SINDROMI CLINICHE CON DISFUNZIONE DIASTOLICA: DIAGNOSI CLINICO-STRUMENTALE E CLASSIFICAZIONE

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CONGRESSO NAZIONALE SIEC

Napoli, 18 Aprile 2015

EMERGENCY ROOM
DYSPNEA AT REST

♂ E.C.

76 y.o., HTS, Db, RENAL TRANSPLANT

B.P. 170/100mmHg

H.R. 95BPM in AFib

SO2 85%, 91% FiO2 35%

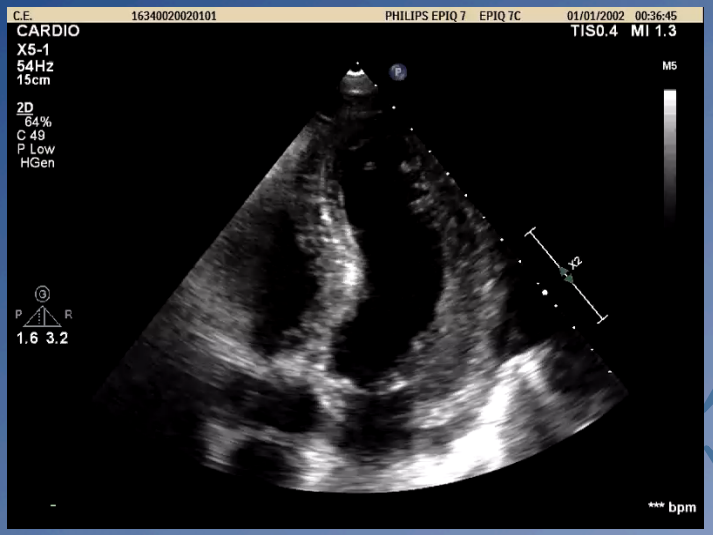
FEVER DAY BEFORE ADMISSION

RALES AND RHONCHI

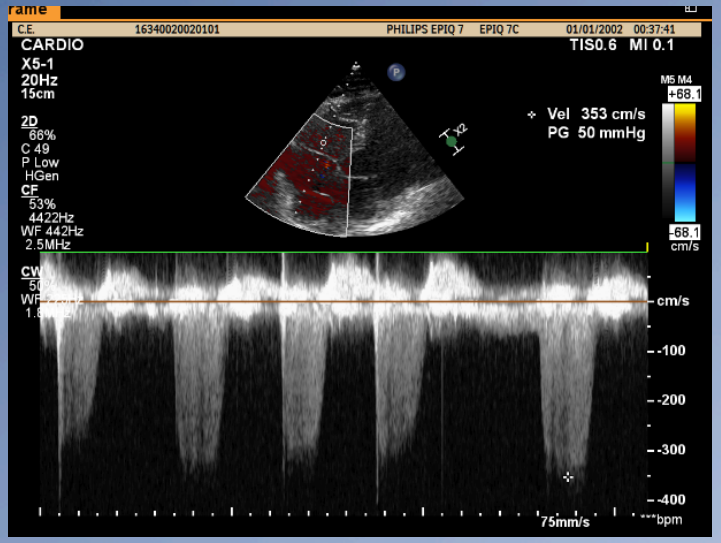
PERIPHERAL OEDEMA

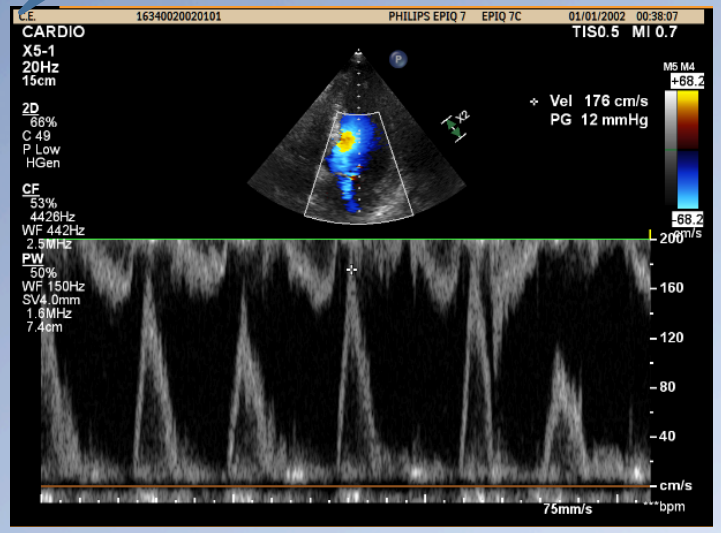
BILATERAL

EMERGENCY ROOM
DYSPNEA AT REST

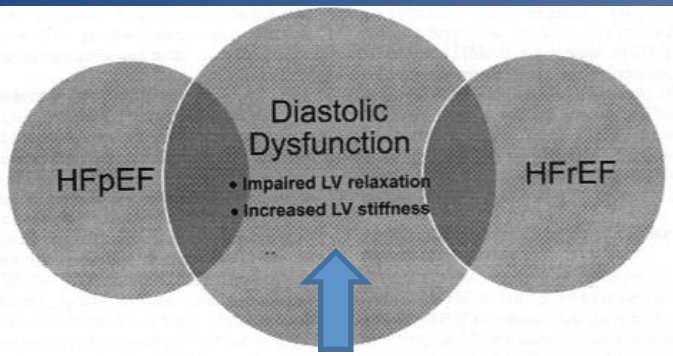


HFpEF:
DIASTOLIC DYSFUNCTION

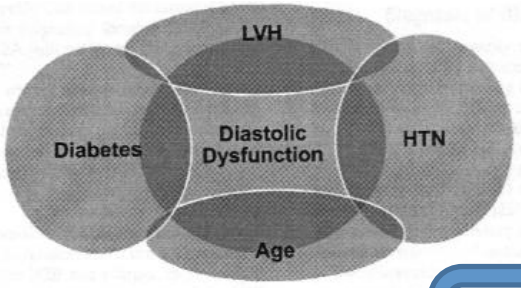




DIASTOLIC DYSFUNCTION
CLINICAL CLASSIFICATION



GENERAL POPULATION:
21% MILD
7% MODERATE/SEVERE

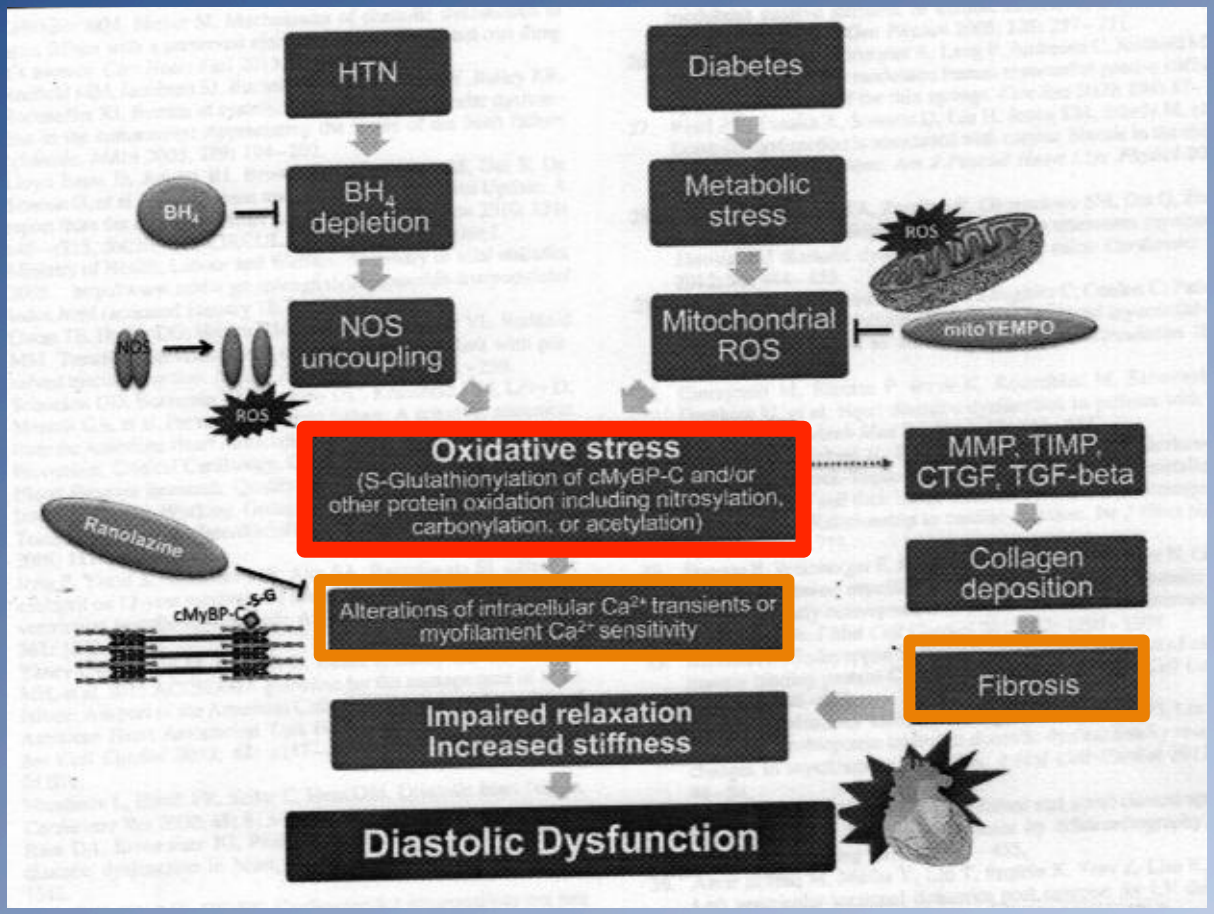


ASYMPTOMATIC:
Elevated LV stiffness
Diastolic filling abnormalities
Normal excercise tolerance

