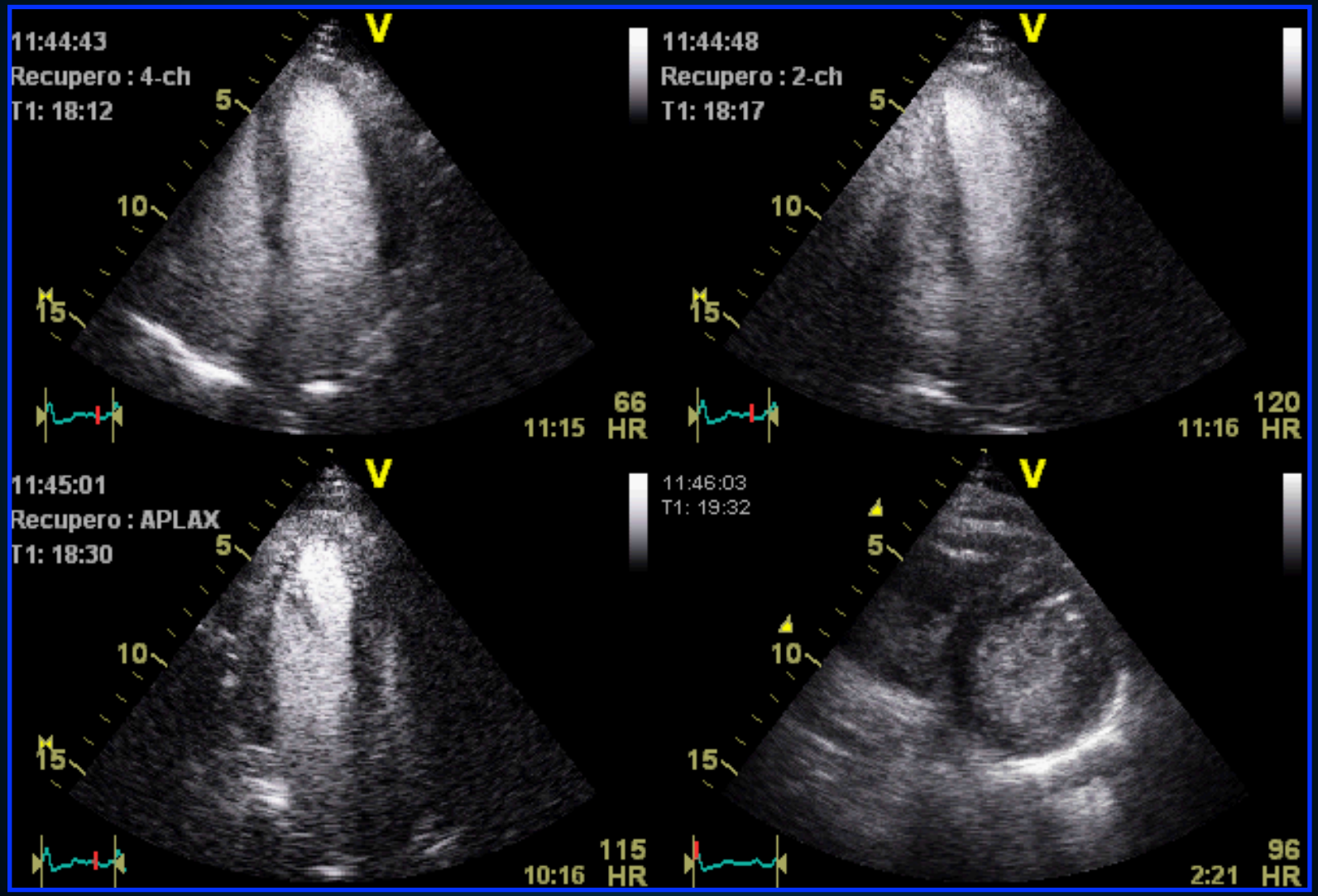




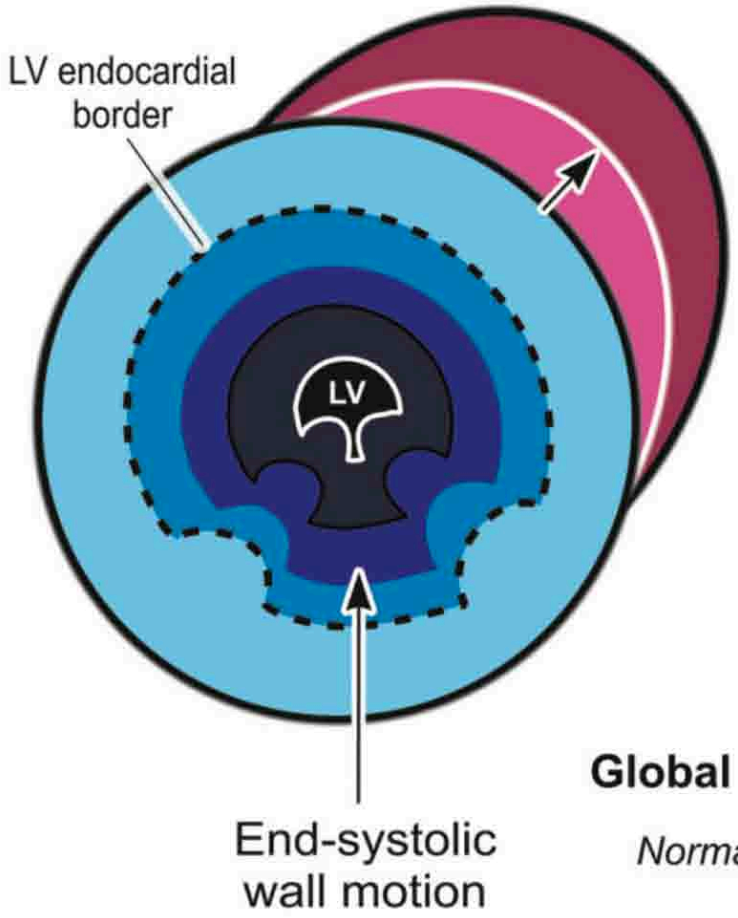




Opacificazione VS (Sonovue)



WALL MOTION SCORE INDEX



WALL MOTION SCORE (WMS)

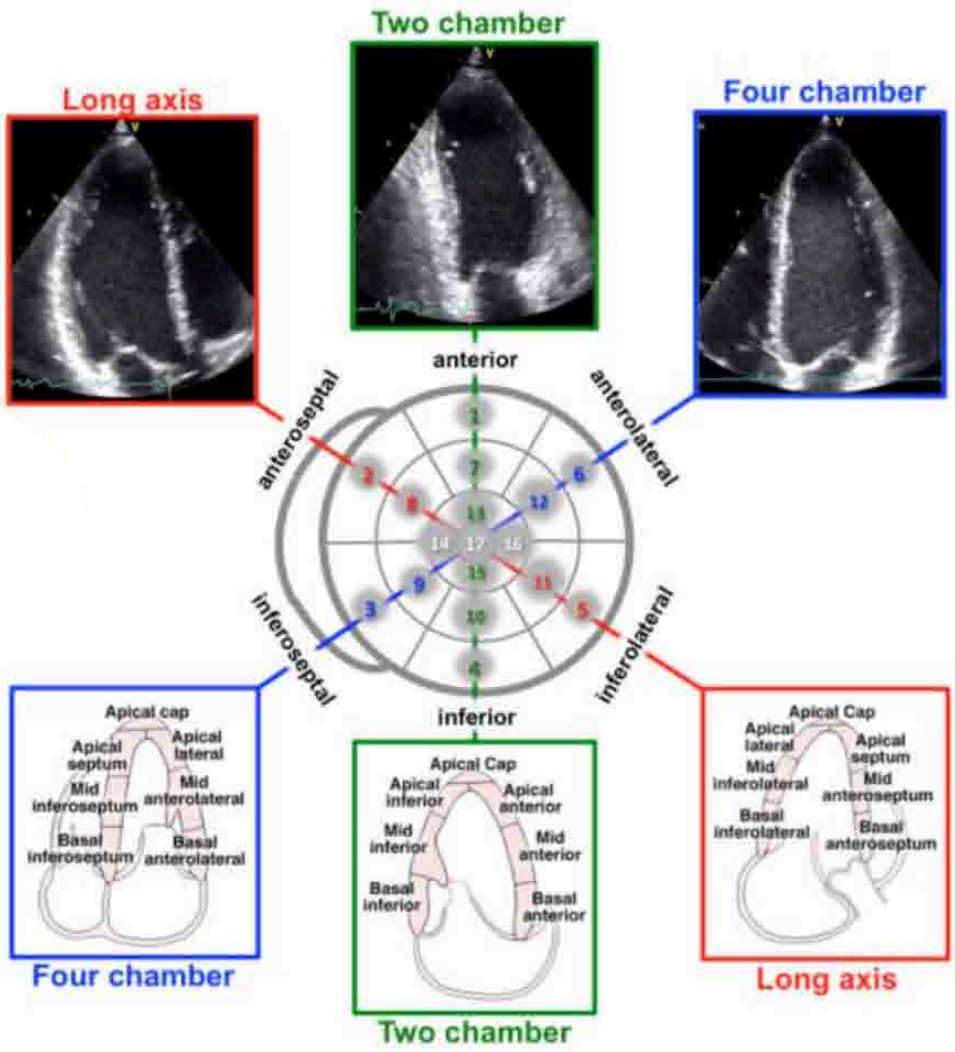
Aneurysmal	5
Dyskinetic	4
Akinetic	3
Hypokinetic	2
Normal	1
Hyperkinetic	

$$\text{WMS Index} = \sum_{n=1}^{n=N} \text{WMS} \div N$$

Global Wall Motion Score (WMS) = 16

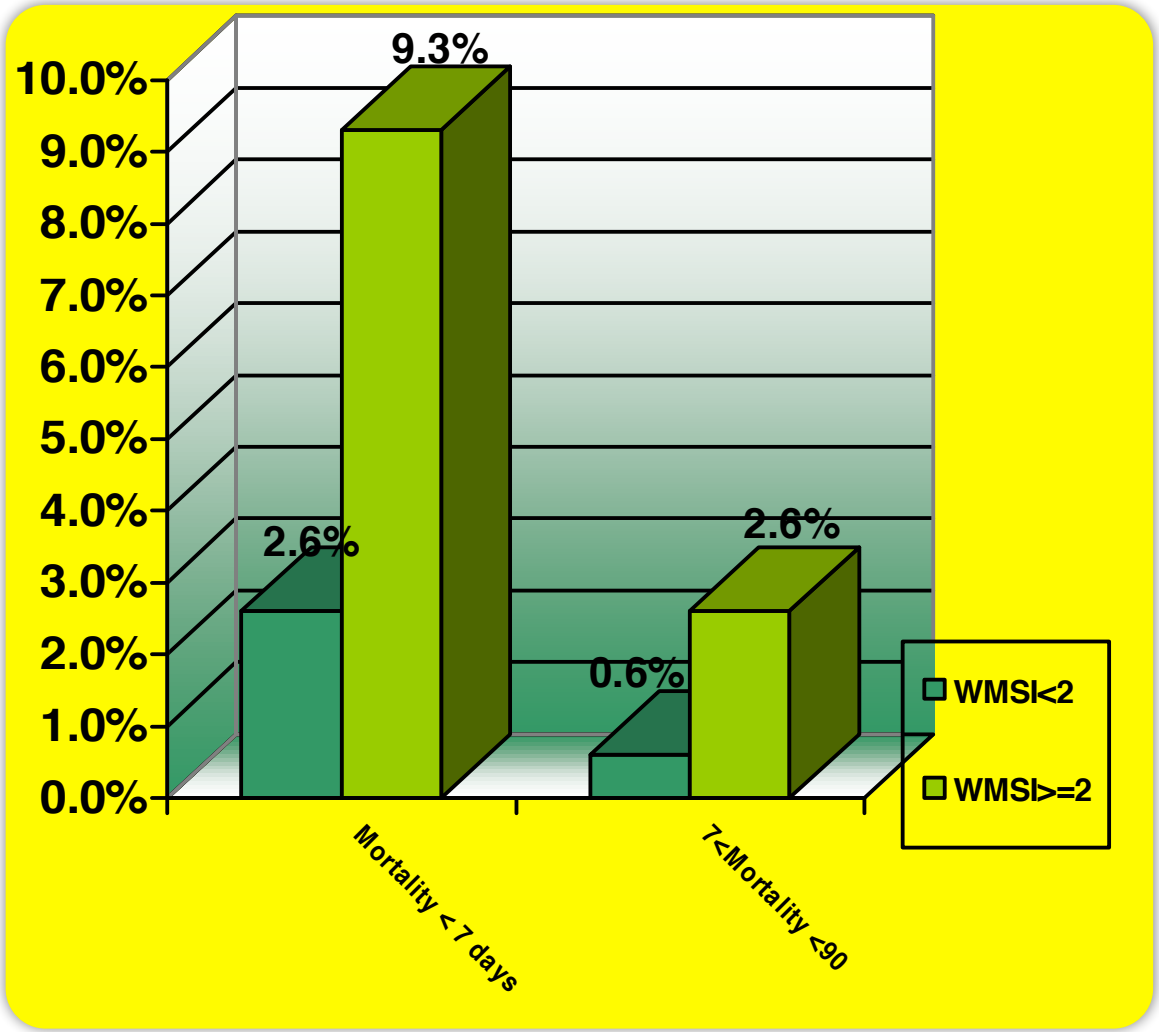
Normal Score for ASE 16-segment model

Normal WMS Index = 1



1. Normal or Hyperkinetic
2. Hypokinetic (reduced thickening)
3. Akinetic (absent or negligible thickening
4. Dyskinetic (systolic thinning or stretching)

WMSI E MORTALITÀ



Quali sono i limiti nella valutazione dell'EF?

Left Ventricular Ejection Fraction

VARIABILITÀ dei "CUT OFF" di EF

	Normal	Mild	Moderate	Severe
2015	>52	51-41	40-30	<30
2005	>55	54-45	44-30	<30

LV Ejection Fraction

VARIABILITÀ dei "CUT OFF" di EF

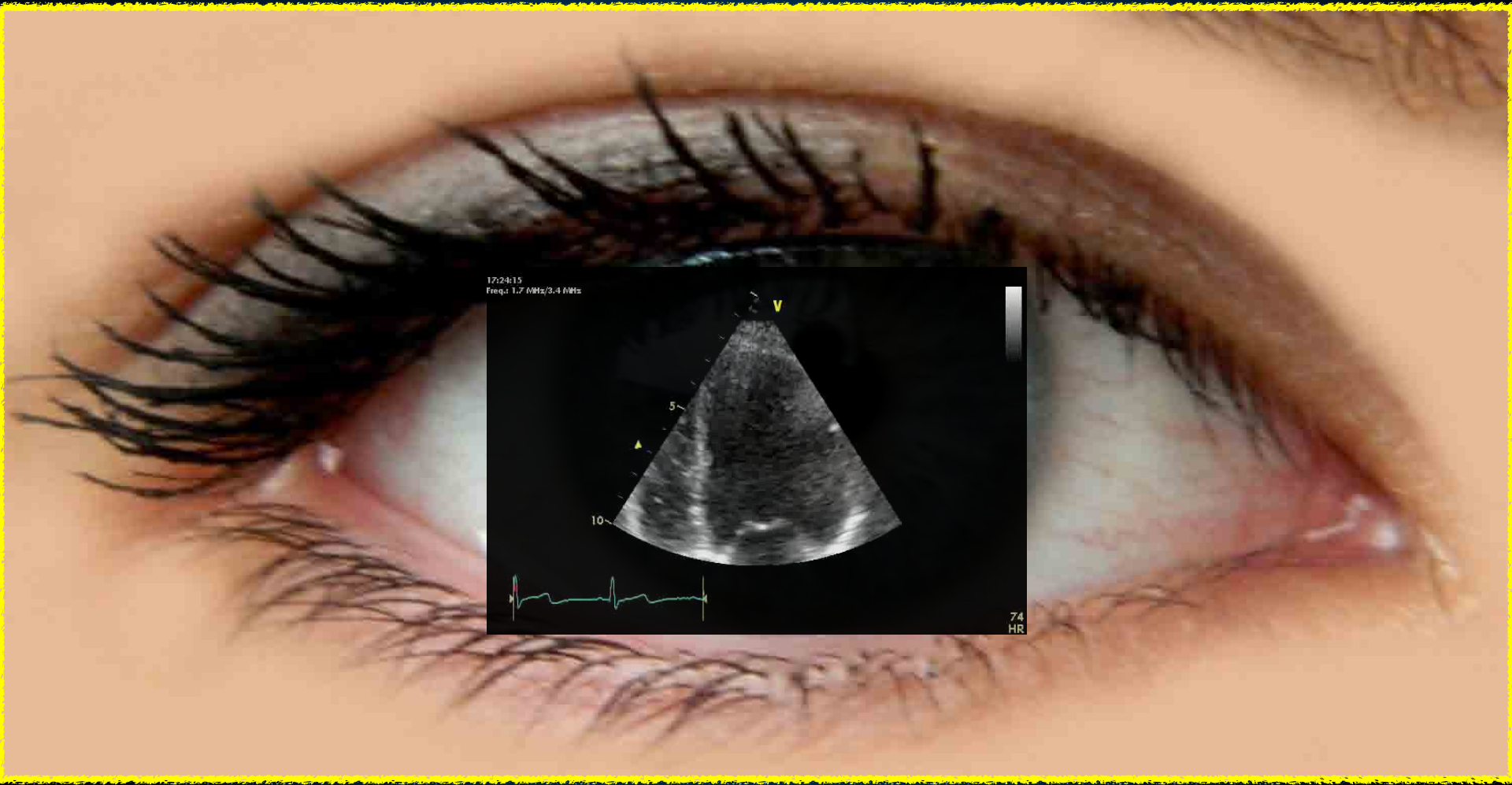
Male

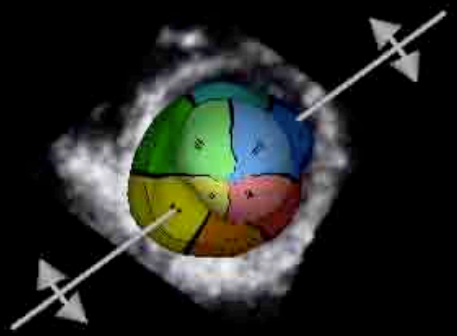
	Normal	Mildly	Moderately	Severely
LVEF	52-72	41-51	30-40	<30