EARLY SYMPTOMATIC:
Pulmonary pressure increase during excercise
Reduced excercise tolerance

AFIB

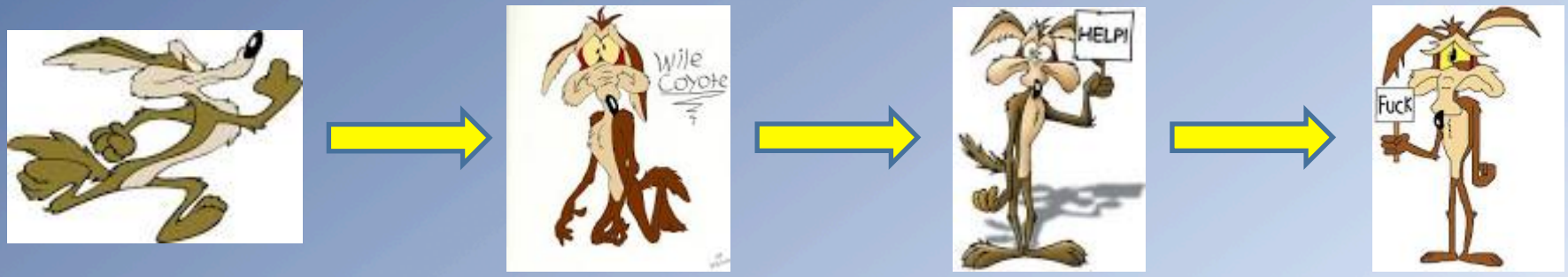
SYMPTOMATIC:
Further increase in filling pressure
Clinical signs of Heart Failure


HTN
Diabetes
BH4
BH4 depletion
Metabolic stress
ROS
NOS
NOS uncoupling
Mitochondrial ROS
mitoTEMPO
ROS
Oxidative stress
(S-Glutathionylation of cMyBP-C and/or other protein oxidation including nitrosylation, carbonylation, or acetylation)
MMP, TIMP, CTGF, TGF-beta
Ranolazine
Collagen deposition
cMyBP-C
Alterations of intracellular Ca2+ transients or myofilament Ca2+ sensitivity
Fibrosis
Impaired relaxation
Increased stiffness
Diastolic Dysfunction

DIASTOLIC DYSFUNCTION AND HF
CLINICAL CLASSIFICATION

ACCF/AHA Stages of HF[38]		NYHA Functional Classification[46]	
A	At high risk for HF but without structural heart disease or symptoms of HF	None	
B	Structural heart disease but without signs or symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.
D	Refractory HF requiring specialized interventions	IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.

EVOLUTION OF HEART FAILURE



DIASTOLIC DYSFUNCTION AND HF

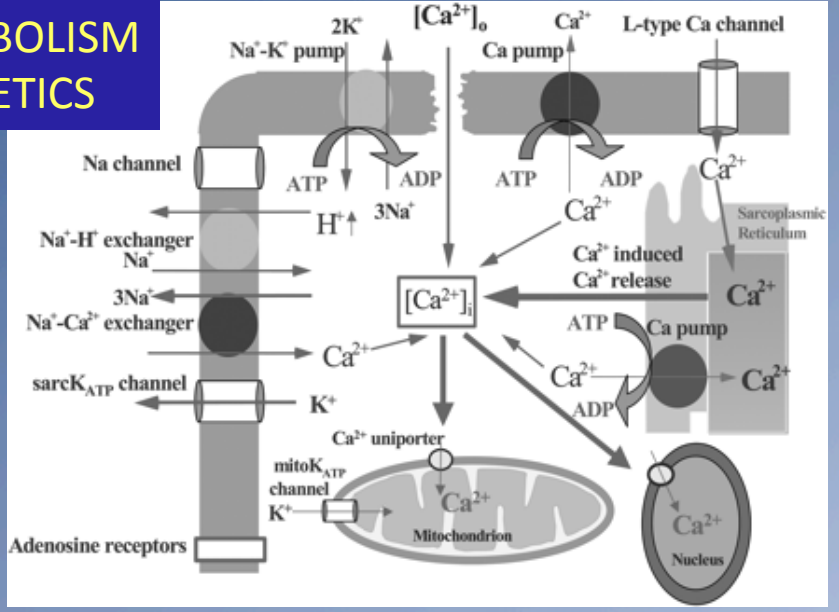
CAUSES

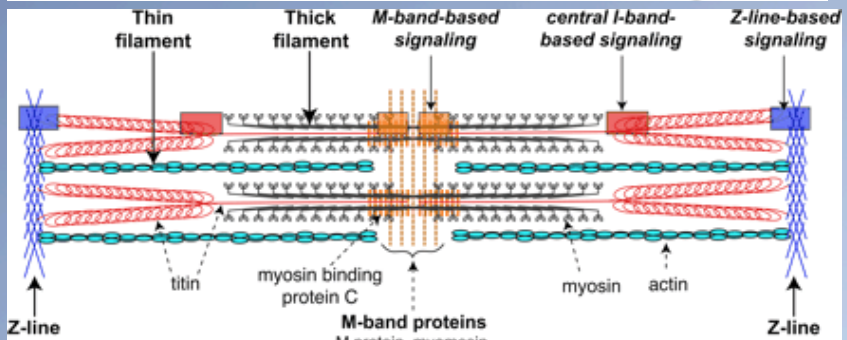
- ATHEROSCLEROSIS ISCHEMIA
- VALVULAR DISEASE
- HYPERTENSIVE DISEASE
- PERICARDIAL DISEASE
- FAMILIAL CMP
- ENDOCRIN/ METABOLIC CAUSE
  - OBESITY
  - DIABETIC CMP
  - TYROID DISEASE
  - GH DISEASE
- TOXIC CMP
  - COCAINE
  - ALCOHOL
  - CANCER THERAPY
- MYOCARDITIS INFLAMMATORY CMP
  - MYOCARDITIS
  - GIANT CELL
  - HIV
  - CHAGAS
  - HYPERSENSITIVITY
  - REUMATHOLOGICAL/ CONNETTIVE DISSUE
- PERIPARTUM CMP
- IRON OVERLOAD CMP
- AMILOIDOSIS
- SARCOIDOSIS

TABLE 1. Diastolic Heart Failure: Mechanisms

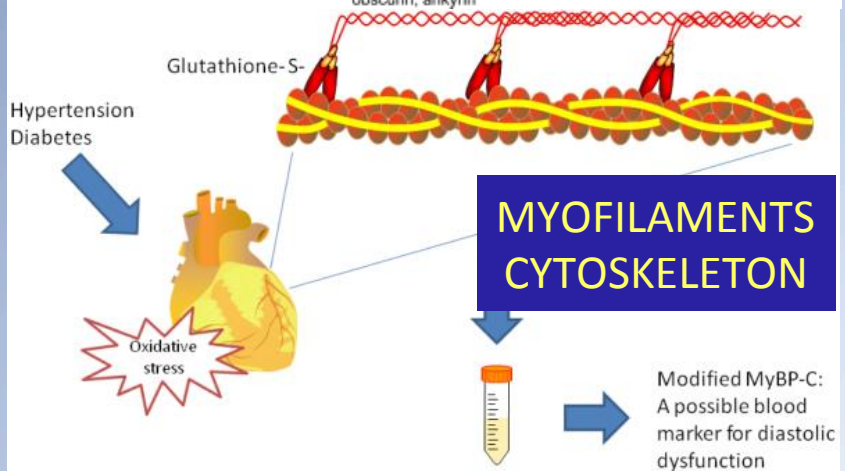
- Extramyocardial
  - Hemodynamic load: early diastolic load, afterload
  - Heterogeneity
  - Pericardium
- Myocardial
  - Cardiomyocyte
    - Calcium homeostasis
      - Calcium concentration
      - Sarcolemmal and SR calcium transport function
      - Modifying proteins (phospholamban, calmodulin, calsequestran)
    - Myofilaments
      - Tn-C calcium binding
      - Tn-I phosphorylation
      - Myofilament calcium sensitivity
      - α/β-myosin heavy chain ATPase ratio
    - Energetics
      - ADP/ATP ratio
      - ADP and Pi concentration
    - Cytoskeleton
      - Microtubules
      - Intermediate filaments (desmin)
      - Microfilaments (actin)
      - Endosarcomeric skeleton (titin, nebulin)
  - Extracellular matrix
    - Fibrillar collagen
    - Basement membrane proteins
    - Proteoglycans
    - MMP/TIMP
  - Neurohormonal activation
    - Renin-angiotensin-aldosterone
    - Sympathetic nervous system
    - Endothelin
    - Nitric oxide
    - Naturetic peptides

Ca METABOLISM ENERGETICS





MYOFILAMENTS CYTOSKELETON



DIASTOLIC DYSFUNCTION AND HFpEF
PHYSICAL FINDINGS

TABLE 1. Prevalence of Specific Symptoms and Signs in Systolic vs Diastolic Heart Failure

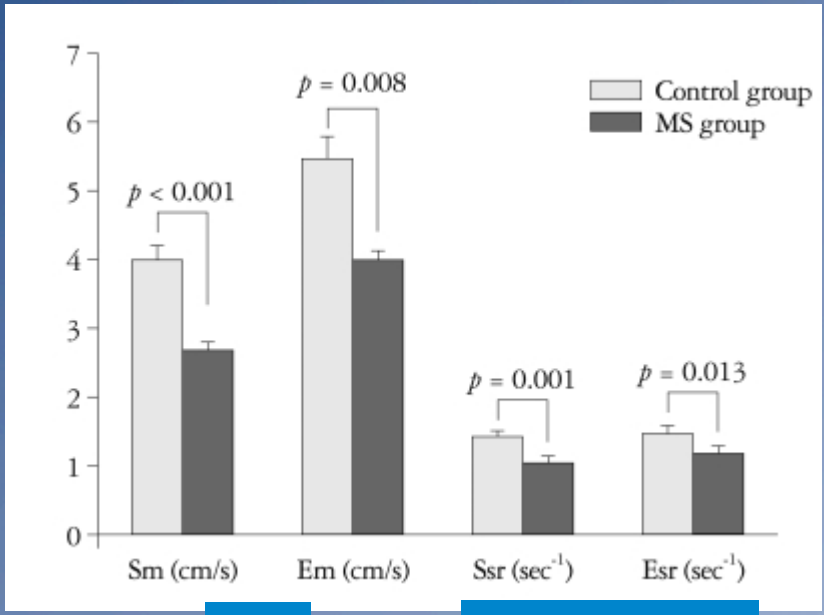
	Diastolic Heart Failure (EF>50%)
Symptoms	
Dyspnea on exertion	85
Paroxysmal nocturnal dyspnea	55
Orthopnea	60
Physical examination	
Jugular venous distension	35
Rales	72
Displaced apical impulse	50
S_3	45
S_4	45
Hepatomegaly	15
Edema	30
Chest radiograph	
Cardiomegaly	90
Pulmonary venous hypertension	75

Data are presented as percent of patients in each group with the listed symptom or sign of heart failure.[25,26] There were no statistically significant differences between patients with an EF >50% vs <50%.

Classification	EF (%)
I. Heart failure with reduced ejection fraction (HF*r*EF)	≤40
II. Heart failure with preserved ejection fraction (HF*p*EF)	≥50
a. HF*p*EF, borderline	41 to 49
b. HF*p*EF, improved	>40

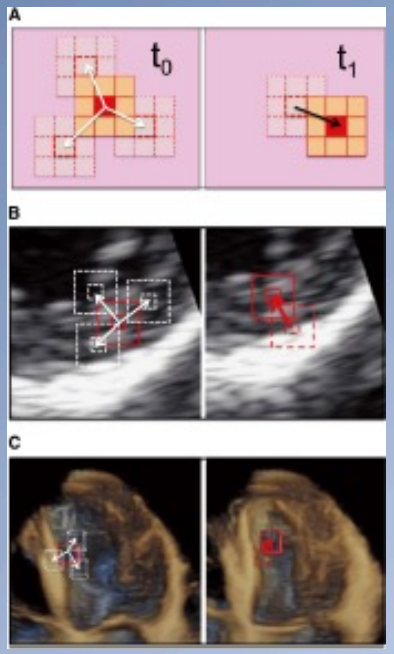
NEW TECHNOLOGIES
EARLY EVALUATION OF SYSTOLIC FUNCTION
SYSTOLIC DYSFUNCTION WITH PRESERVED EF

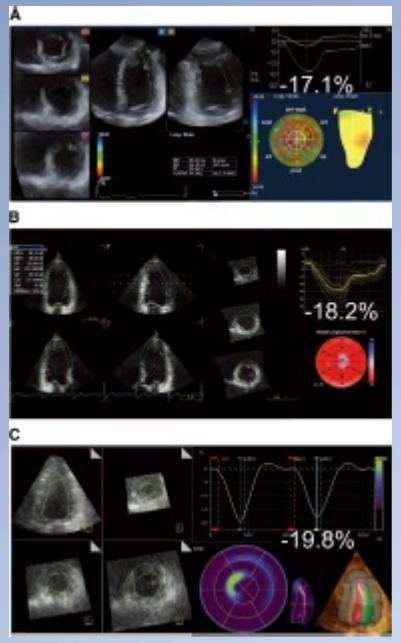
METABOLIC SYNDROME
NORMAL EJECTION FRACTION