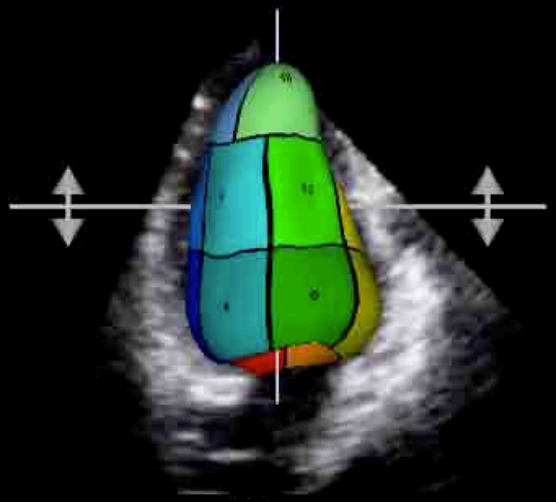
Female

	Normal	Mildly	Moderately	Severely
LVEF	54-74	41-53	30-40	<30

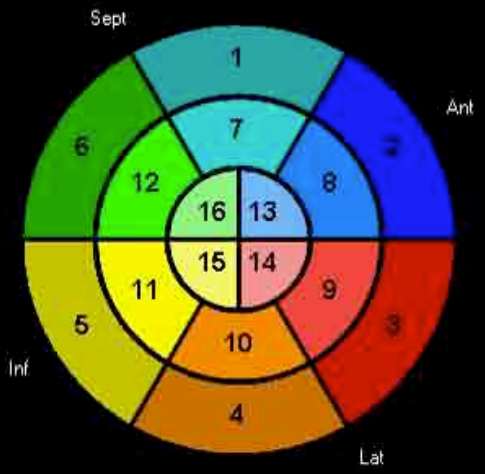
LIMITI dell'ECOCARDIOGRAFIA







3D


Sept
Ant
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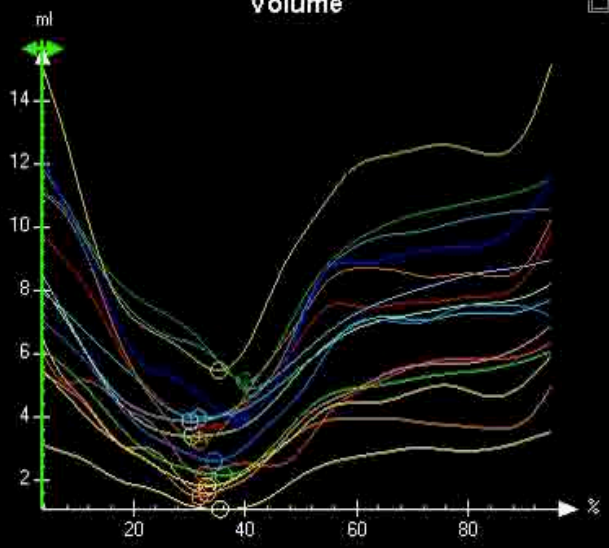
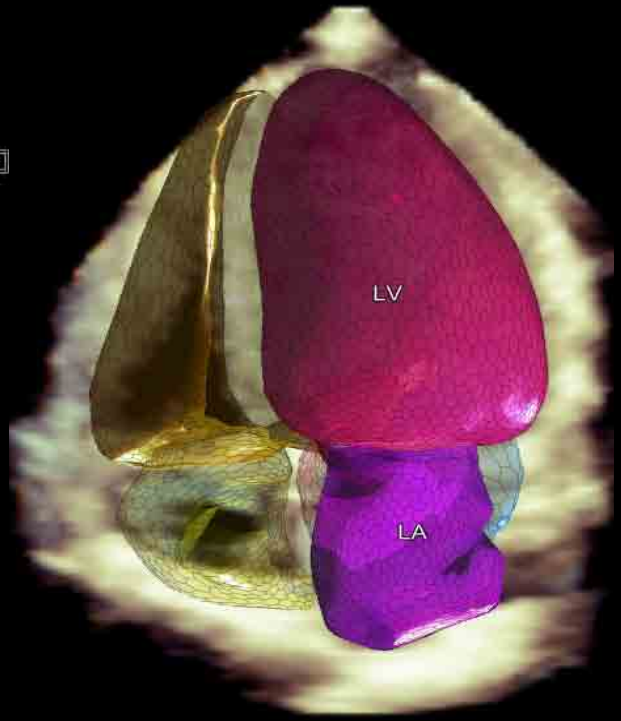
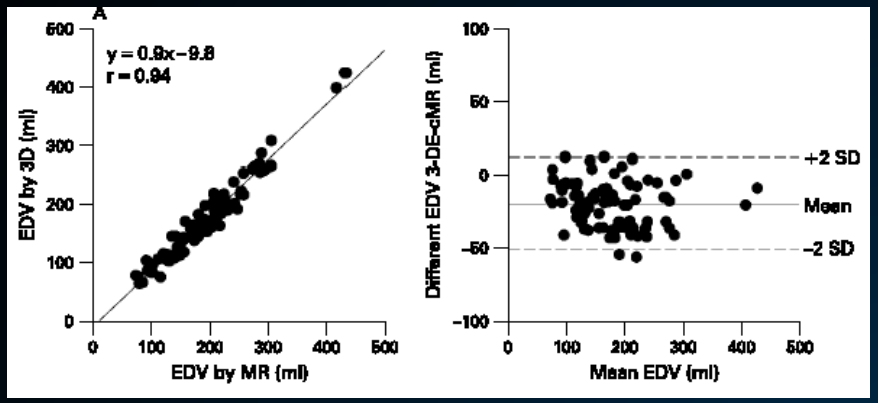

Volume
ml
14
12
10
8
6
4
2
20
40
60
80
%


LV
LA

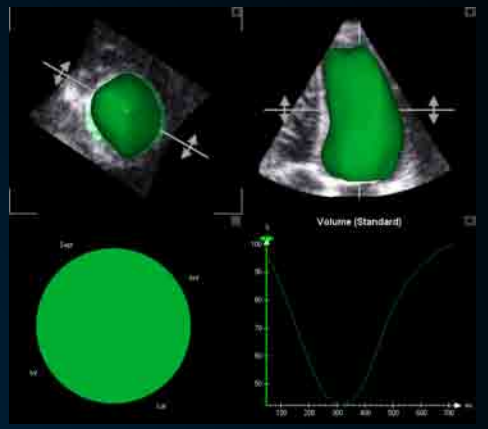
3D echocardiography for evaluating the left ventricle: key points

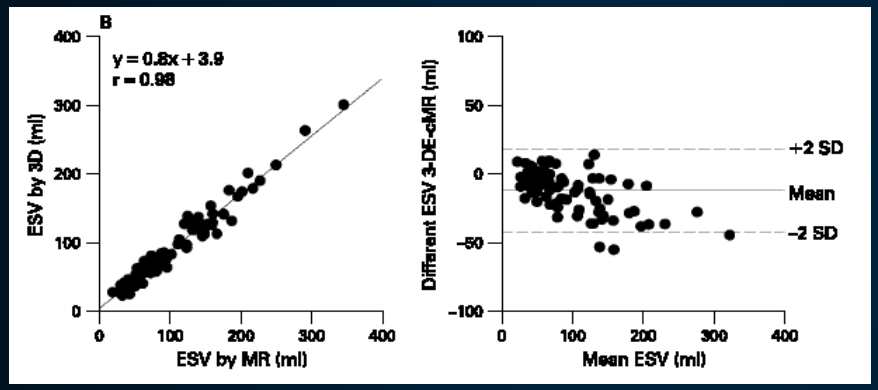
- Left ventricular (LV) morphology and function most common echocardiography request
- M mode and 2D echocardiography make incorrect geometric assumptions about the LV
- Inaccurate and poor reproducibility of M mode/2D analysis
- 3D echocardiography makes no geometric assumptions
- 3D sees the LV "as it is"
- 3D measures endocardial position at >700 points
- 3D echocardiography has excellent correlation with cardiac magnetic resonance (CMR) for volume, mass, and ejection fraction
- 3D reproducibility comparable with CMR

Eco 3D vs MRI in pz con/senza anomalie del wall motion: Volumi e Frazione di Eiezione

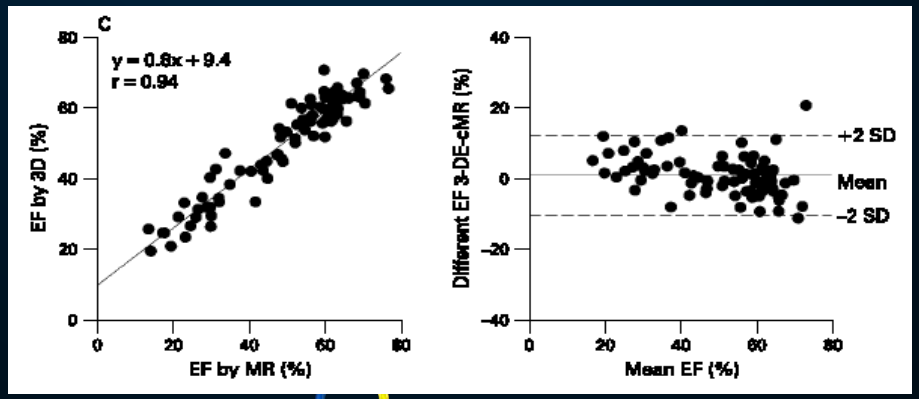


-20 ± 31





-12 ± 21



5 ± 10

Pouleur AC et al, Heart 2008;94:1050-1057

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http://dx.doi.org/10.1016/j.jacc.2012.09.035

Cardiac Imaging

Reproducibility of Echocardiographic Techniques for Sequential Assessment of Left Ventricular Ejection Fraction and Volumes

Application to Patients Undergoing Cancer Chemotherapy

Paaladinesh Thavendiranathan, MD, MSc, Andrew D. Grant, MD, Tomoko Negishi, MD, Juan Carlos Plana, MD, Zoran B. Popović, MD, PhD, Thomas H. Marwick, MD, PhD, MPH

Cleveland, Ohio

Confronto tra 2D-biplano, 2D-biplano/contrasto, Triplano, Triplano/contrasto, 3D, 3D/contrasto

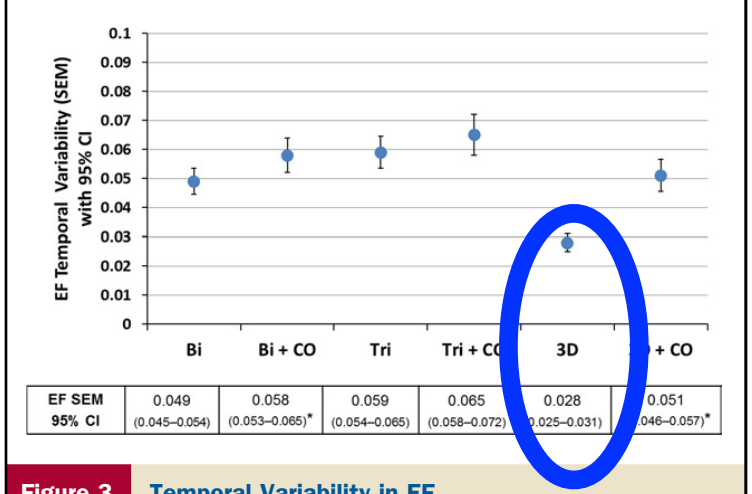


Figure 3 Temporal Variability in EF

Accurate calculation of LVEF should be done with the **best method available** in the echo laboratory (ideally **3DE**)

Conc ar of

follow-up. (J Am Coll Cardiol 2013;61:77–84) © 2013 by the American College of Cardiology Foundation

Table 2 Interobserver and Intraobserver Variability and Minimal Detectable Change for EF Measurements by All 6 Techniques

	Bi	Bi + Co	Tri	Tri + Co	3D	3D + Co
Intraobserver	0.033*	0.035*	0.038*	0.037*	0.017	0.026
Min Δ detectable	0.090	0.098	0.104	0.102	0.048	0.072
Interobserver	0.040	0.051*	0.049*	0.048*	0.027	0.038
Min Δ detectable	0.111	0.142	0.135	0.133	0.075	0.100
Interobserver test-retest	0.047*	0.055*	0.058*	0.069*	0.022	0.042*
Min Δ detectable	0.013	0.152	0.162	0.192	0.060	0.115

Noncontrast 3D had the lowest intraobserver and interobserver test-retest observer variability and the smallest minimal detectable change. An ejection fraction (EF) of .033 corresponds to 3.3%. *$p < 0.01$ *t* test compared with noncontrast 3D.

Bi = biplane Simpson's; BP + Co = biplane Simpson's with contrast; Tri = triplane; Tri + Co = triplane + contrast; 3D = 3-dimensional; 3D + Co = 3-dimensional with contrast.

EF e PITFALLS

- Ogni Pt è caratterizzato da condizioni funzionali ed emodinamiche diverse
- L'EF non riflette accuratamente lo stato contrattile del miocardio, essendo influenzata dalle **condizioni di carico** (⟶annotare FC e PAO durante gli esami!)
- **L'EF non sempre riflette la portata cardiaca**, che può:
  - essere conservata in Pts con bassa EF, ma VS di volumetria aumentata
  - essere ridotta in Pts con EF normale, ma piccola volumetria ventricolare / ipertrofia o insufficienza mitralica severa o compromissione della funzione diastolica

VALUTAZIONE dell'EF: LIMITI

- ↓ *EF = perdita di cardiomiociti (danno irreversibile)*
- *EF normale anche con alterazioni cinesi segmentaria*

- ***EF = indice tardivo, poco sensibile e poco specifico, con bassa accuratezza diagnostica e scarso potere predittivo***

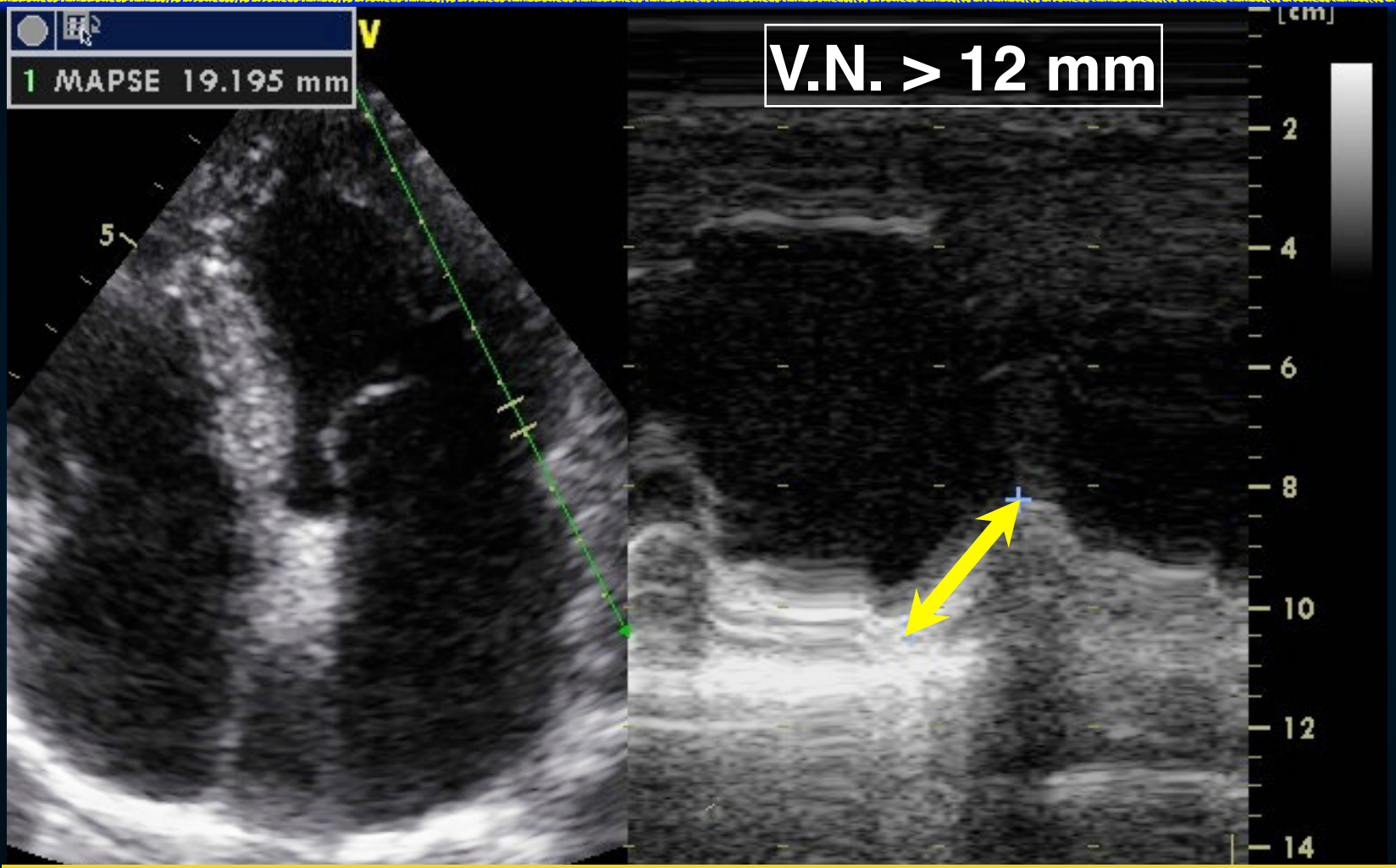
OBIETTIVO DEL CARDIONCOLOGO:

identificazione precoce dei Pts a rischio di sviluppare una disfunzione VS → personalizzazione del programma terapeutico cht e cardioprotezione

(= identificazione del danno in fase pre-clinica)

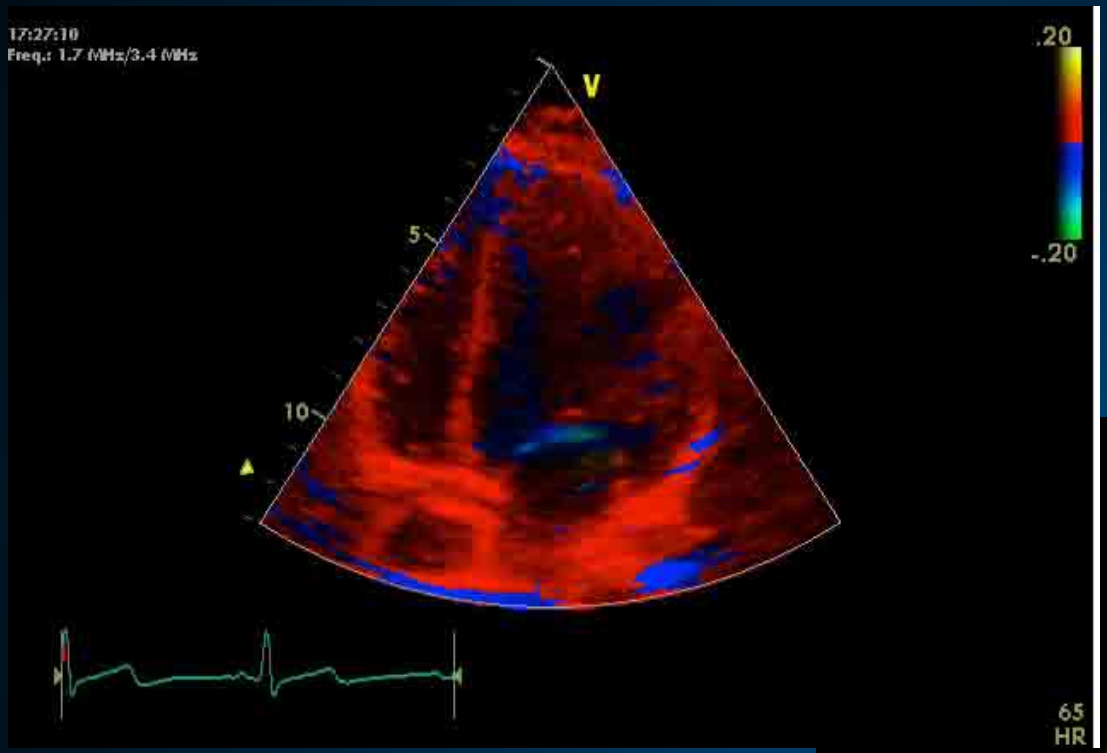
Esistono altre tecnologie per evidenziare una CTX, prima della riduzione dell'EF?