DTI

STRAIN RATE



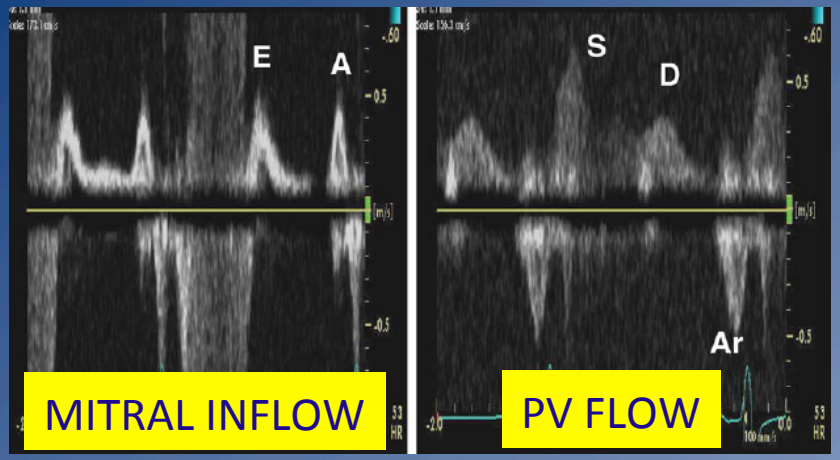


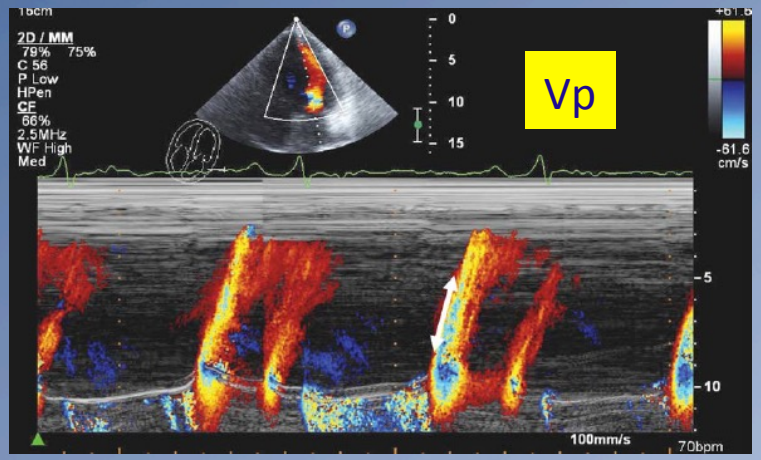
SUBCLINICAL MYOCADIAL DYSFUNCTION

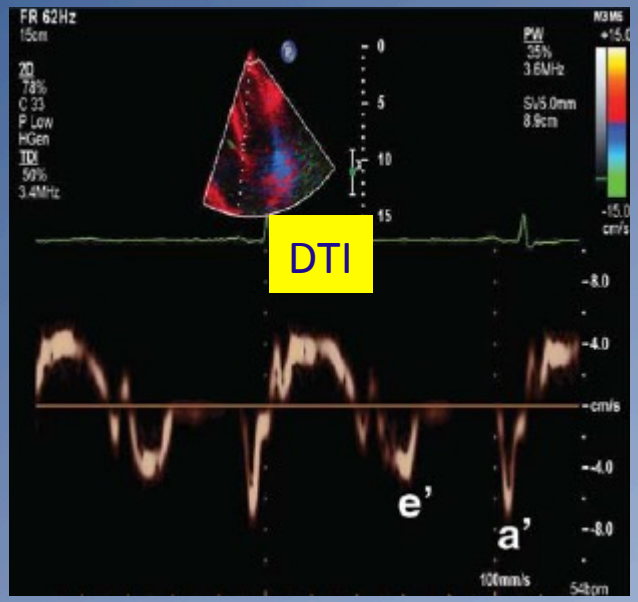
SPECKLE TRACKING ECHOCARDIOGRAPHY

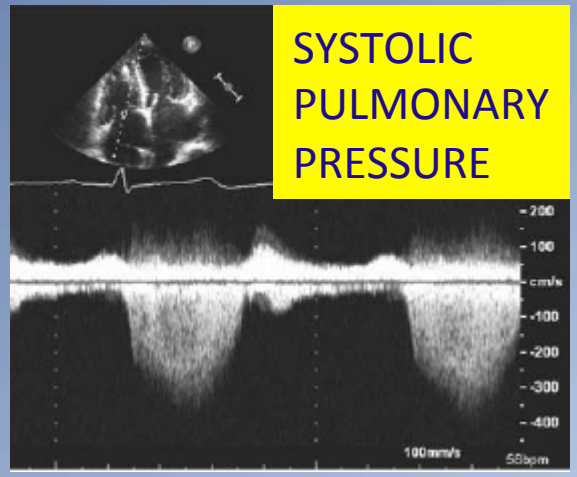
DIASTOLIC DYSFUNCTION

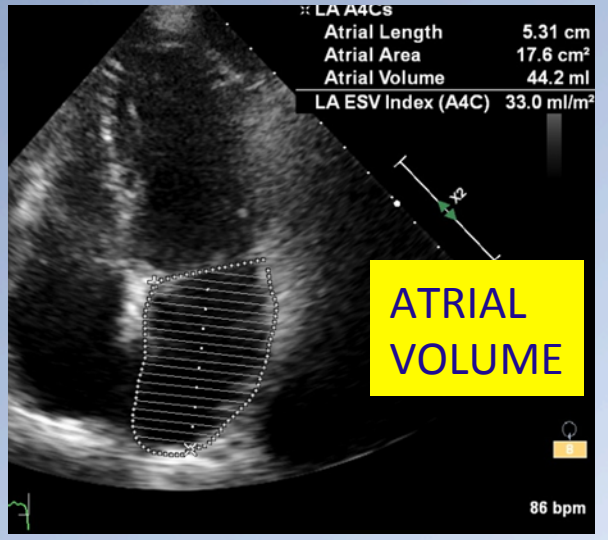
ULTRASOUND CLASSIFICATION TOOLS







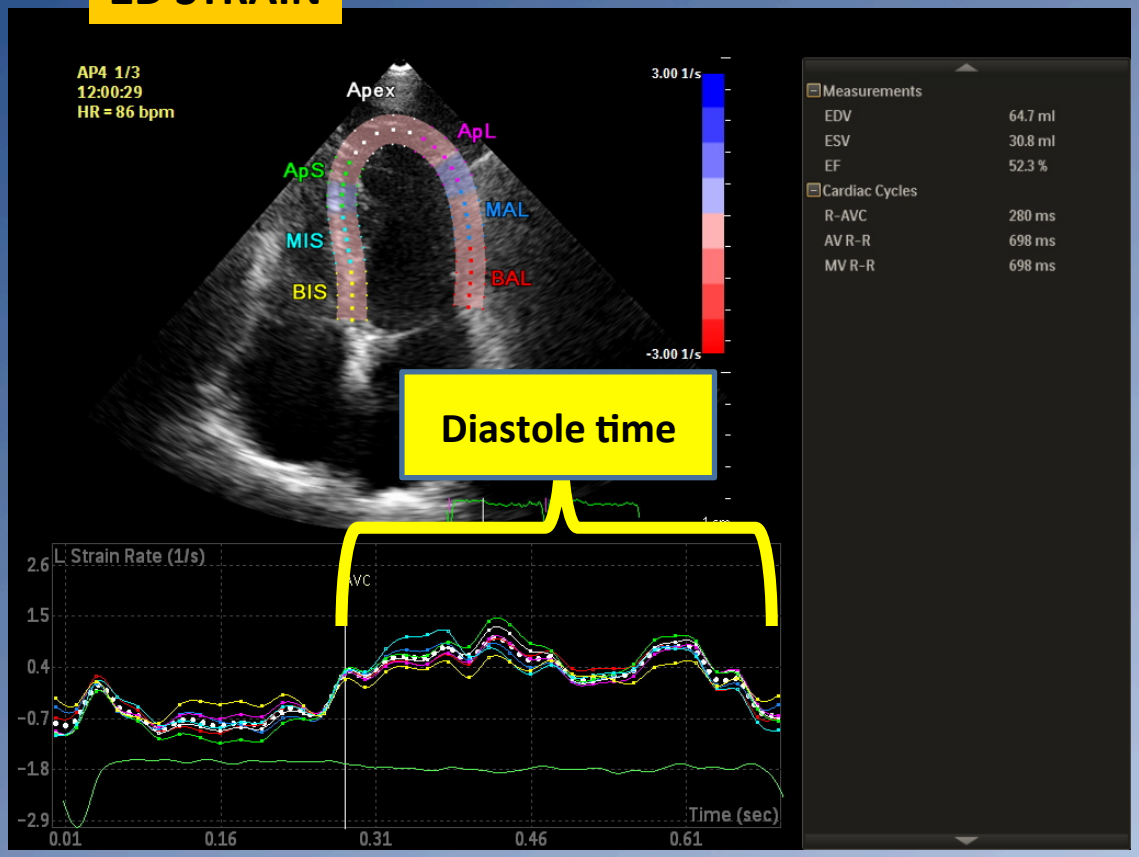




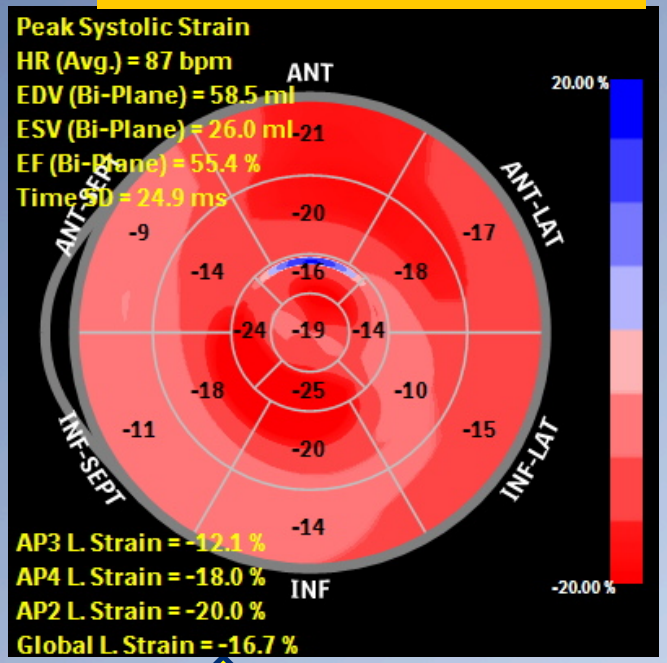
DIASTOLIC DYSFUNCTION

Differents modalities by Speckle Tracking approch

2D STRAIN



GLOBAL LONG. STRAIN



GLS for LV function

SPECKLE for DIASTOLIC ANALYSIS
Diastolic Function index

QLAB-CMQ SW derived parameters of left ventricular function provide a simple and reliable method for the evaluation of the diastolic dysfunction

Speckle Parameters obtain from dV/dt

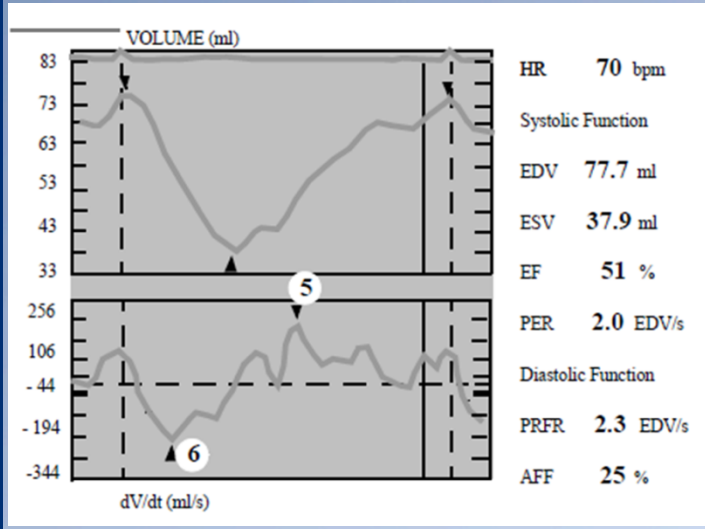
The time rate of volume change, also referred to as the volume "slope," the "derivative of volume versus time," and the "dV/dt" waveform, shows changes in the rate at which the blood volume is increasing or decreasing. The units are displayed in ml/sec for volume.