MAPSE

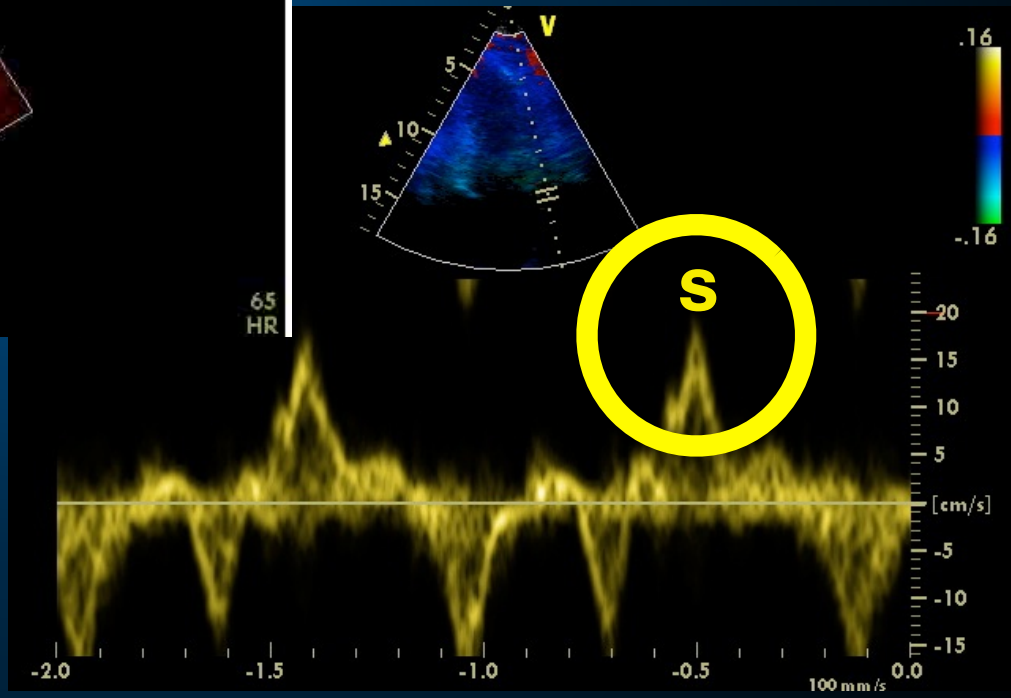


MAPSE = “**M**itral **A**nnular **P**lane **S**ystolic **E**xcursion"

DOPPLER TISSUTALE

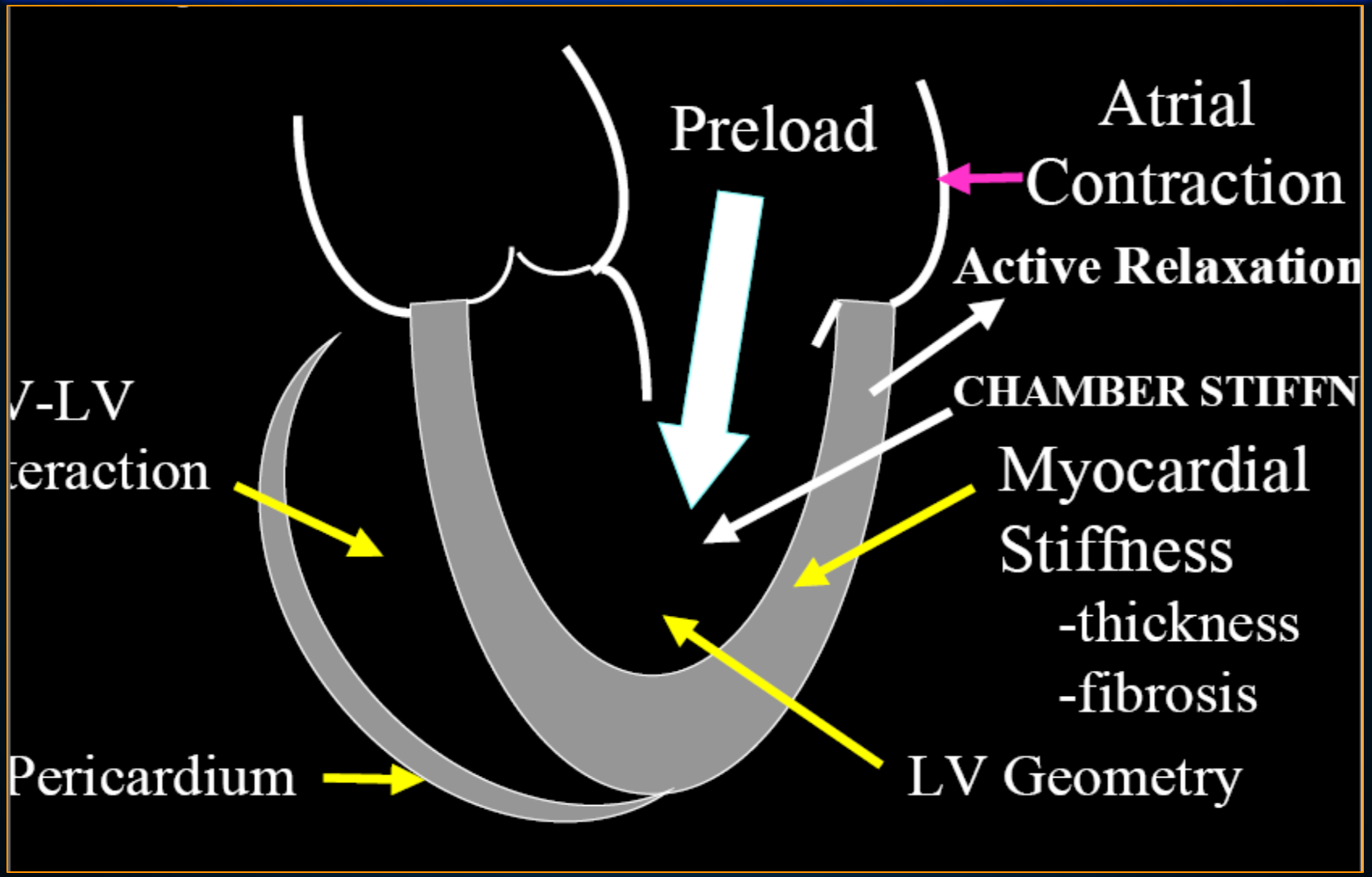


S2 ≧ 8 cm/s

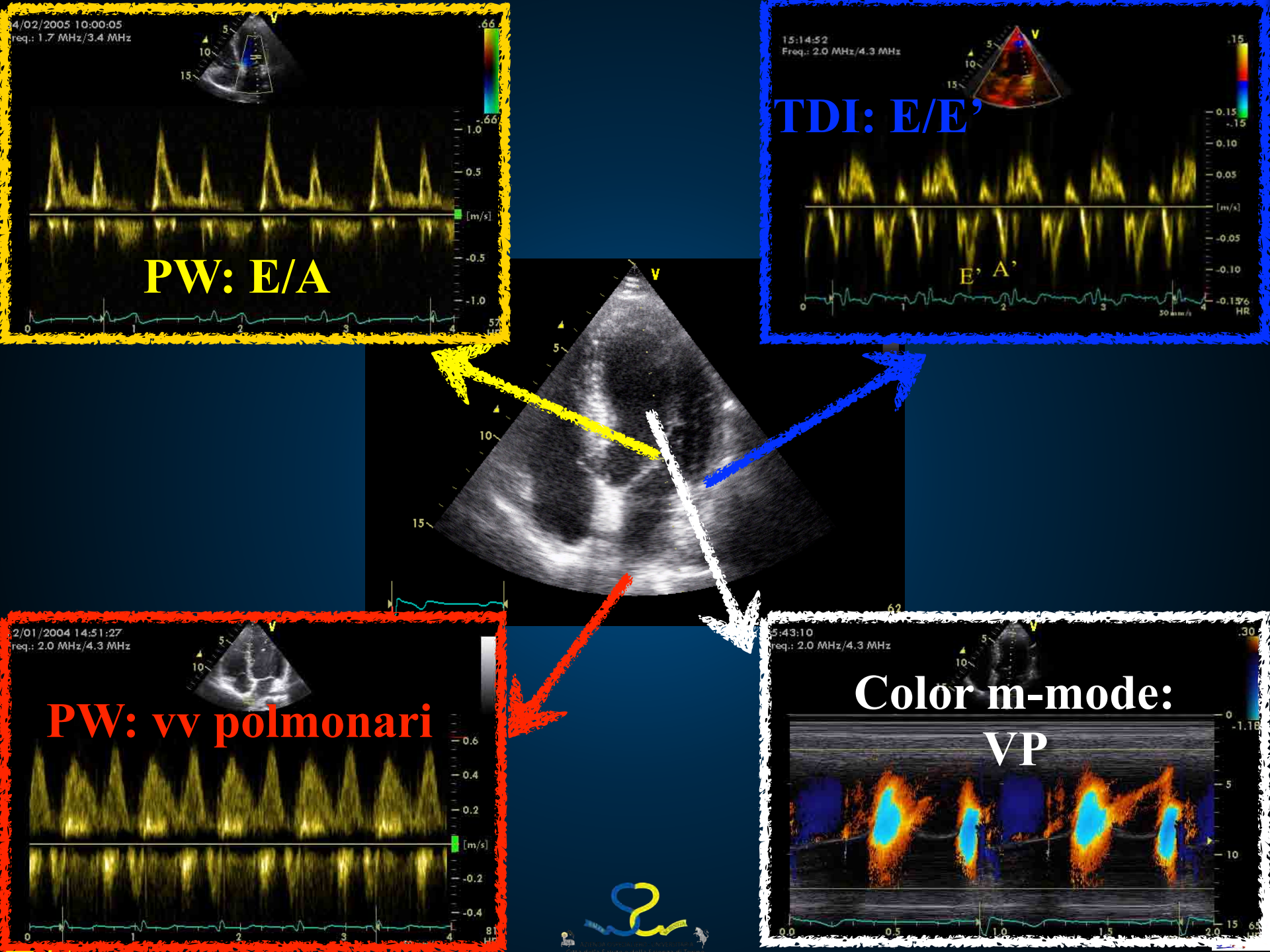


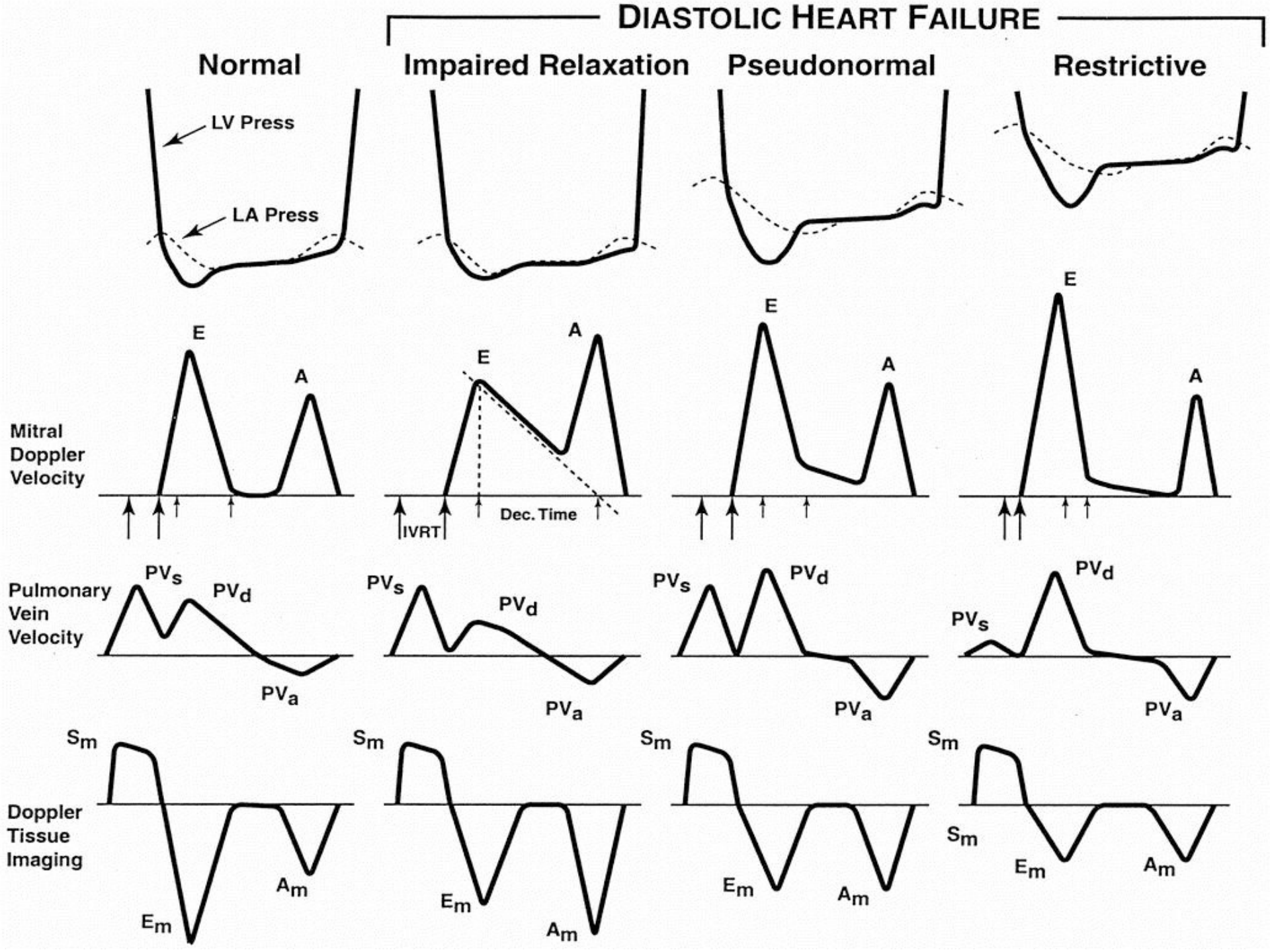
S1: evidente in ipertensione, ipertrofia, anziani, CMP ipocinetica, CAD

FUNZIONE DIASTOLICA



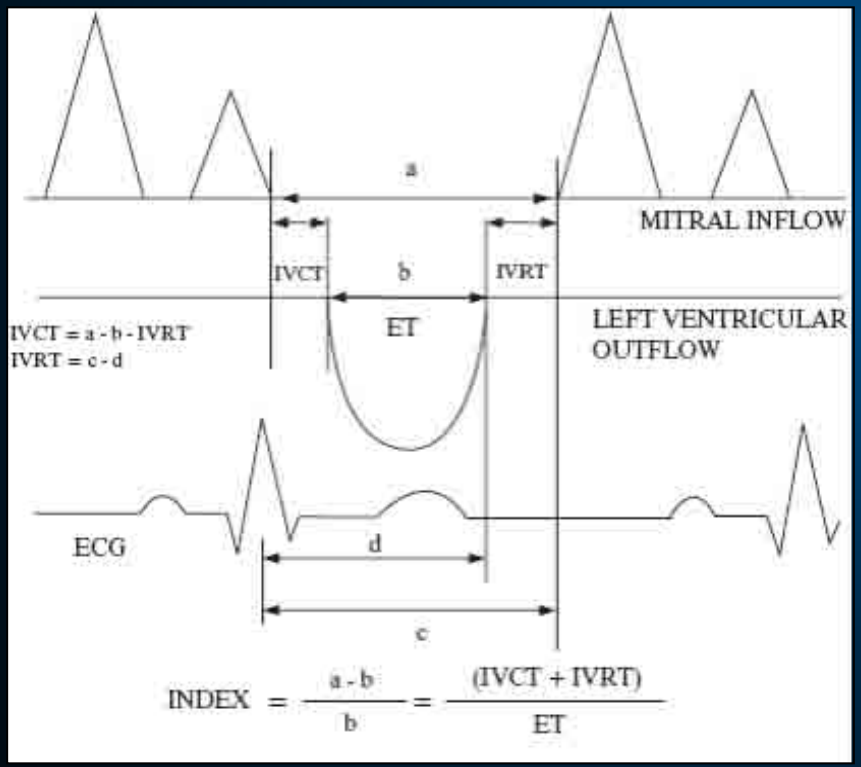
Quinones ASE Review 2007

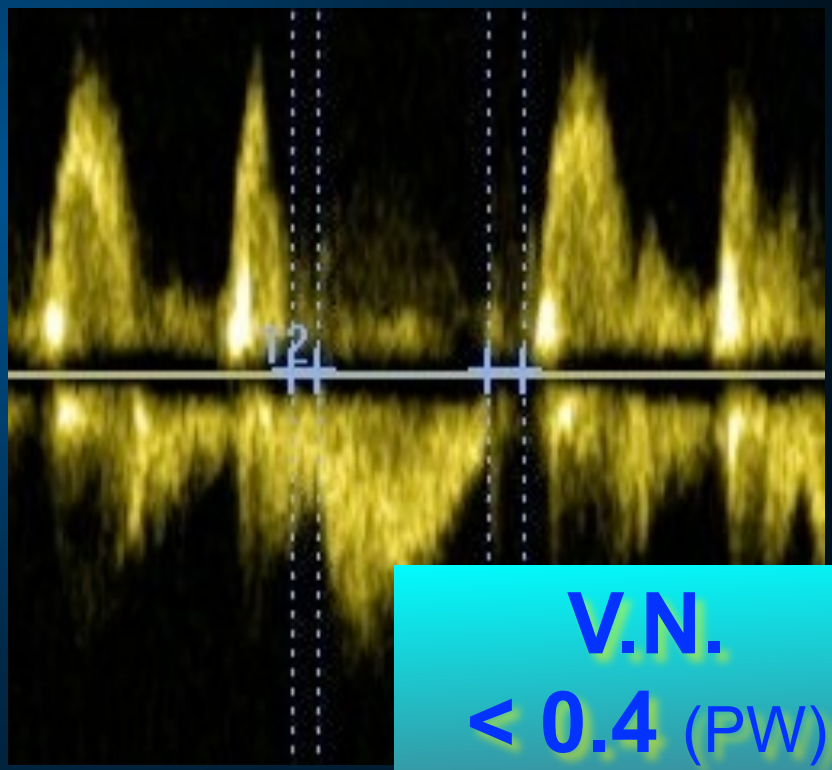

PW: E/A
TDI: E/E’
E’ A’
PW: vv polmonari
Color m-mode:
VP


DIASTOLIC HEART FAILURE
Normal
Impaired Relaxation
Pseudonormal
Restrictive
LV Press
LA Press
Mitral Doppler Velocity
E
A
IVRT
Dec. Time
Pulmonary Vein Velocity
PVs
PVd
PVa
Doppler Tissue Imaging
Sm
Em
Am