PHILIP CMQ uses the dV/dt values to calculate :

5. Peak Rapid Filling Rate (PRFR) – The highest positive value in the rapid filling phase on dV/dt waveform. This number expresses the fastest rate (ml/sec) at which ventricular filling occurs between ESV and the end of slow filling marker.

6. Peak Ejection Rate (PER) – The lowest negative value on the dV/dt waveform. This number expresses the fastest rate (ml/sec) at which ventricular ejection occurs.

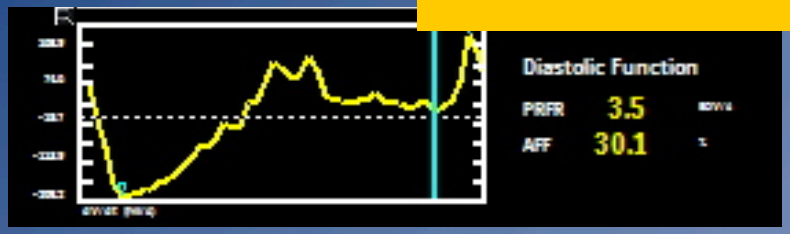
To more accurately assess patients with and without dilated left ventricles, the PRFR and PER rates are normalized by dividing them by the end diastolic volume.

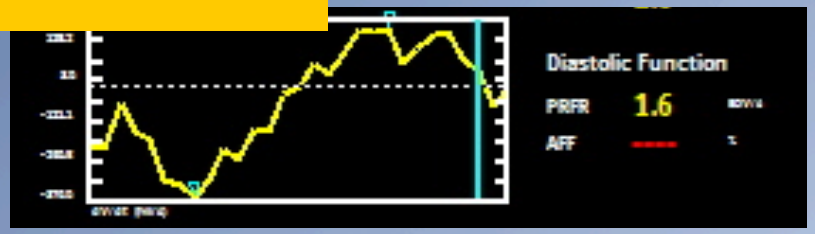


SPECKLE for DIASTOLIC ANALYSIS
Diastolic Function index

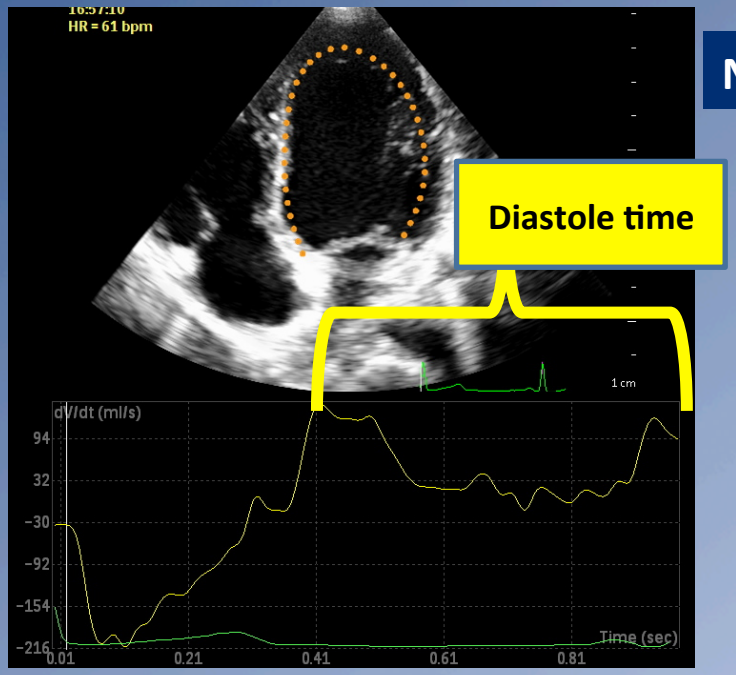
QLAB-CMQ SW derived parameters of left ventricular function provide a simple and reliable method for the evaluation of the diastolic dysfunction

Peak Rapid Filling Rate (PRFR) ⇨ **COMPLIANCE**

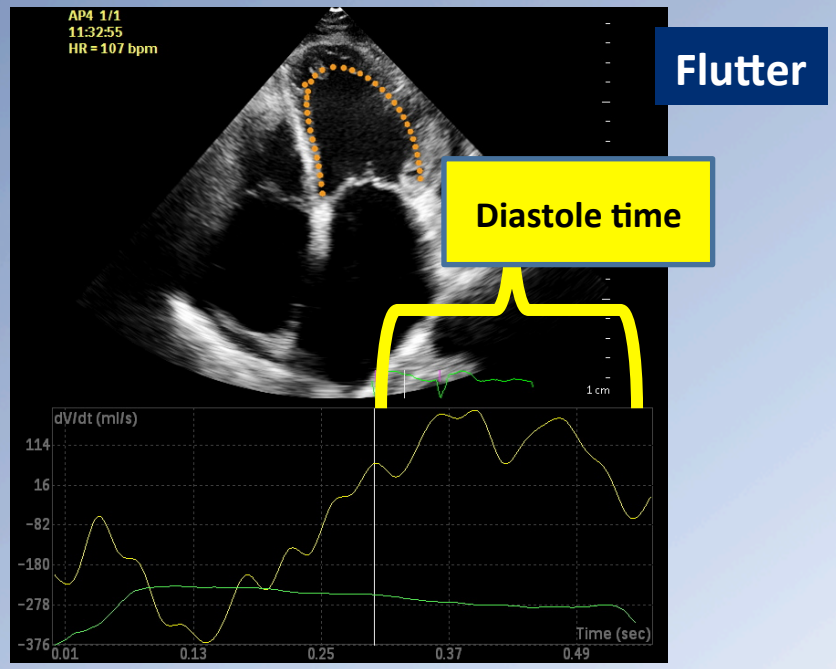




Normal



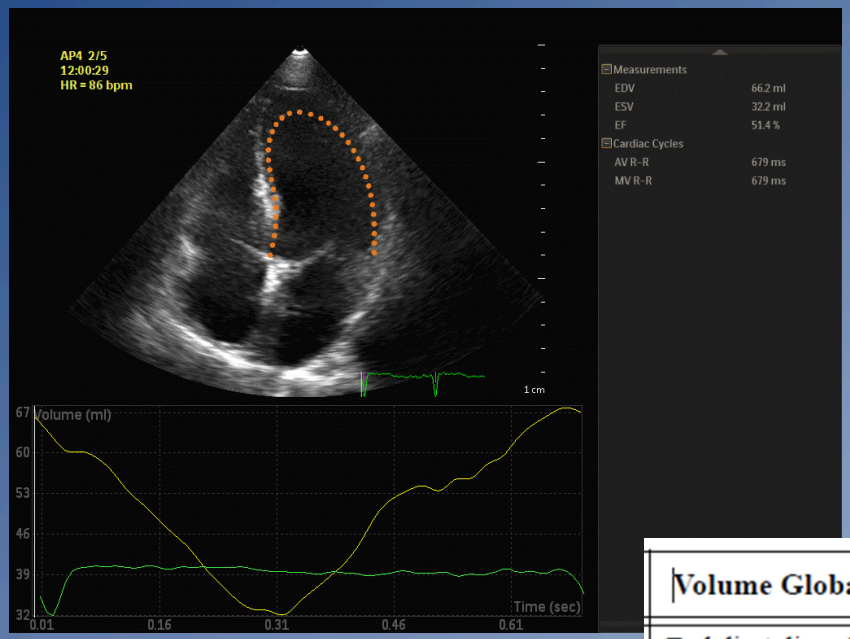
Flutter

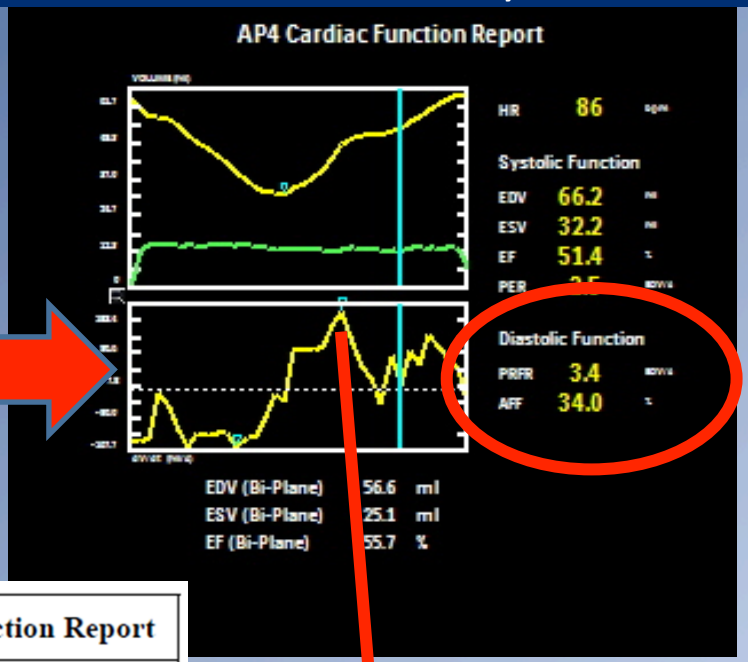


SPECKLE for DIASTOLIC ANALYSIS

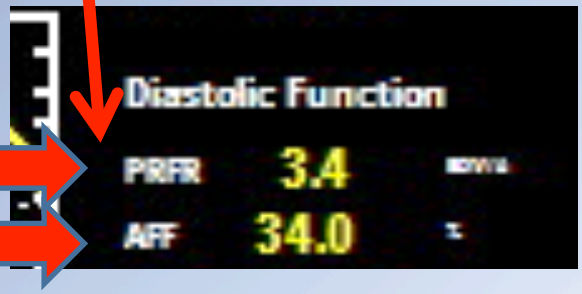
Diastolic Function index

QLAB-CMQ SW derived parameters of left ventricular function provide a simple and reliable method for the evaluation of the diastolic dysfunction