Index of Myocardial Performance (IMP)

Valutazione sisto-diastolica: durata del periodo di contrazione isovolumetrica (IVCT) e di rilasciamento isovolumetrico (IVRT) su eiezione ao (ET) = *TEI Index*





V.N.
< 0.4 (PW)
< 0.55 *(TDI)*

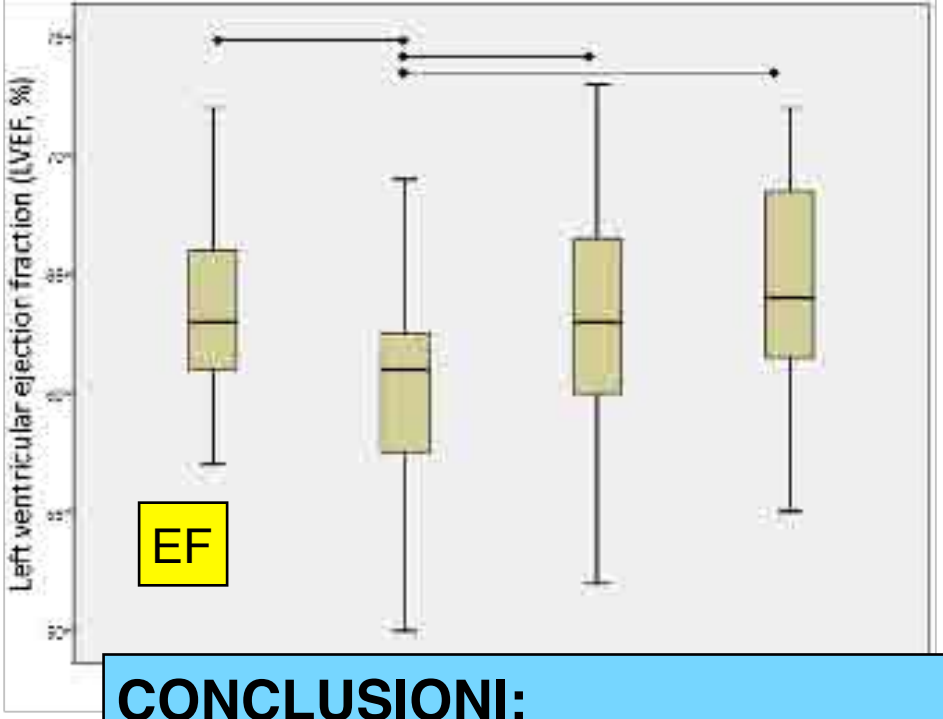
Temporal Changes in Standard and Tissue Doppler Imaging Echocardiographic Parameters After Anthracycline Chemotherapy in Women With Breast Cancer

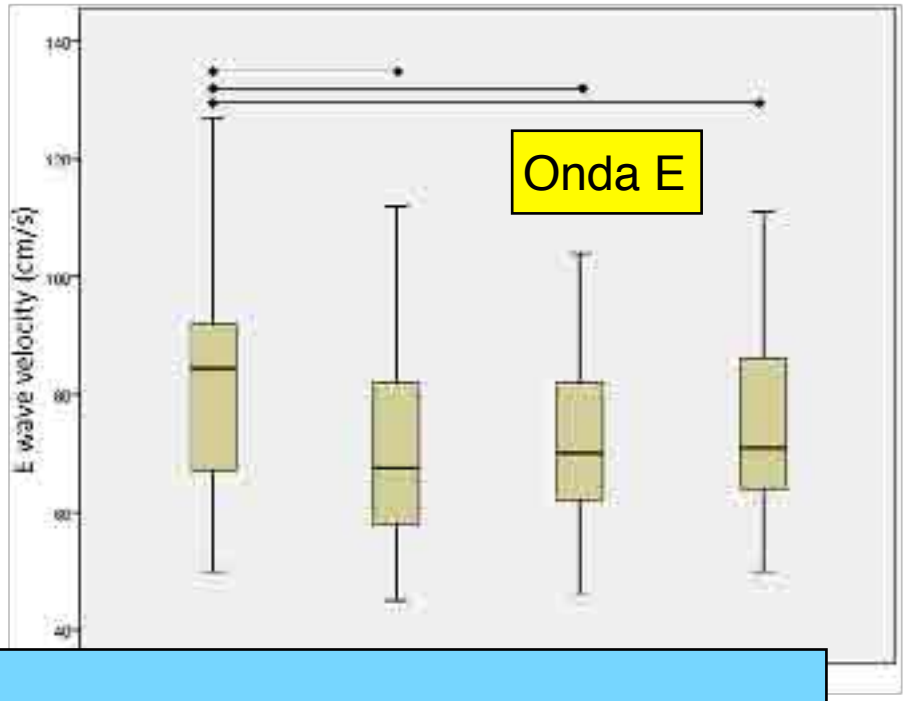
Marzia Lotriónte, MD[a], Elena Cavarretta, MD, PhD[b], Antonio Abbate, MD, PhD[c], Eleonora Mezzaroma, PhD[c], Eugenia De Marco, MD[a], Silvia Di Persio, RN[a], Francesco Loperfido, MD[a], Giuseppe Biondi-Zoccai, MD[b,*], Giacomo Frati, MD[b,d], and Giovanni Palazzoni, MD, PhD[e]

Anthracyclines are established cardiotoxic agents; however, the exact extent and time course of such cardiotoxicity has not been appraised in detail. We aimed to exploit serial measurements of standard and tissue Doppler imaging (TDI) echocardiographic parameters collected in a prospective clinical trial to clarify the outlook of cardiac function during and long after anthracycline chemotherapy. Women enrolled in a randomized trial focusing on liposomal doxorubicin-based chemotherapy for breast cancer and providing ≥4 separate echocardiographic assessments were included. Repeat-measure nonparametric analyses were used to appraise changes over time in the standard and tissue Doppler imaging echocardiographic parameters. A total of 39 patients with serial imaging evaluations were enrolled. Significant temporal changes were found for the left ventricular ejection fraction and diastolic parameters, despite different temporal trends. Specifically, the left ventricular ejection fraction exhibited a V-shaped trend, decreasing initially from 63% to 61% but then recovering to 64% ($p < 0.001$), with a similar trend in the TDI E/Em ratio ($p = 0.011$). In contrast, persistent impairments typical of an L-shaped trend were found for the E wave ($p = 0.006$), TDI lateral Em wave ($p = 0.001$), and TDI septal Em wave ($p = 0.001$). In conclusion, subclinical temporal changes in the standard and TDI echocardiographic parameters after anthracycline chemotherapy showed a distinctive pattern of transient impairment followed by full recovery of the left ventricular ejection fraction versus a persistent impairment of the diastolic parameters, which must be taken into account in the everyday treatment of such patients. (Am J Cardiol 2013;112:1005–1012)

39 ♀, liposomal-doxo, 4 f.u.: fine, 6, 12, 18-24 m

EF e funzione diastolica

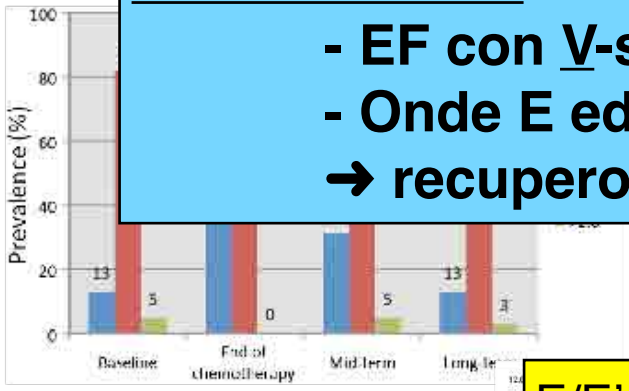


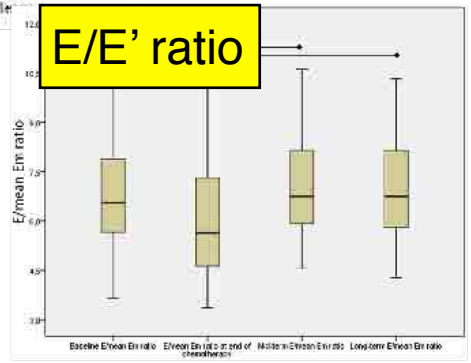


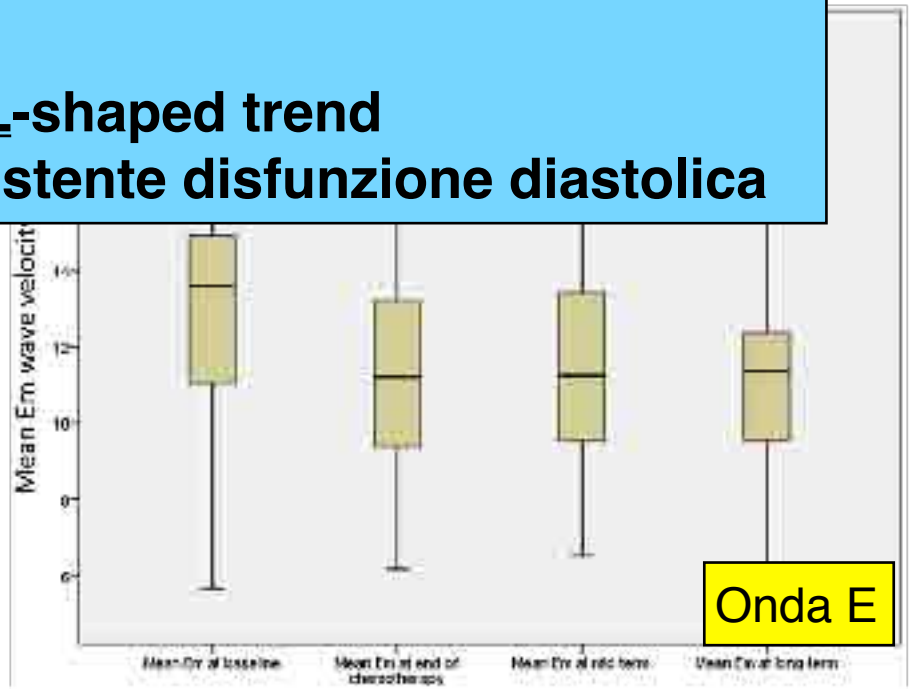
CONCLUSIONI:

- **EF con V-shaped trend**
- **Onde E ed E'$_{lat/sett}$ con L-shaped trend**

➜ recupero EF, ma persistente disfunzione diastolica







Evaluation of early subclinical cardiotoxicity of chemotherapy in breast cancer

Hayri Ahcı, Ozan Balakan, Süleyman Ercan, Musa Çakıcı, Fethi Yavuz, Verdat Davutoğlu

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Department of Oncology, Faculty of Medicine, Sütçü İmam University, Kahramanmaraş-*Turkey*
Department of Cardiology, Faculty of Medicine, Gaziantep University, Gaziantep-*Turkey*
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Clinic of Cardiology, Dr. Ersin Arslan State Hospital, Gaziantep-*Turkey*

Tissue Doppler imaging may be more sensitive than ECG, conventional ECHO and Doppler for determining the subclinical cardiac damage.

Methods: Fifty-one patients consecutively enrolled to this prospective cohort study. All patients were diagnosed as breast cancer at oncology hospital in University of Gaziantep. Before chemotherapy, all of the patients underwent to detailed ECG and echocardiography (ECHO) examinations. After 6 months, detailed ECG and ECHO examinations were repeated and compared with baseline values. Statistical analysis was performed using Shapiro-Wilk tests, Student t-test and Spearman correlation test.

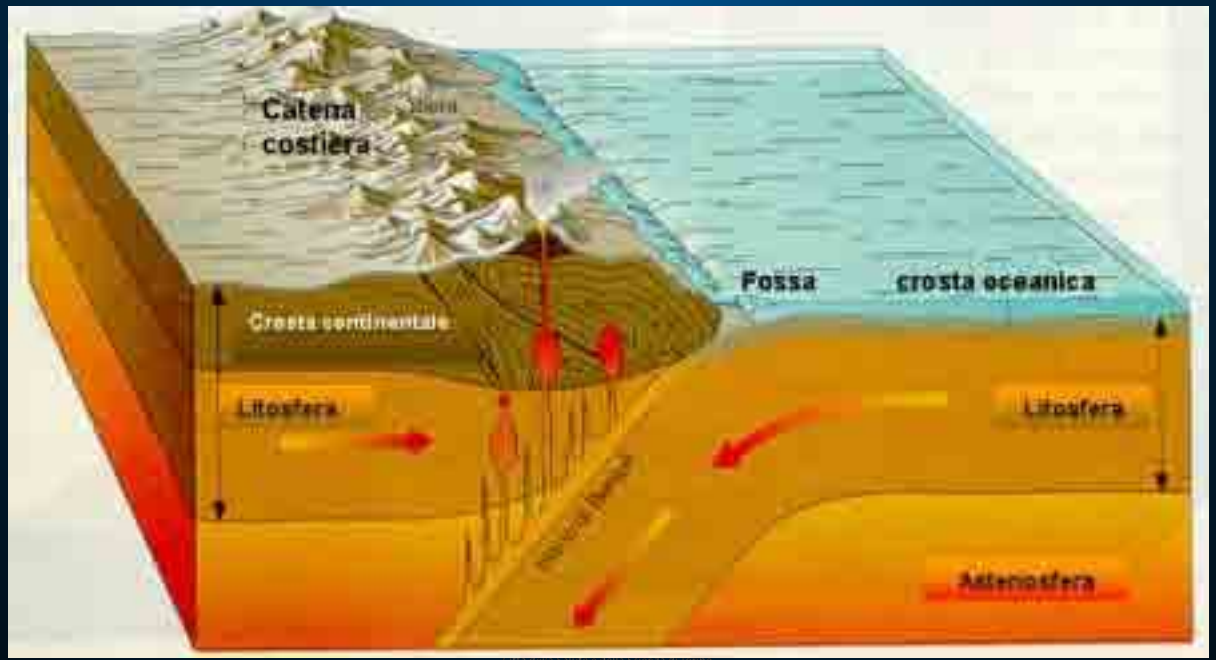
Results: The average age of patients was 51 and one was male. Statistically significant decrease in ejection fraction was found after treatment (62.3%±3.3 and 59.9%±5.9, p=0.002). Evaluation of diastolic parameters; significant increase in the transmitral A flow velocity and significant decrease of E/A ratio were observed on Doppler ECHO analysis (77.4±19.1 cm/sec versus 86±18 cm/sec, p<0.001; 1.01±0.3 versus 0.9±0.2, p=0.03, respectively). On tissue Doppler analysis we observed that significant reduction in the value of E' and significantly increase E/E' ratio were present (12.5±3.6 cm/sec versus 10.7±2.9 cm/sec, p=0.001; 6.6±2.9 versus 7.7±3.3, p=0.04, respectively).

Conclusion: Chemotherapy has detrimental subclinical effect on both of systolic and diastolic function in early six months period despite the prescription of lower dosage of chemotherapy than well-known cardiac safety dosage limits. Tissue Doppler imaging may be more sensitive than ECG, conventional ECHO and Doppler for determining the subclinical cardiac damage. *(Anadolu Kardiyol Derg 2015; 15(0): 000-000)*

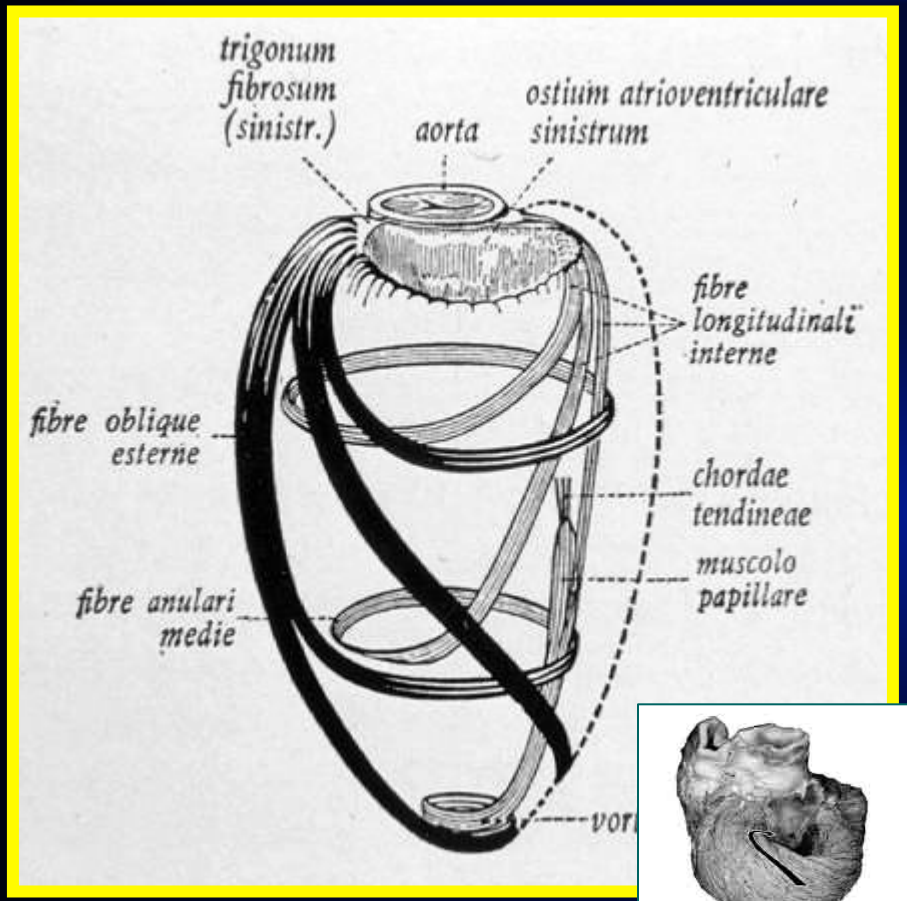
Key words: breast cancer, chemotherapy, echocardiography, tissue Doppler imaging, cardiotoxicity