Volume Global Function Report
End diastolic volume (EDV) End systolic volume (ESV)
Heart Rate (HR)
Ejection Fraction (EF)
Peak ejection rate (PER)
Peak rapid filling rate (PRFR)
Atrial Filling fraction (AFF)

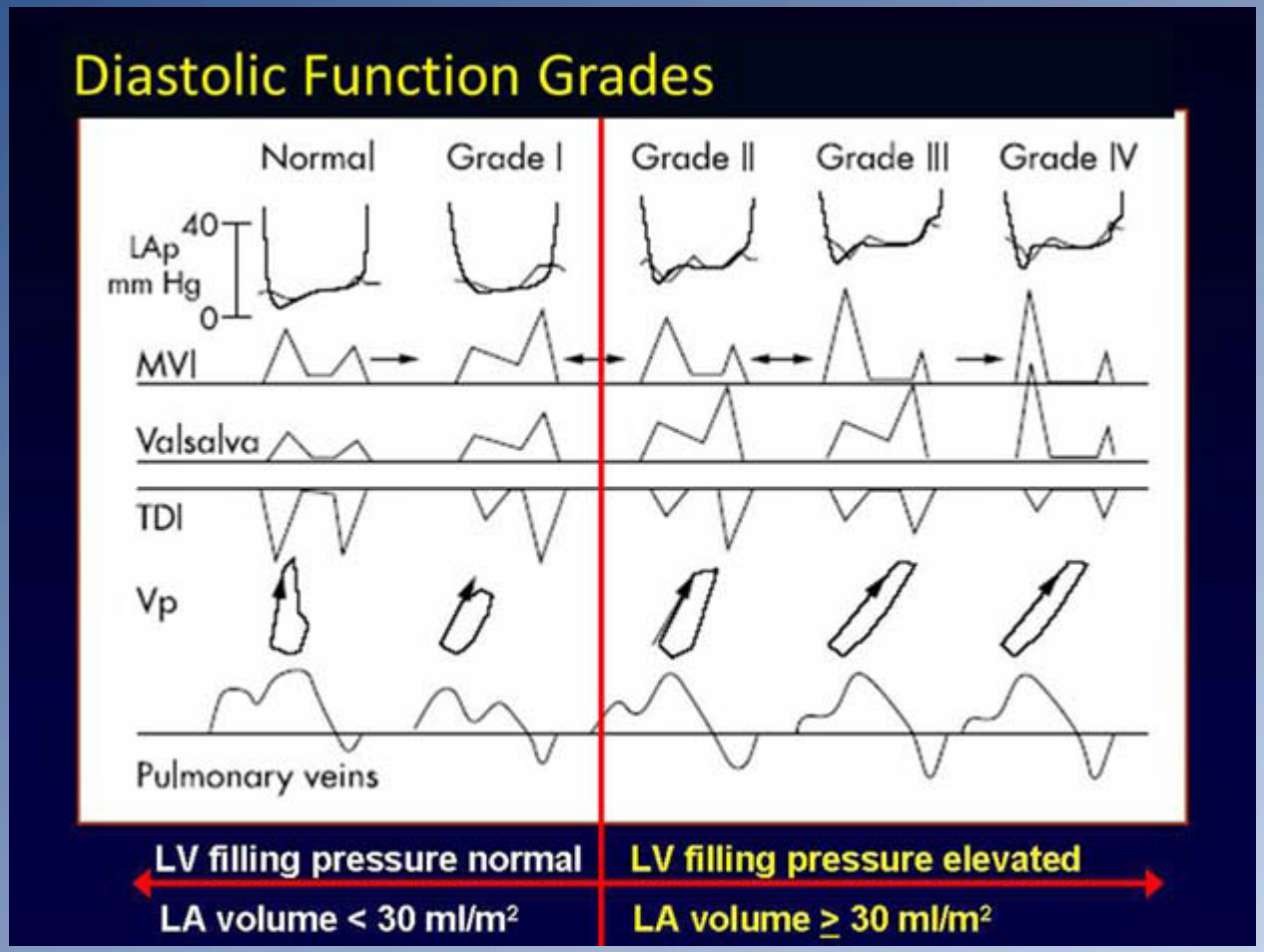


DIASTOLIC DYSFUNCTION
ULTRASOUND CLASSIFICATION

Table 1. Grades of Diastolic Dysfunction as Categorized by Echocardiography

	Normal	Grade I Abnormal relaxation	Grade II Pseudonormal	Grade III Restrictive (reversible)	Grade IV Restrictive (fixed)
NYHA		I–II	II–III	III–IV	IV
Mitral inflow (PW)					
Mitral inflow on valsalva					
Mitral anular motion (TDI)					
Vp (Color M-mode)					
Pulmonary venous flow (PW-Doppler)					
LV relaxation (tau)					
LV compliance					
LA pressure					
LV blood filling					
LV volume index					

DIASTOLIC DYSFUNCTION
ULTRASOUND CLASSIFICATION



NYHA I-II

NYHA ≥ II

Practical approach to Grade Diastolic Disfunction

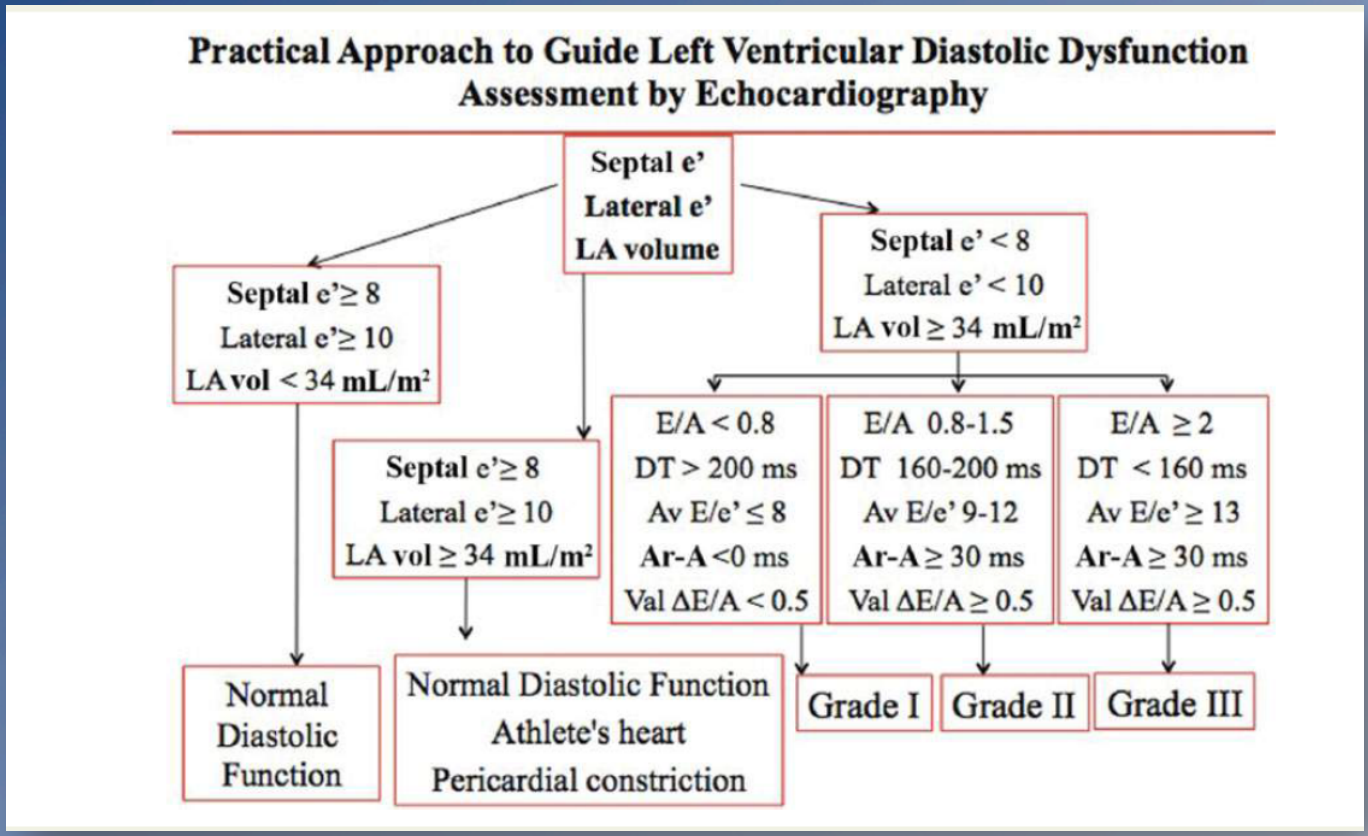
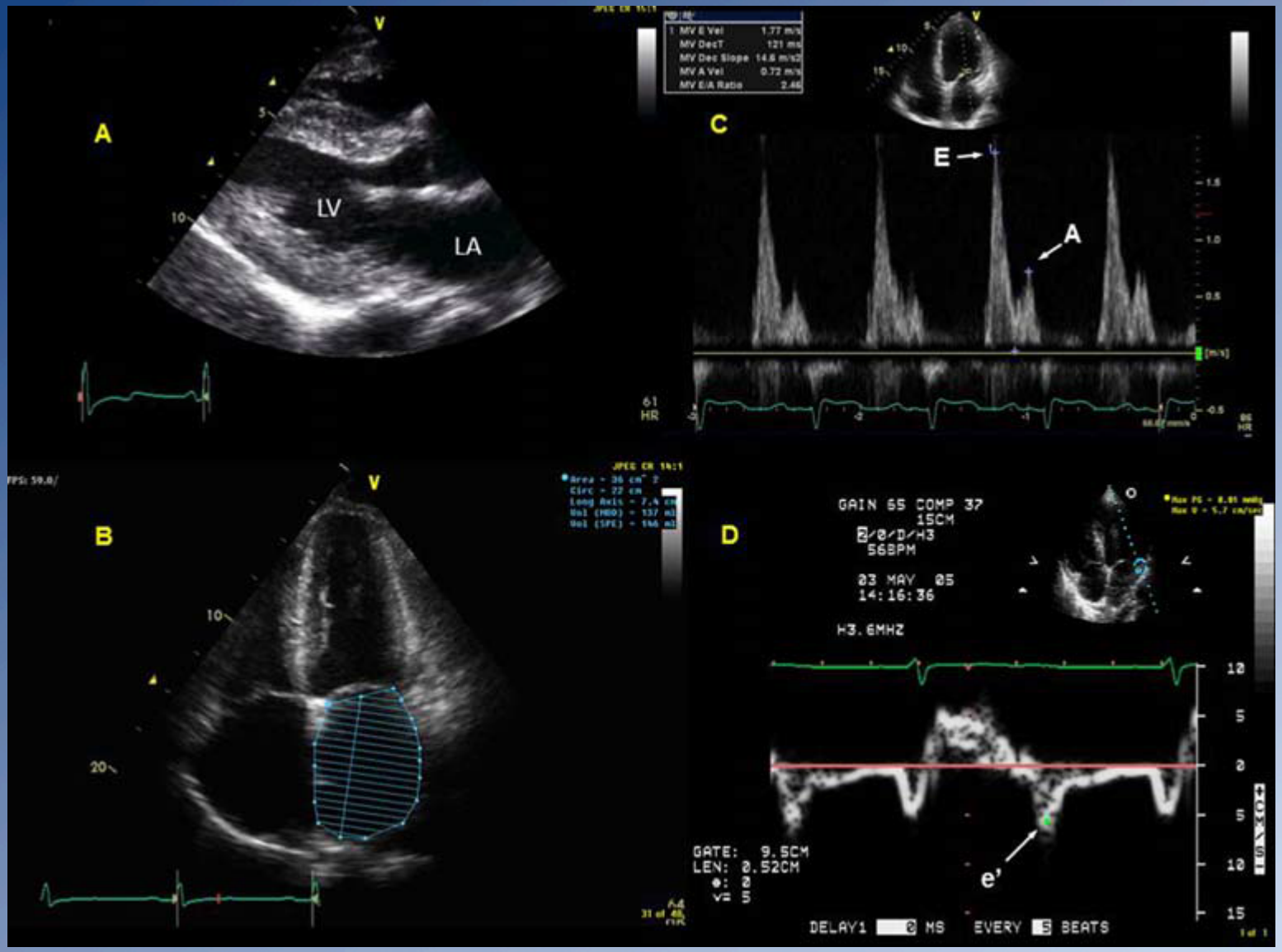


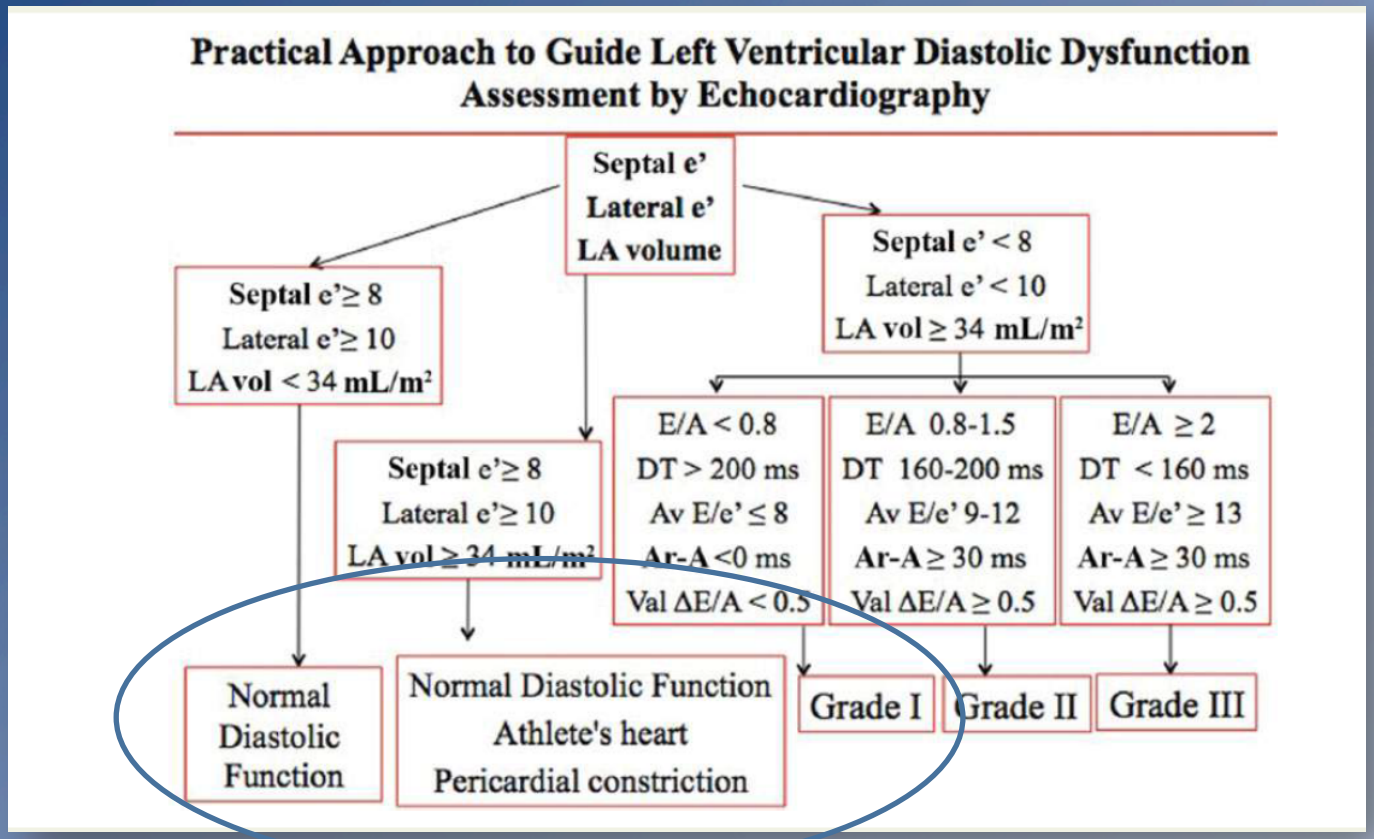
Figure 8: Practical approach to grade diastolic dysfunction by echocardiography. Adapted from the EACVI/ASE recommendations for the evaluation of left ventricular diastolic function by echocardiography.53 LA: left atrial; vol: volume; DT: E wave velocity deceleration time; Av: average, Val: Valsalva manoeuvre; E: early mitral inflow velocity; e′: early diastolic mitral annular velocity; A: duration of the pulmonary flow reversal; Ar: pulmonary venous atrial flow reversal.