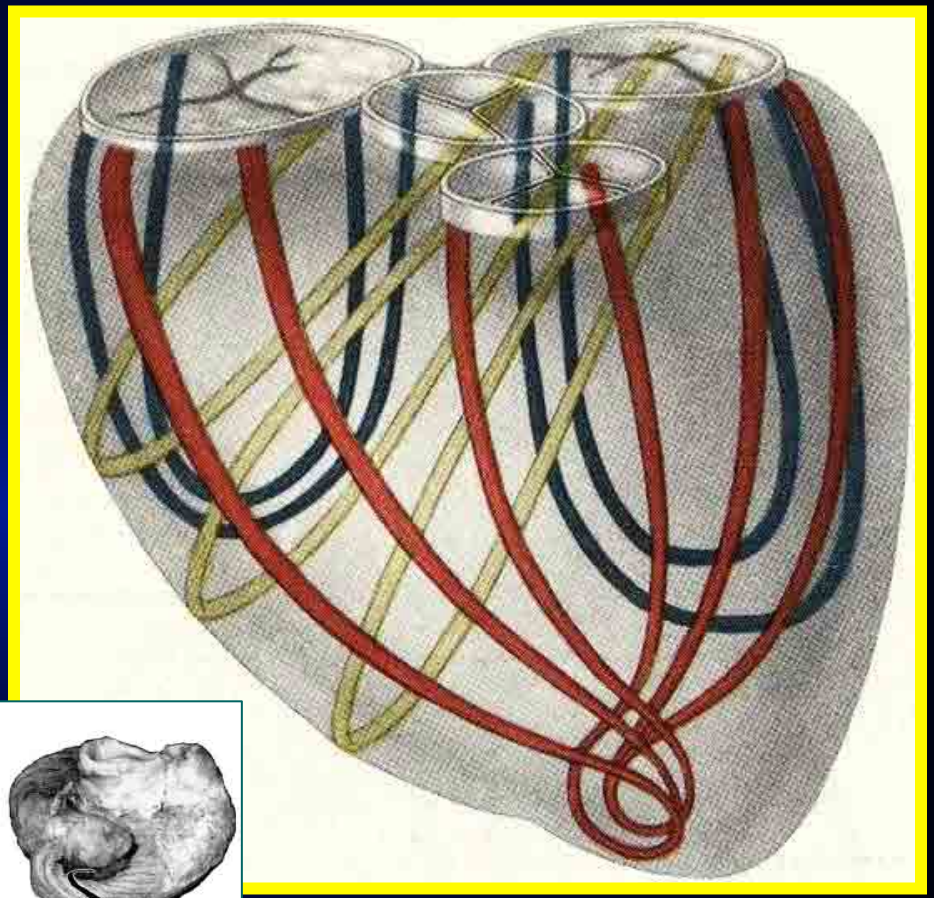
Nelle ultime Linee Guida si dà molta rilevanza allo STRAIN

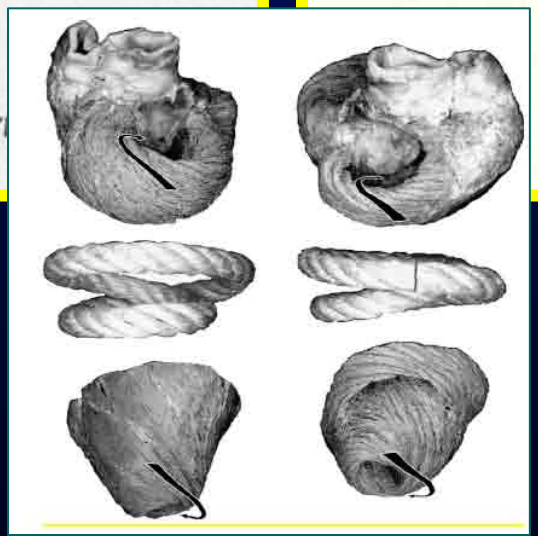
LO STRAIN


Catena costiera
Fossa
crosta oceanica
Crosta continentale
Litosfera
Litosfera
Astenosfera

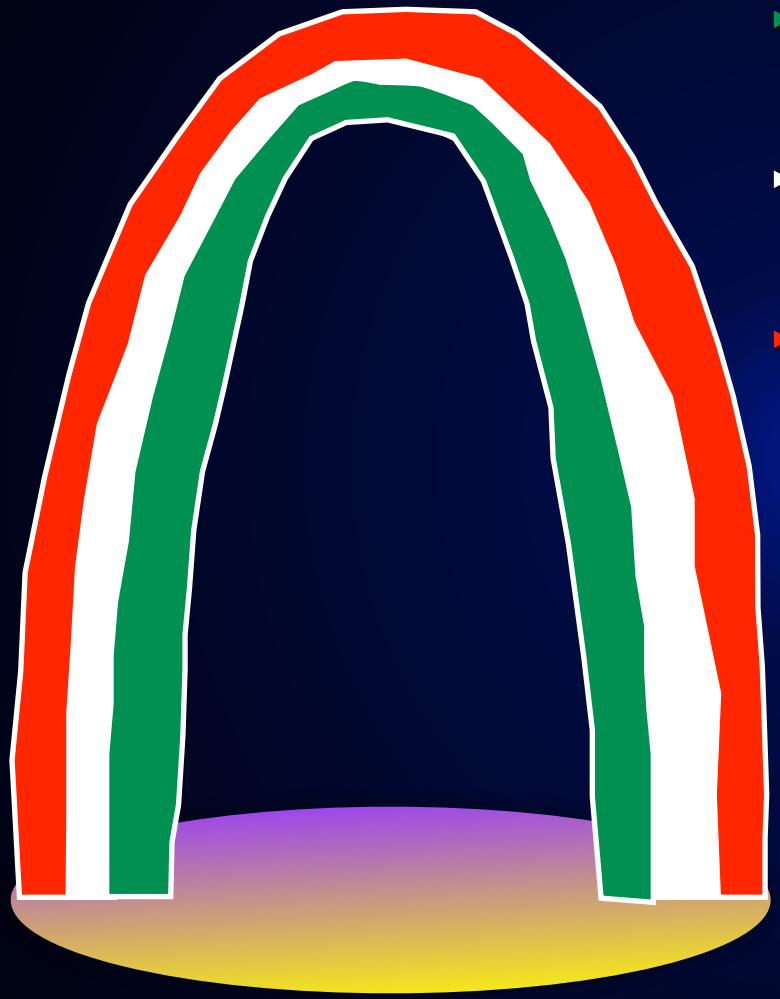
Il cuore: i fasci muscolari







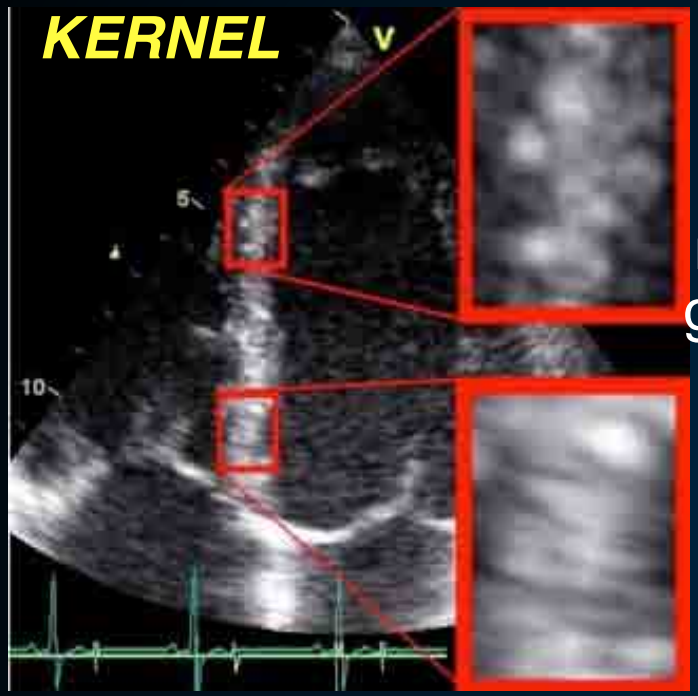
Le FIBRE MIOCARDICHE



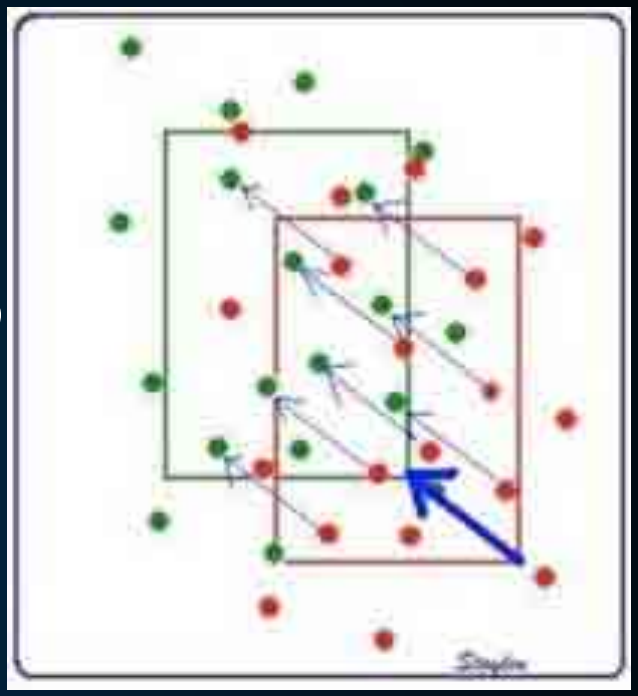
- Subendocardio: longitudinali
- Midwall: circonferenziali
- Subepicardio: longitudinali (radiali)

L'EF valuta solo l'accorciamento radiale, ma l'accorciamento longitudinale contribuisce al 60% della contrazione !

SPECKLE TRACKING



Lo **speckle** è una nuova metodica in grado di valutare lo strain tramite un'acquisizione standard 2D

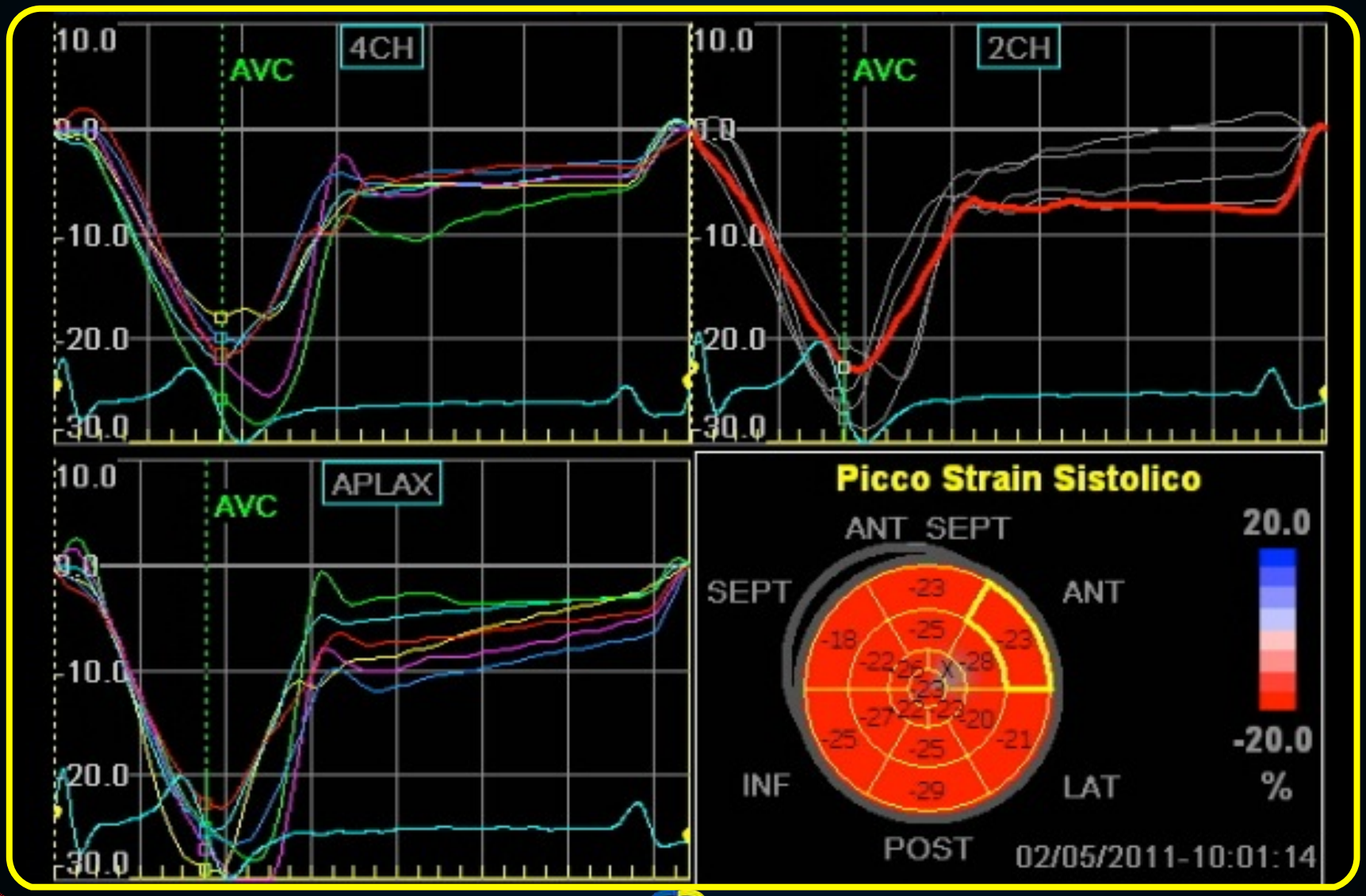


• The random distribution of the speckles ensures that each region of the myocardium has an unique pattern, a fingerprint.

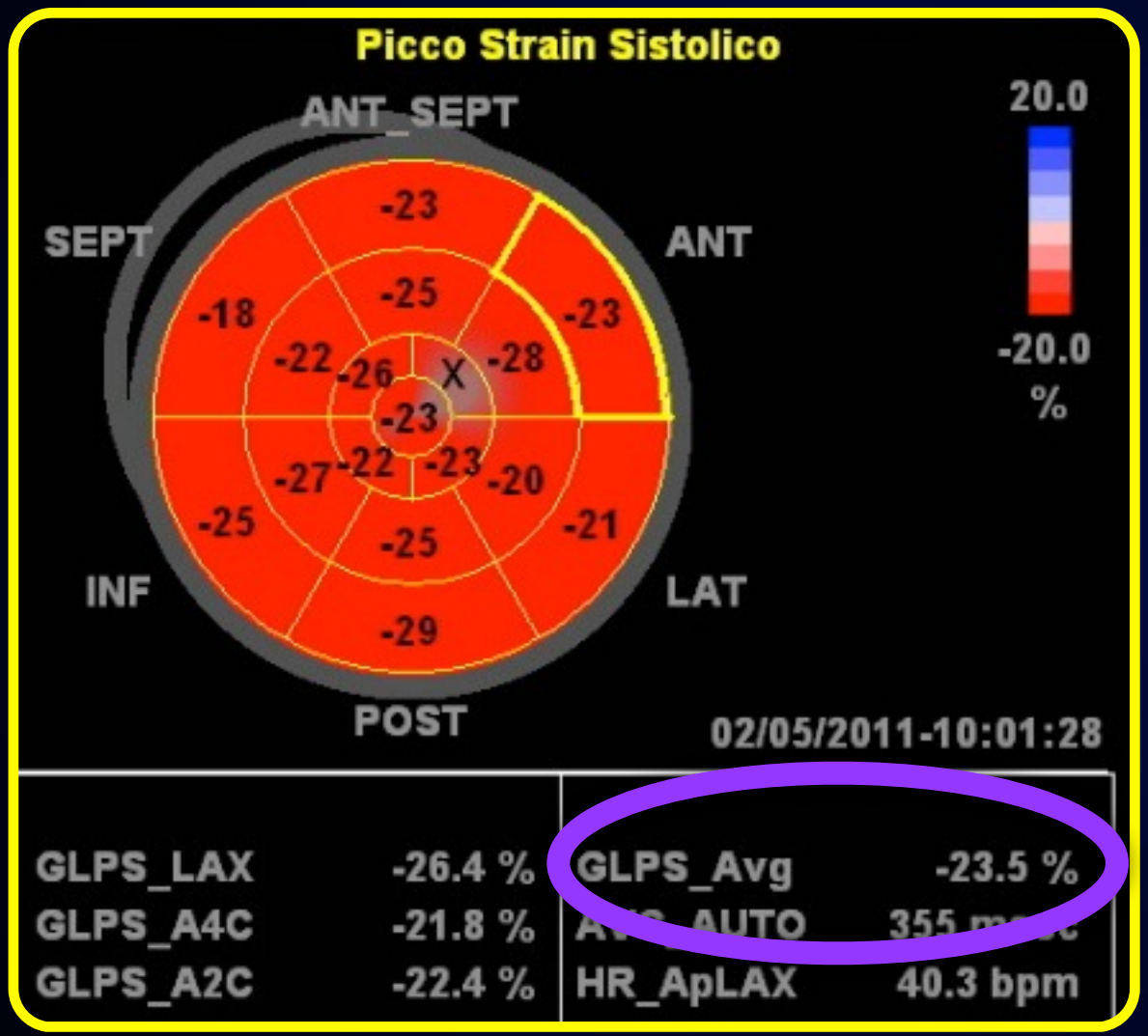
•The speckles follow the motion of the myocardium so when the myocardium moves from one frame to the next, the position of this fingerprint will shift slightly, remaining fairly constant.

•Thus, if a region (***kernel***) is defined in one frame, a search algorithm will be able to recognise the lie sized and shaped area with the most similar speckle pattern in the next frame, within a defined search area and hence, to find the new position of the kernel

2D STRAIN: AFI



2D STRAIN: AFI - BULL'S EYE

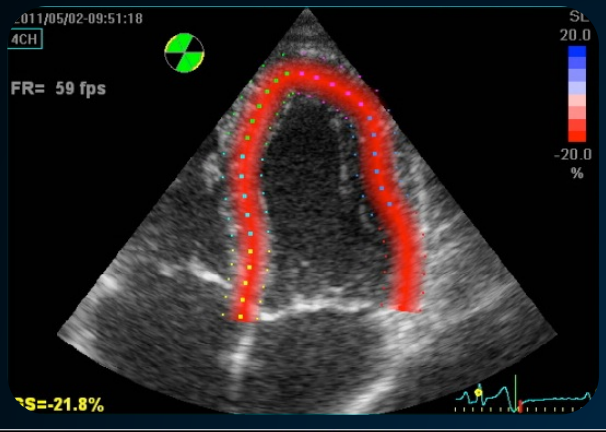


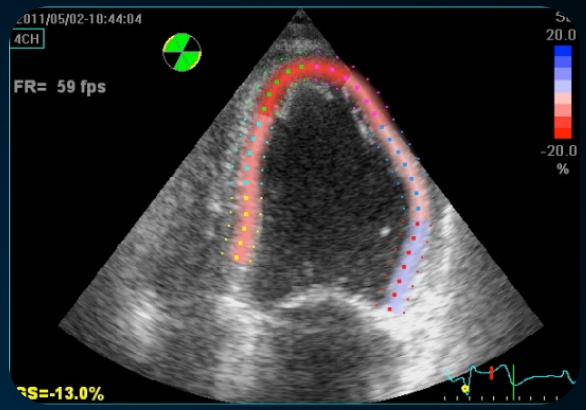
GLPS

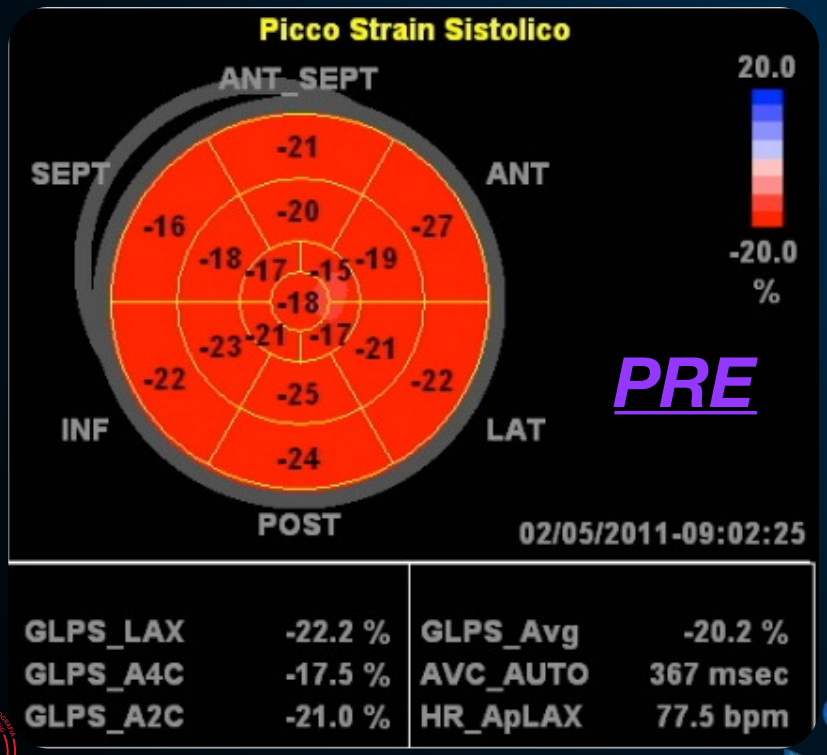
Global
Longitudinal
Peak
Systolic

V.N. < -18%

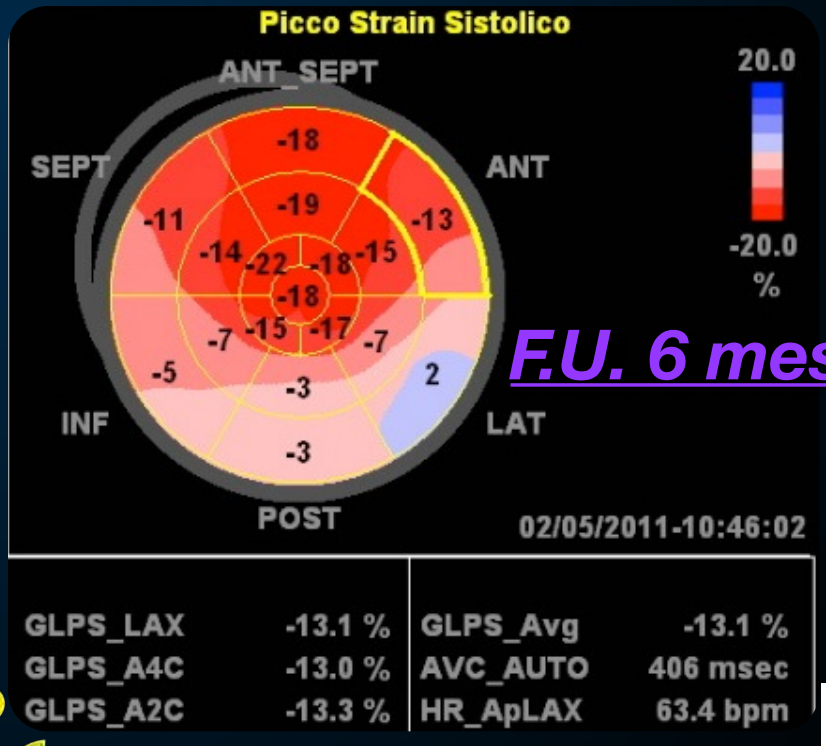
K mammella: PRE / POST CT-RT



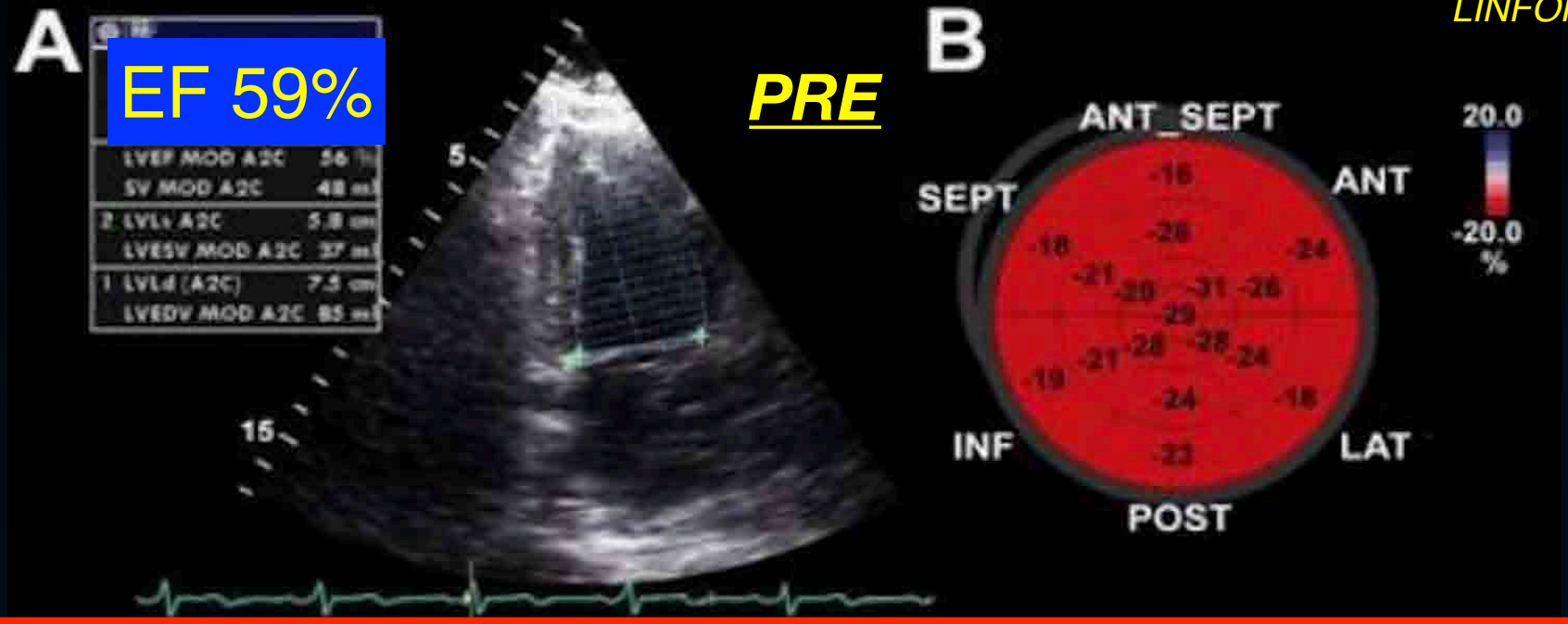


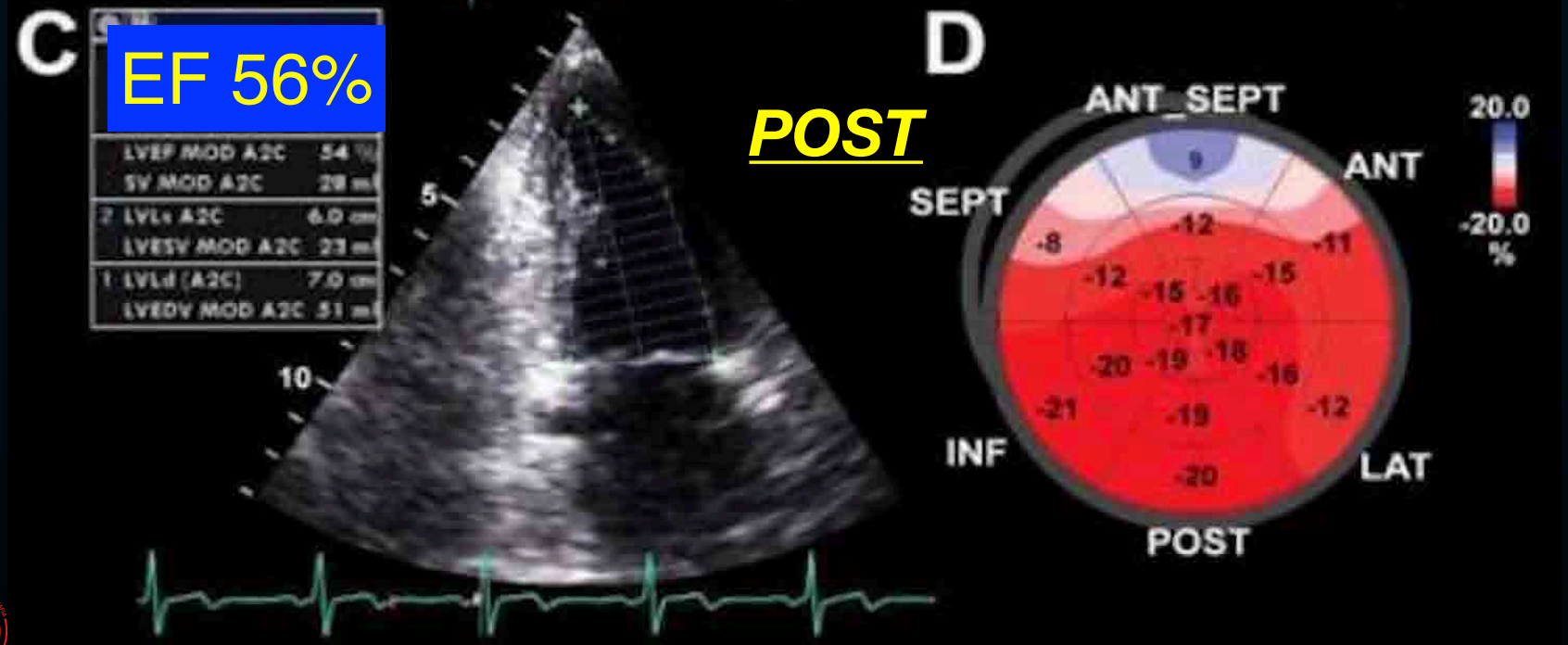


PRE



F.U. 6 mesi


A
EF 59%
LVEP MOD A2C 56
SV MOD A2C 48 ml
LVLs A2C 5.8 cm
LVESV MOD A2C 37 ml
LVLd (A2C) 7.5 cm
LVEDV MOD A2C 85 ml
5
15
PRE
B
ANT_SEPT
ANT
SEPT
INF
LAT
POST
20.0
-20.0
%


C
EF 56%
LVEP MOD A2C 54
SV MOD A2C 28 ml
LVLs A2C 6.0 cm
LVESV MOD A2C 23 ml
LVLd (A2C) 7.0 cm
LVEDV MOD A2C 51 ml
5
10
POST
D
ANT_SEPT
ANT
SEPT
INF
LAT
POST
20.0
-20.0
%

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http://journals.tbzmed.ac.ir/jcvtr

Original Article

Two-dimensional strain echocardiography for detection of cardiotoxicity in breast cancer patients undergoing chemotherapy

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[1]Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
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[3]Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

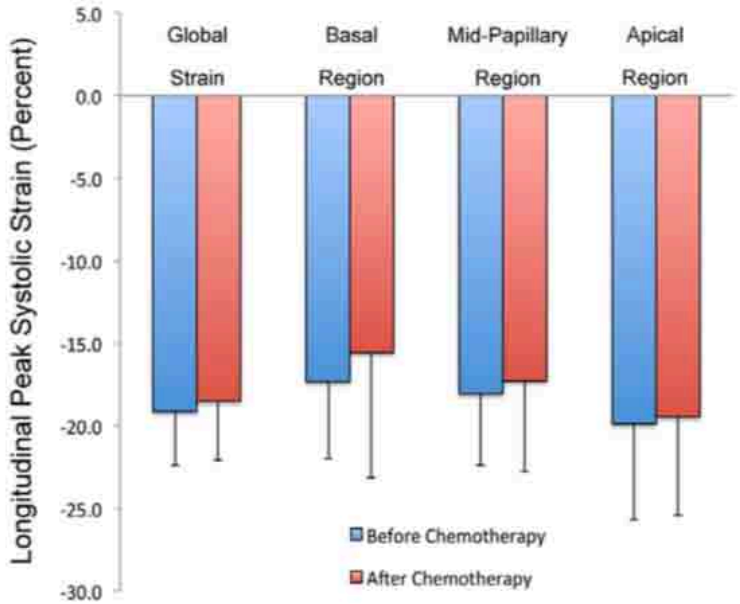
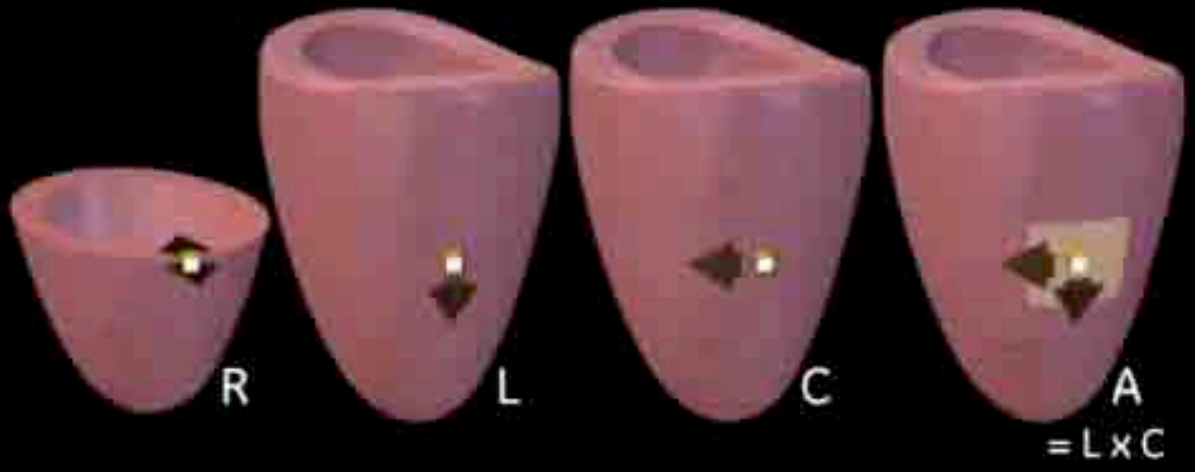


Figure 2. Two-dimensional strain echocardiography values at before and after chemotherapy.

4D STRAIN

Radial strain, Longitudinal strain,
Circumferential strain and Area strain.



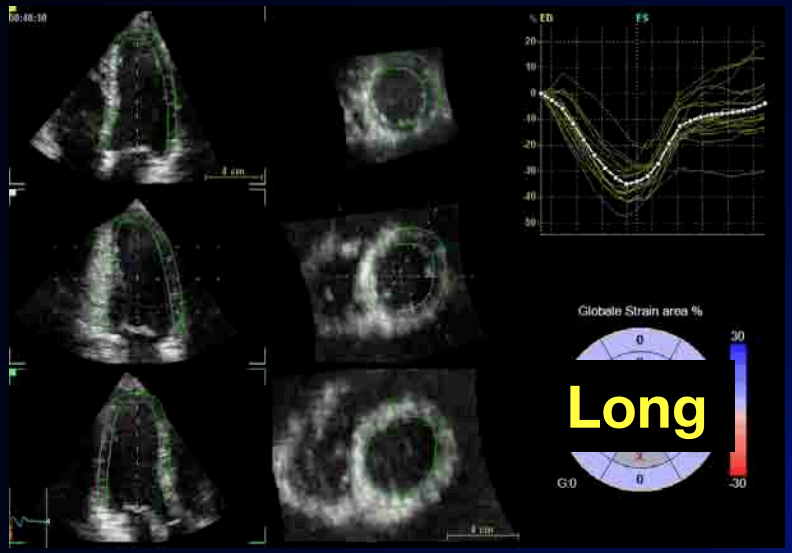
STRAIN

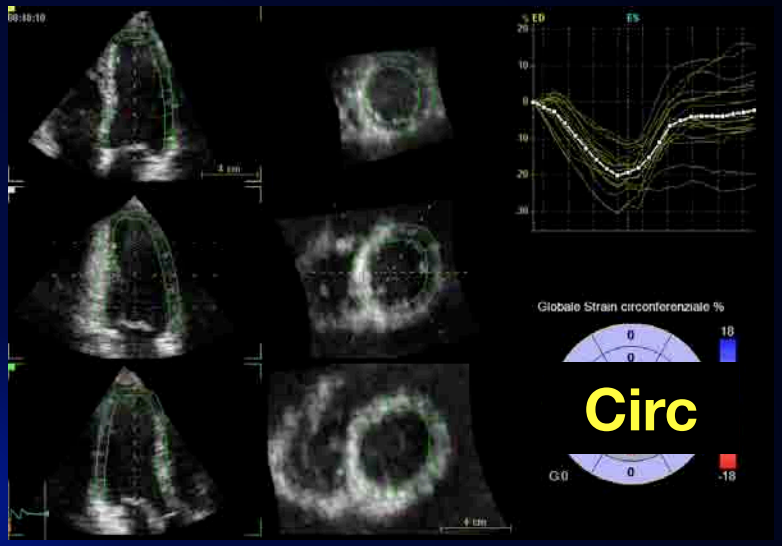
LONGITUDINALE

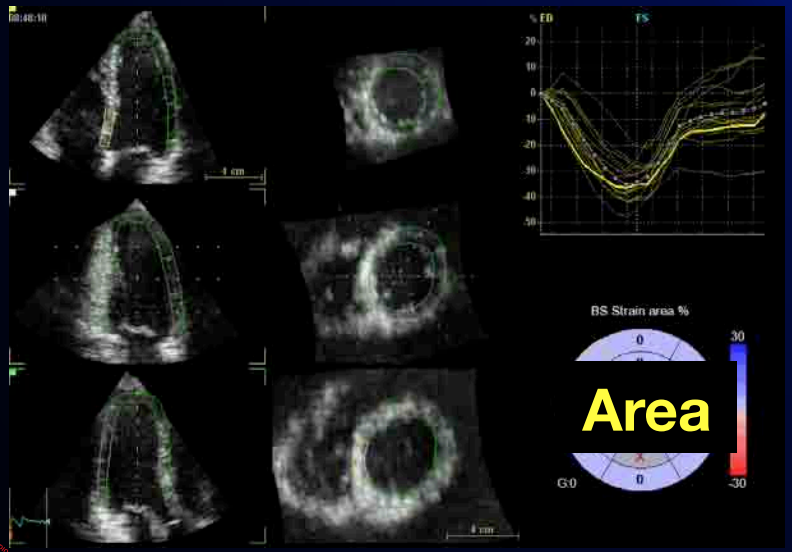
CIRCONFERENZIALE

RADIALE

4D STRAIN


Globale Strain area %
Long


Globale Strain circonferenziale %
Circ


BS Strain area %
Area

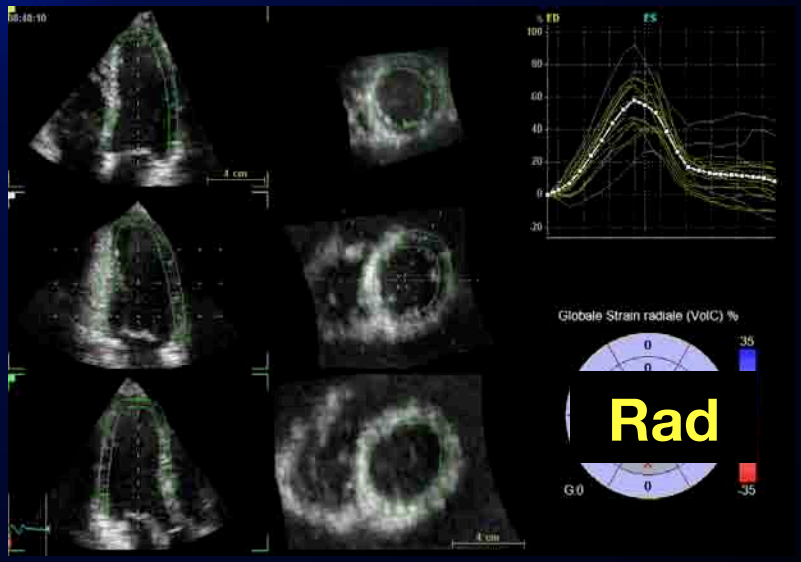

Globale Strain radiale (VolC) %
Rad

Table 4 Clinical studies using STE-derived deformation indices during or early after cancer treatment

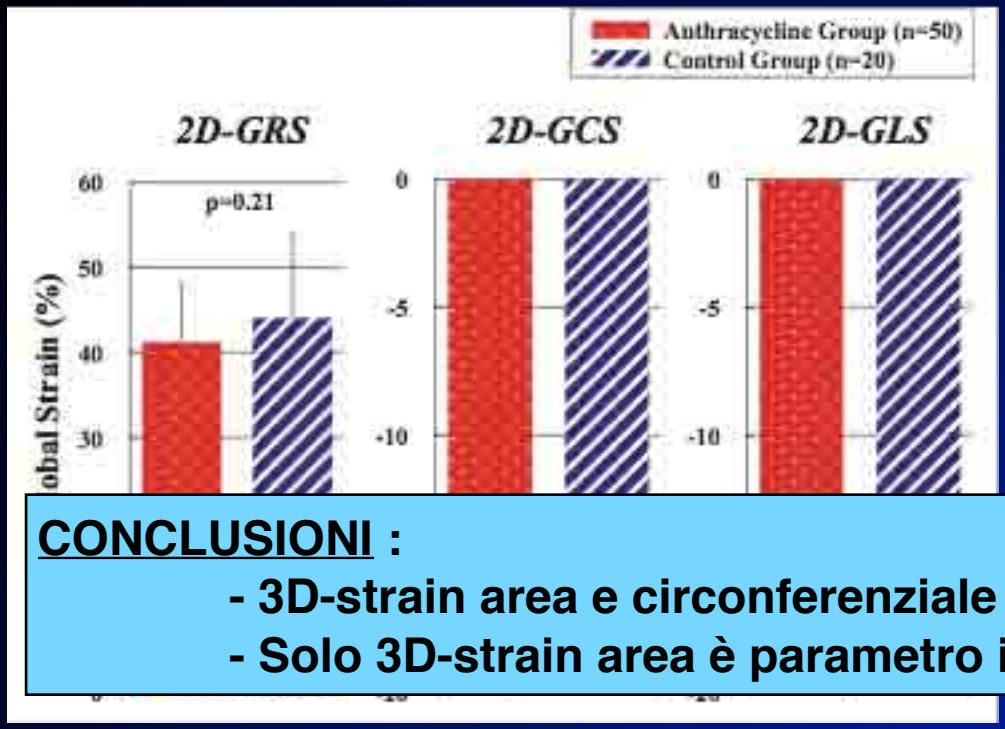
Study	Echocardiographic method	Cancer type	n	Age, yrs	Female, %	Treatment	Echocardiography timing	Pre-echo	Post-echo	Cardiotoxicity Rate (%)	Thresholds for Toxicity Prediction	Vendor, Reproducibility
Mornos *et al.* (2013)[234]	STE	Breast lymphoma, ALL, AML, osteosarcoma	74 & 37 controls	51 ±11	58	Anthracyclines	Pre, post, and 6, 12, 24 and 52 weeks	GLS -21.2 ± 2.5% GRS 47.8 ± 5.3%	GLS -19.0 ± 2.4% GRS 41.1 ± 5.4% (6 weeks)	13	ΔGLS 2.8% (13.1% relative), sensitivity 79% and specificity 73% at 6 weeks for toxicity at 24 -52 weeks	GE, intraobserver ICC for GLS 0.95, interobserver 0.91
Negishi *et al.* (2013)[155]	STE	Breast	81	50 ± 11	100	Trastuzumab, doxorubicin 46% RT 62%	Pre-trastuzumab, and 6 and 12 months later	GLS -20.7 ± 2.6% GLSR -1.17 ± 0.24/s GLSR-E 1.36 ± 0.28/s	GLS -18.3 ± 2.1% GLSR -1.00 ± 0.15/s GLSR-E 1.20 ± 0.28/s (at 6 months in patients who later had toxicity)	30	GLS change ≥11% between pre-treatment and 6 months, sensitivity 65%, spec 95% or absolute GLS >-20.5 at 6 months, sensitivity 96%, spec 66% for toxicity at 12 months	GE, intraobserver ICC (95% CI) for GLS 0.85 (0.54%-0.96%), GSLR 0.91 (0.70-0.98/s), GLSR-E 0.90 (0.66-0.97/s), Interobserver 0.71 (0.23%-0.92%), 0.85 (0.28-0.97/s), 0.87 (0.56-0.97/s)
Baratta *et al.* (2013)[235]	STE	Breast	36	47 ± 16	58	Doxorubicin 58% trastuzumab 22%	Pre- and 2,3,4, and 6 months after start of therapy	GLS -20.3 ± 2.7% GRS 53.1 ± 4%	GLS -18.9 ± 2.5% (3 months) GRS 50 ± 3.9% (4 months)	19.4	GLS fall ≥ 15% at 3 months, sensitivity 86%, spec 86%. GRS fall ≥ 10% at 4 months, sensitivity 86% spec 69%	GE, mean (SD) absolute difference inter/intraobserver GLS 0.6 (1.4%)/0.2 (1/1%), GRS 3.4 (7.1%)/3.2 (6.6%)
Sawaya *et al.* (2012)[160]	STE	Breast	81	50 ± 10	100	Doxorubicin, epirubicin, trastuzumab, RT 60%	Pre-anthracycline and at 3, 6, 9, 12, and 15 months	GLS -21 ± 2% GRS 53 ± 15% GCS -18 ± 4%	GLS -19 ± 2% GRS 50 ± 17% GCS -16 ± 4% at 3 months	32	Absolute GLS < -19% at 3 months, sensitivity 74%, spec 73% for subsequent toxicity	GE, same variability as in previous study (153)
Sawaya *et al.* (2011)[153]	STE	Breast	43	49 ± 10	100	Doxorubicin, epirubicin, trastuzumab, RT 11.6%	Pre-anthracycline and at 3 and 6 months	GLS -20.5 ± 2.2% GCS 18 ± 4%	GLS -19.3 ± 2.4% GCS 15 ± 4%	21	GLS fall > 10% at 3 months, sensitivity 78%, spec 79% for toxicity at 6 months	GE, intraobserver as absolute mean error (SD) GLS -0.14 (1.1%), interobserver 0.5 (1.5%)
Fallah-Rad *et al.* (2011)[156]	STE	Breast	42	47 ± 9	100	Epirubicin, doxorubicin, trastuzumab, RT 98%	Pre-anthracycline, Pre-trastuzumab and at 3, 6, 9, and 12 months	GLS -19.8 ± 1.8% GLS 41.4 ± 15.2%	GLS -16.4 ± 1.1% GRS 34.5 ± 15.2% (3 months into trastuzumab)	24	Absolute GLS fall of 2.0%, sensitivity 79%, spec 82%. Absolute GRS fall of 0.8%, sensitivity 86%, spec 81% for subsequent toxicity	GE, intraobserver as ICC (COV) GLS 0.94 (3.5%), GRS 0.91 (3.2%). Interobserver 0.90 (5.2%), 0.82 (5.4%)
Hare *et al.* (2009)[162]	TDI and STE	Breast	35	51 ± 8	100	Doxorubicin, epirubicin, trastuzumab, RT 77%	Pre- and/or post-anthracycline and at 3-month	STE GLSR -1.30 ± 0.21/s STE RSR 2.02 ± 0.61/s	STE GLSR -1.24 ± 0.18/s (by 3 months) STE RSR 1.75 ± 0.41/s (by	14	A >1 SD drop in GLSR (toxicity at mean follow-up of 22 ± 6 months)	GE, intra/interobserver as ICC for 2D GLS 0.94/0.91, GLSR

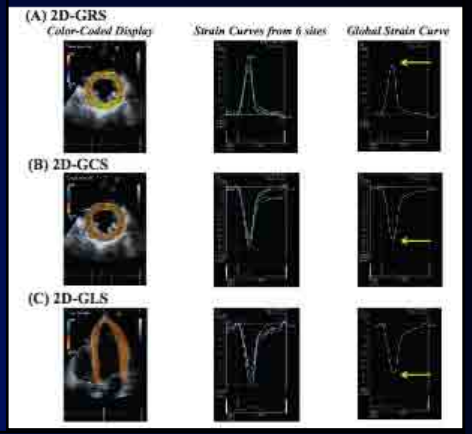
Left Ventricular Endocardial Dysfunction in Patients with Preserved Ejection Fraction after Receiving Anthracycline

Tatsuya Miyoshi, M.D.,* Hidekazu Tanaka, M.D., Ph.D.,* Akihiro Kaneko, M.D., Ph.D.,* Kazuhiro Tatsumi, M.D., Ph.D.,* Kensuke Matsumoto, M.D.,* Hironobu Minami, M.D., D.Med.Sci.,† Hiroya Kawai, M.D., Ph.D.,* and Ken-ichi Hirata, M.D., Ph.D.*

*Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe, Japan; and †Division of Medical Oncology and Hematology, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe, Japan

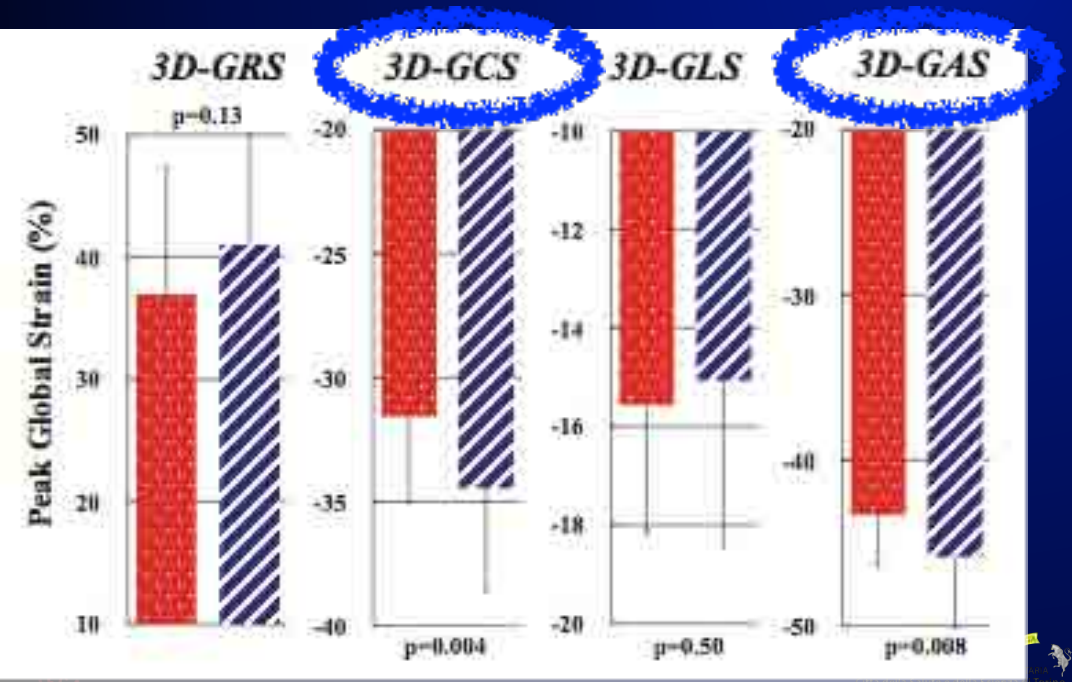
Background: Anthracycline chemotherapy generates progressive dose-dependent left ventricular (LV) dysfunction associated with a poor prognosis. Early detection of minor LV myocardial dysfunction caused by the cardiotoxicity of anthracycline is thus important for predicting global LV dysfunction. Methods: Fifty patients with preserved ejection fraction (all ≥55%) after receiving anthracycline chemotherapy were recruited for this study. Two-dimensional speckle tracking was used to assess global radial and circumferential strains from mid-LV short-axis views and global longitudinal strain from the apical four- and two-chamber view as peak global strain curves. Three-dimensional (3D) radial, circumferential, and longitudinal myocardial function was quantified as a peak global strain curve using 3D speckle tracking from all 16 LV segments. 3D speckle tracking imaging was used to evaluate LV endocardial area change ratio (area strain) quantified as peak global area strain curve (3D-GAS) to determine LV endocardial function. Twenty age-, gender-, and EF-matched normal volunteers were studied for comparisons. Results: Only 3D-GAS and peak 3D global circumferential strains of the anthracycline group were significantly worse than those of the control group (-43.3 ± 3.1 vs. $-45.8 \pm 4.3\%$ and $-31.6 \pm 3.5\%$ vs. $-34.4 \pm 4.2\%$, respectively; $P = 0.008$, $P = 0.004$) even though global LV systolic and diastolic functions were similar. 3D-GAS correlated significantly with the cumulative doxorubicin dose ($r = 0.316$, $P = 0.026$). It was noteworthy that multivariate analysis showed only 3D-GAS ($\beta = 0.323$, $P = 0.025$) was independently associated with cumulative doxorubicin dose. Conclusions: Three-dimensional speckle tracking area strain was found useful for early detection of minor LV endocardial dysfunction associated with the use of anthracycline, and may thus prove to be clinically useful for predicting global LV dysfunction. (Echocardiography 2014;31:848–857)

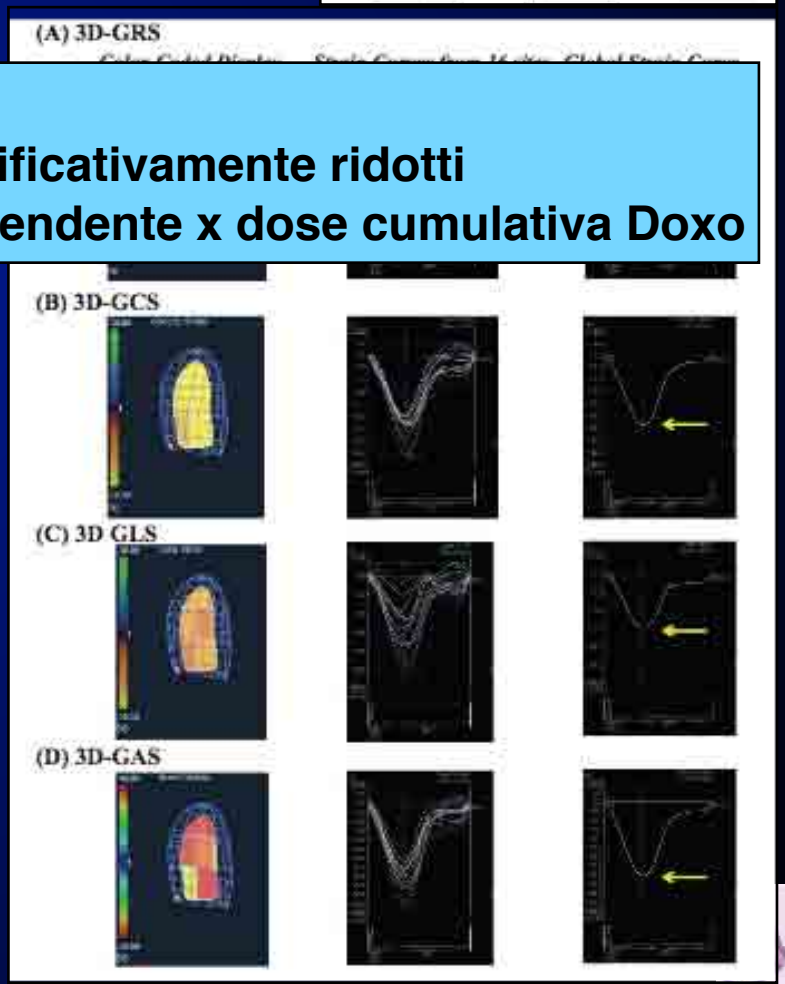




CONCLUSIONI :

- 3D-strain area e circonferenziale significativamente ridotti
- Solo 3D-strain area è parametro indipendente x dose cumulativa Doxo





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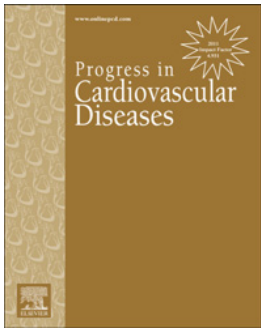

Cardio-Oncology: Role of Echocardiography

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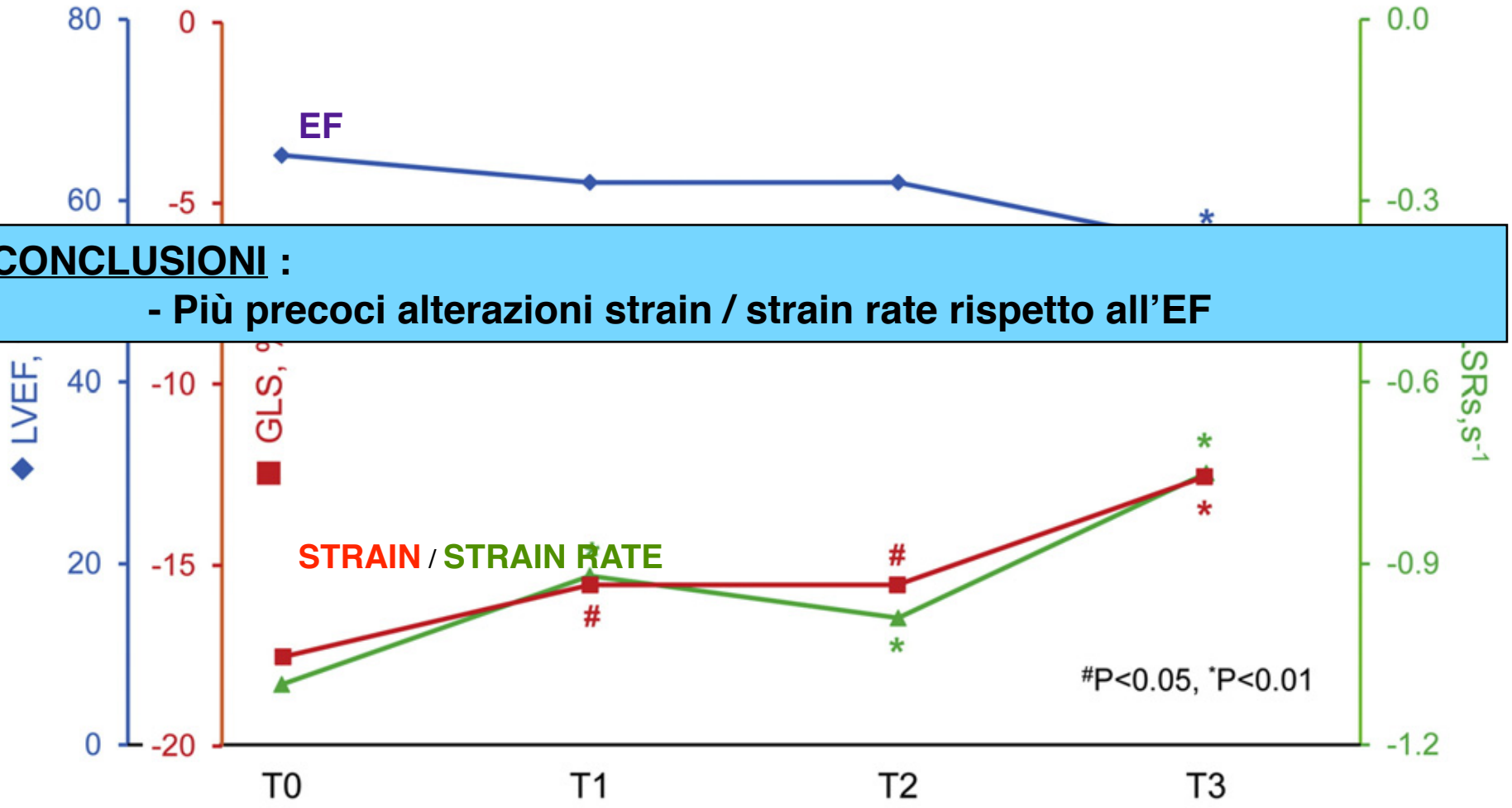
ARTICLE INFO

Keywords:
Cardio-oncology
Strain
Radiotherapy
Breast cancer
Lymphoma

ABSTRACT

Current therapies for cancer have improved life expectancy of patients. Breast cancer and lymphoma survivors in up to 26% of cases can develop complications as a consequence of the chemotherapeutic and radiotherapeutic treatments. Echocardiography is a noninvasive method that can in all stages of cancer treatment perform a comprehensive evaluation and detect coronary, myocardial, valve and pericardial disease complications secondary to the therapeutic regimen used (radiotherapy and/or chemotherapy). Three-dimensional echocardiography derived left ventricular ejection fraction (LVEF) has an excellent correlation with cardiac magnetic resonance imaging and can be used to monitor LVEF; 2-dimensional speckle tracking echocardiography (2D-STE) derived strain and strain rate can detect changes in myocardial mechanics before changes in LVEF occur and can predict a future decrease in ejection fraction to less than 50% or of greater than 10% indicative of cardiotoxicity. Echocardiography should be used as the method of choice to evaluate serial changes in heart function, detect late side effects of treatment, and to identify patients at risk of a future decrease in LVEF.

Dynamic changes of LVEF, GLS% and GLSRs s^{-1} at different time points (T0 – T3)



CONCLUSIONI :

- Più precoci alterazioni strain / strain rate rispetto all'EF

Modified from: Xu Y, Hermann J, Pellikka PA, Ansell SM, Cha S, **Villarraga HR**. Can early changes in 2-dimensional speckle tracking echocardiography predict a future decrease in left ventricular ejection fraction in lymphoma patients undergoing anthracycline chemotherapy? JASE. 2013; 26:B52

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STATE-OF-THE-ART PAPERS

Use of Myocardial Strain Imaging by Echocardiography for the Early Detection of Cardiotoxicity in Patients During and After Cancer Chemotherapy

A Systematic Review

Paaladinesh Thavendiranathan, MD,*† Frédéric Poulin, MD,* Ki-Dong Lim, MD,*

Miglior predittore CTX =

Global Longitudinal Strain S.T.: ⬇10-15%

small trials in the research setting. In this systematic review of the current literature, we describe echocardiographic myocardial deformation parameters in 1,504 patients during or after cancer chemotherapy for 3 clinically-relevant scenarios. The systematic review was performed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines using the EMBASE (1974 to November 2013) and MEDLINE (1946 to November 2013) databases. All studies of early myocardial changes with chemotherapy demonstrate that alterations of myocardial deformation precede significant change in left ventricular ejection fraction (LVEF). Using tissue Doppler-based strain imaging, peak systolic longitudinal strain rate has most consistently detected early myocardial changes during therapy, whereas with speckle tracking echocardiography (STE), peak systolic global longitudinal strain (GLS) appears to be the best measure. A 10% to 15% early reduction in GLS by STE during therapy appears to be the most useful parameter for the prediction of cardiotoxicity, defined as a drop in LVEF or heart failure. In late survivors of cancer, measures of global radial and circumferential strain are consistently abnormal, even in the context of normal LVEF, but their clinical value in predicting subsequent ventricular dysfunction or heart failure has not been explored. Thus, this systematic review confirms the value of echocardiographic myocardial deformation parameters for the early detection of myocardial changes and prediction of cardiotoxicity in patients receiving cancer therapy. (J Am Coll Cardiol 2014;63:2751–68) © 2014 by the American College of Cardiology Foundation

STRAIN CUT-OFF for INTERVENDORS

Table 1 – Values of strain and systolic strain rate (S and SRs) with standard deviation (SD).

	Strain %	Longitudinal SRs s^{-1}	Circumferential Strain %	Circumferential SRs s^{-1}	Radial Strain	Radial SRs s^{-1}
GE[40]	−18.6 ± 5.1		−22.9 ± 4.4		54.6 ± 12.6	
VVI[36]	−17.3 ± 2.5	−1.0 ± 0.1	−21.9 ± 4.0	1.3 ± 0.3	44.8 ± 21.7	**2.3 ± 0.7**
TOMTEC[38] (30FPS)	−16.1 ± 4.9		−22.3 ± 7.4		30.4 ± 13.5	
Toshiba[41]	−19.9 ± 2.4		−30.5 ± 3.8		51.4 ± 8.0	
Philips[41]	−18.9 ± 2.5		−22.2 ± 3.2		36.3 ± 8.2	

Abbreviation: SRs: systolic strain rate.

STRAIN

- Myocardial deformation (strain) can be measured using DTI or 2D STE. The latter is favored because of a lack of angle dependency.
- GLS is the optimal parameter of deformation for the early detection of subclinical LV dysfunction.
- Ideally, the measurements during chemotherapy should be compared with the baseline value. In patients with available baseline strain measurements, a relative percentage reduction of GLS of <8% from baseline appears not to be meaningful, and those >15% from baseline are very likely to be abnormal.
- When applying STE for the longitudinal follow-up of patients with cancer, the same vendor-specific ultrasound machine should be used.

EUROPEAN SOCIETY OF CARDIOLOGY®

CASISTICA MOLINETTE

- 73 pazienti ♀
- carcinoma mammario
- ecocardiogramma 2D 3D Doppler prima della CT e al F.U. 9 mesi
- valutazione EF e altri indici sisto-diast

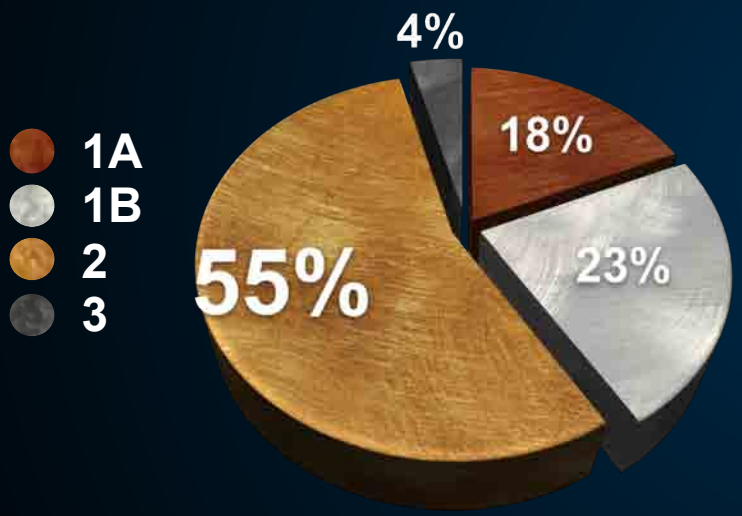
S.C. Cardiologia2 Marra: M.Giorgi, A. Fava, G. Alunni, F. Astegiano
COES Ciuffreda: M. Donadio, M. Mistrangelo

VARIABILITÀ INTEROPERATORE

EF	t -	p value
2D	2,07	0,04
3D Triplano	2,04	0,04
3D Full	2,1	0,03

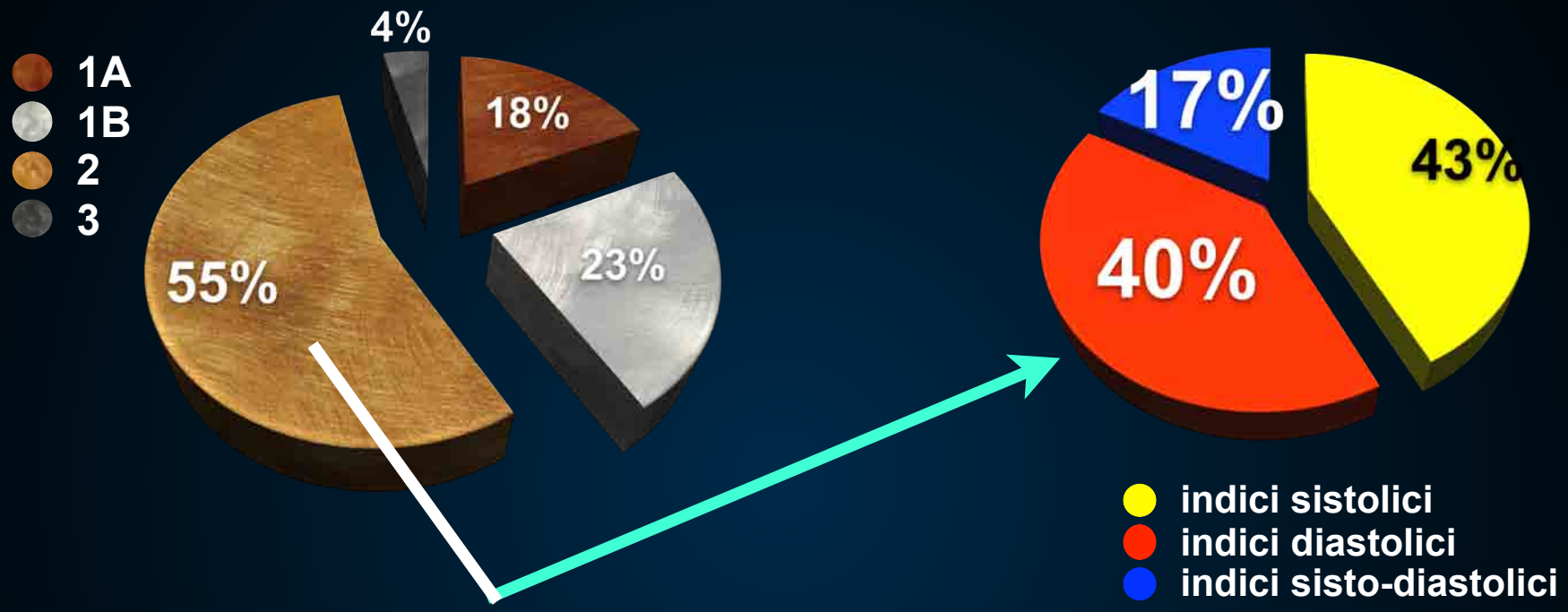
L' ECHO 3D full-volume si è dimostrata la metodica con maggior riproducibilità

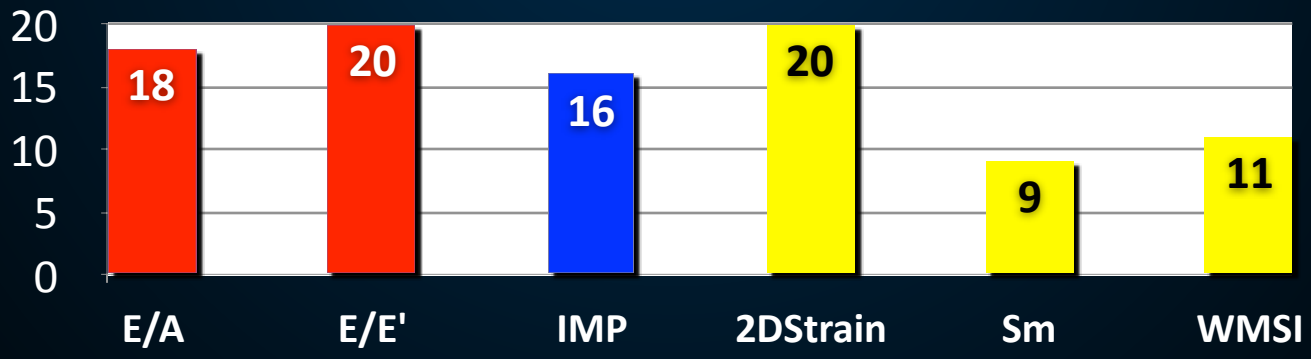
RISULTATI



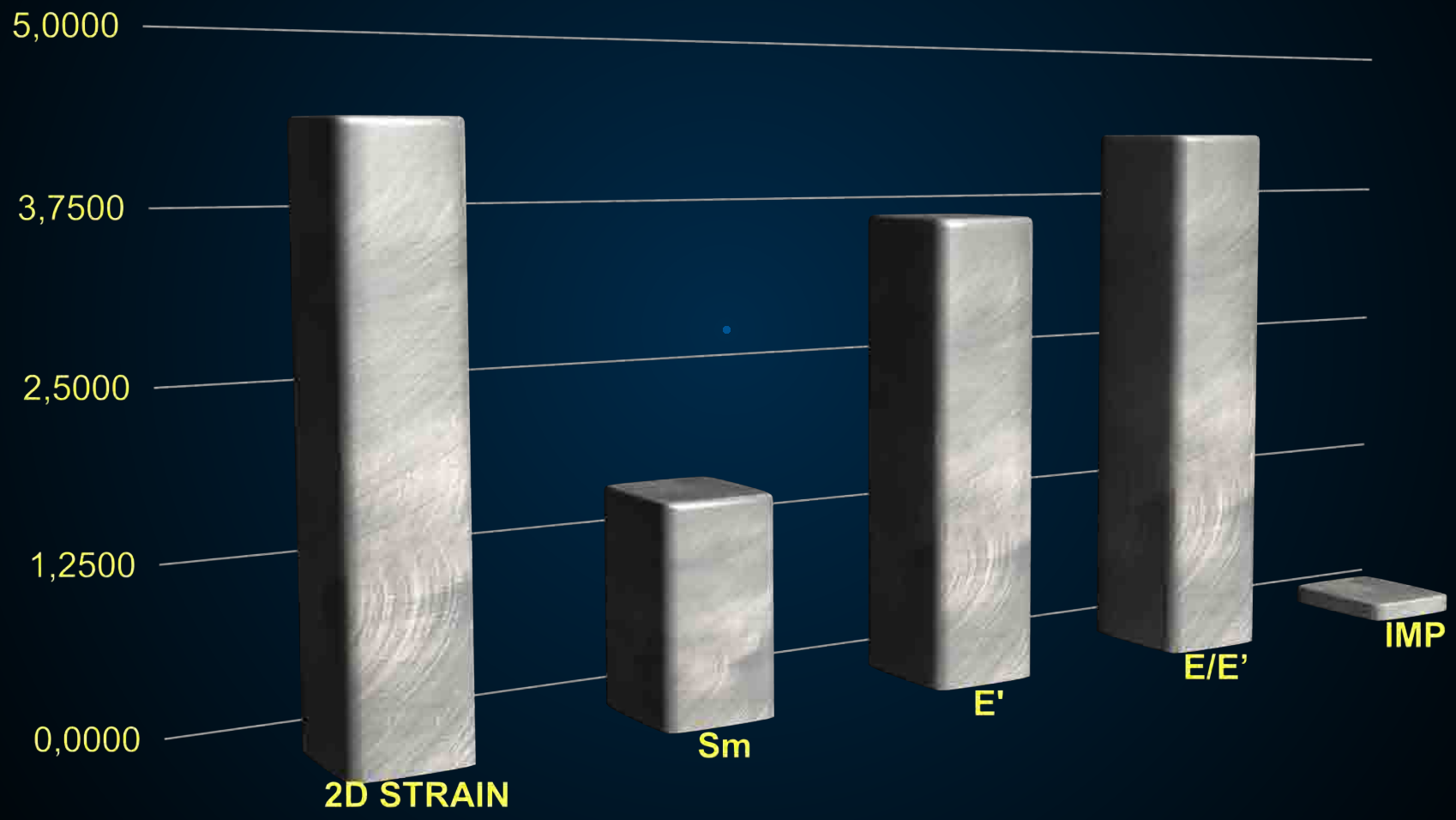
- **GRUPPO 1A**: 13 pazienti (18%) senza alterazioni dell'EF, né degli altri indici
- **GRUPPO 1B**: 17 pazienti (23%) con EF inalterata ed alterazioni "ab initio" di altri indici, non progredite al follow-up
- **GRUPPO 2: 40 pazienti (55%) con EF inalterata ed alterazioni di altri indici al follow-up**
- **GRUPPO 3**: 3 pazienti (4%) con alterazioni significative dell'EF

EF INVARIATA - ALTRI INDICI





ANALISI della VARIANZA



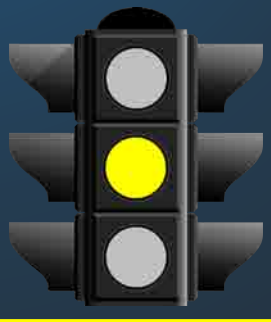
CASISTICA MOLINETTE

- L'**EF** si è confermata parametro molto specifico, ma tardivo e poco sensibile di CTX (alterazione significativa solo 4%)
- 55% Pts ha evidenziato almeno un'alterazione di altri **indici**
- Le Pts con riduzione dell'EF hanno mostrato alterazione di tutti i nuovi indici (diastolici, sistolici e sisto-diastolici)
- Lo **strain sistolico (2D e 4D)** è un indicatore precoce di cardiotossicità insieme all'alterazione della **funzione diastolica**

MANAGEMENT

WALL DYNAMICS (STRAIN) e DIASTOLE

NORMALE ALTERATO

EF	NORMALE		*iniziale disfunzione*
	ALTERATA		


That's all Folks!
Any Question ?