DIASTOLIC HEART FAILURE



HYPERTENSIVE HEART DISEASE

Practical approach to Grade Diastolic Disfunction



ASYMPTOMATIC AT REST - EXERTIONAL DYSPNEA

DIASTOLIC STRESS ECHO

Table 2. Echo-Doppler findings indicating a positive diastolic stress echocardiogram

1. Increase (from rest) in the E velocity with exercise (to ≥ 80 m/s)
2. Increase in the E/A ratio with exercise (to ≥ 1)
3. Increase in E/e′ (to ≥ 12)
4. Increase in peak TR velocity (to ≥ 3.5 m/s). *This finding must accompany one of the 3 above, to distinguish from exercise induced isolated pulmonary hypertension.*

A = late transmitral diastolic velocity; E = early transmitral diastolic velocity; TR = tricuspid regurgitation.

HIGH-RISK PATIENTS

EXCERCISE INDUCED DIASTOLIC DYSFUNCION → ELDERLY
HYPERTENSIVE
DIABETIC
FEMALE

IDEAL PATIENT → EXERTIONAL DYSPNEA
GRADE I DIASTOLIC DYSFUNCTION

DIASTOLIC FUNTION
ECHO ASSESSMENT AND PARAMETERS

Table 3. Strengths and limitations of individual echo-Doppler variables for diastolic assessment

Variable	Strength	Limitations
Left ventricular (LV) hypertrophy		
LV ejection fraction		
Left atrial volume		
Mitral inflow (E, A, E/A, DT)		
Tissue Doppler early diastolic relaxation (e′ and E/e′)		
Flow Propagation Velocity (Vp)		
Pulmonary venous Doppler		
Pulmonary artery pressure (by peak TR velocity)		
LV speckle strain		

A = late transmitral diastolic velocity; Ar = pulmonary venous atrial reversal; DT = mitral deceleration time; E = early transmitral diastolic velocity; LA = left atrial; TR = tricuspid regurgitation.

«MINIMAL» MULTIPARAMETRIC APPROACH

CONCLUSION

RIGHT TOOL IN THE RIGHT HANDS
FOR THE RIGHT PATIENT

NAPOLI
A WARM WELCOME AND GOOD-BY!

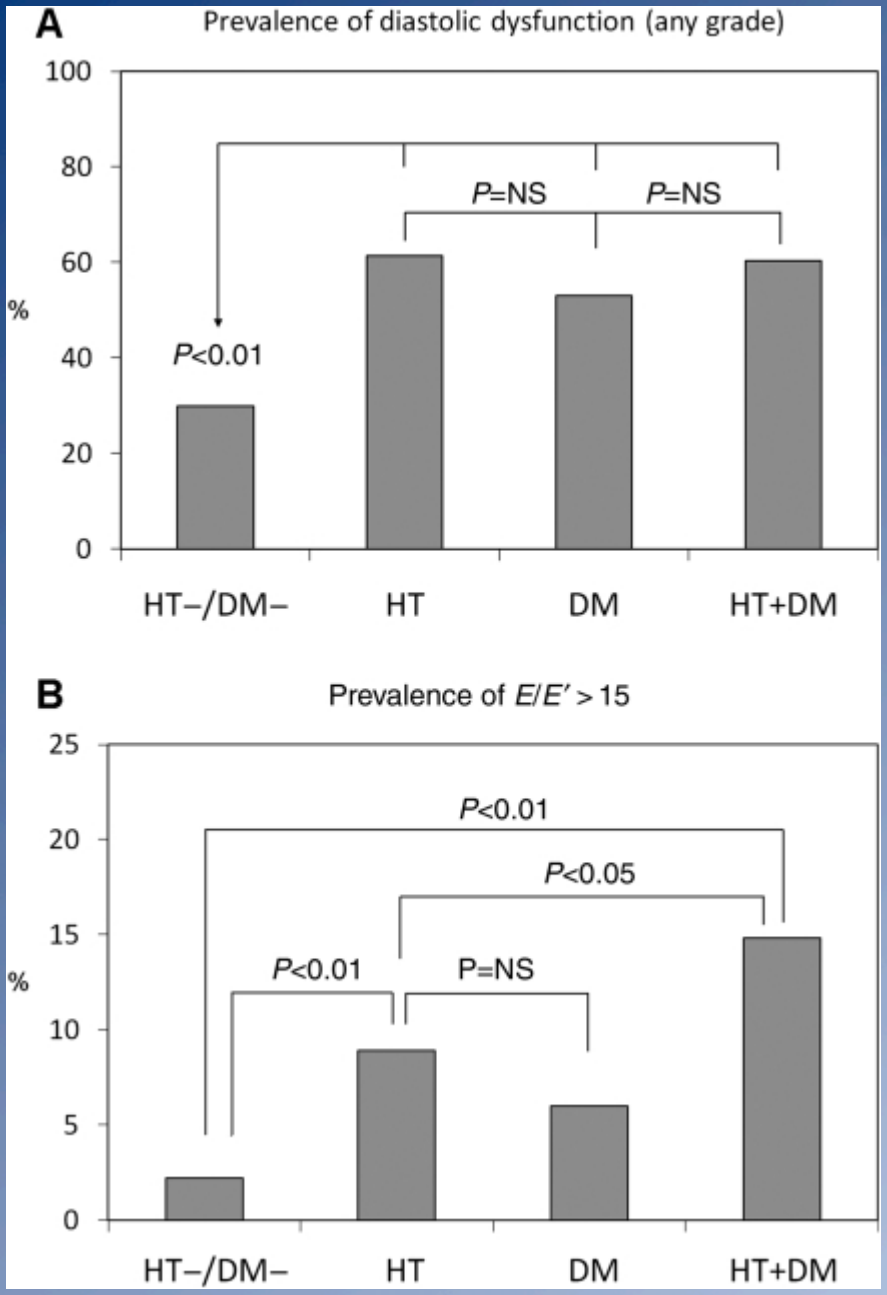
VESUVIO - SUNRISE

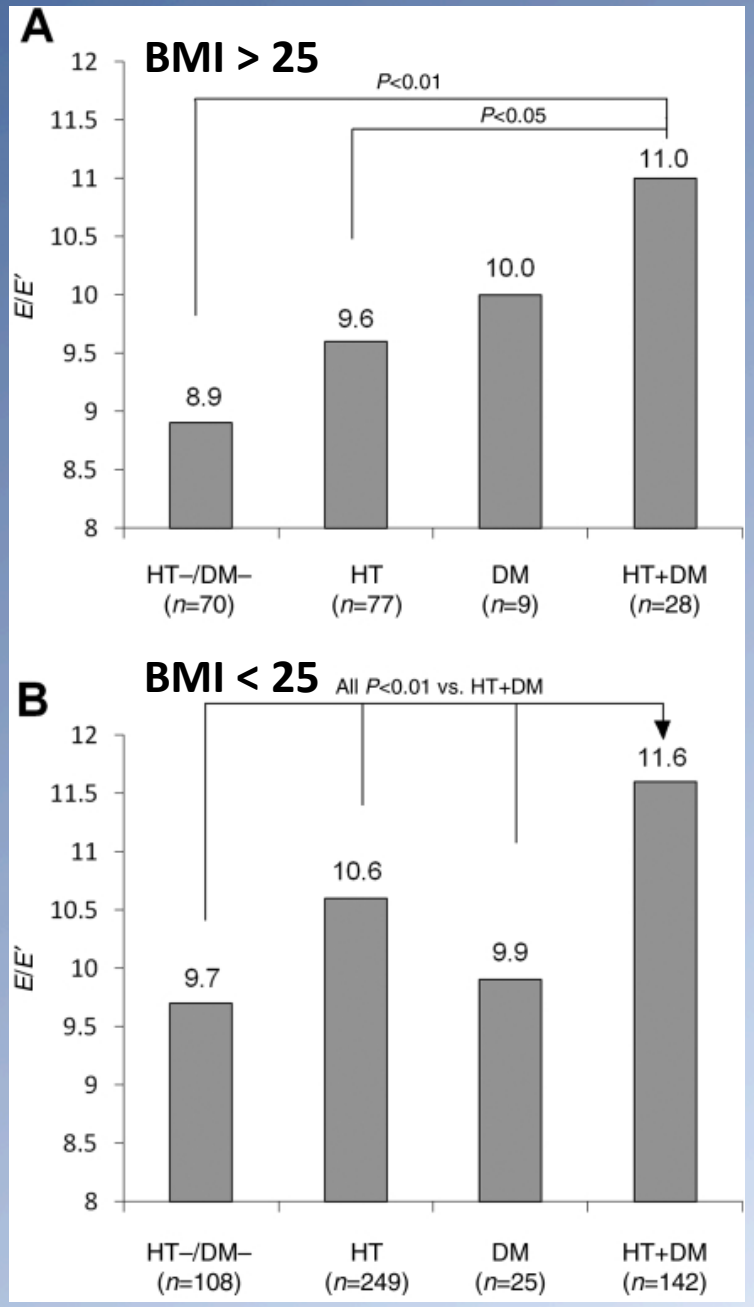
NISIDA - SUNSET

DIASTOLIC DYSFUNCTION

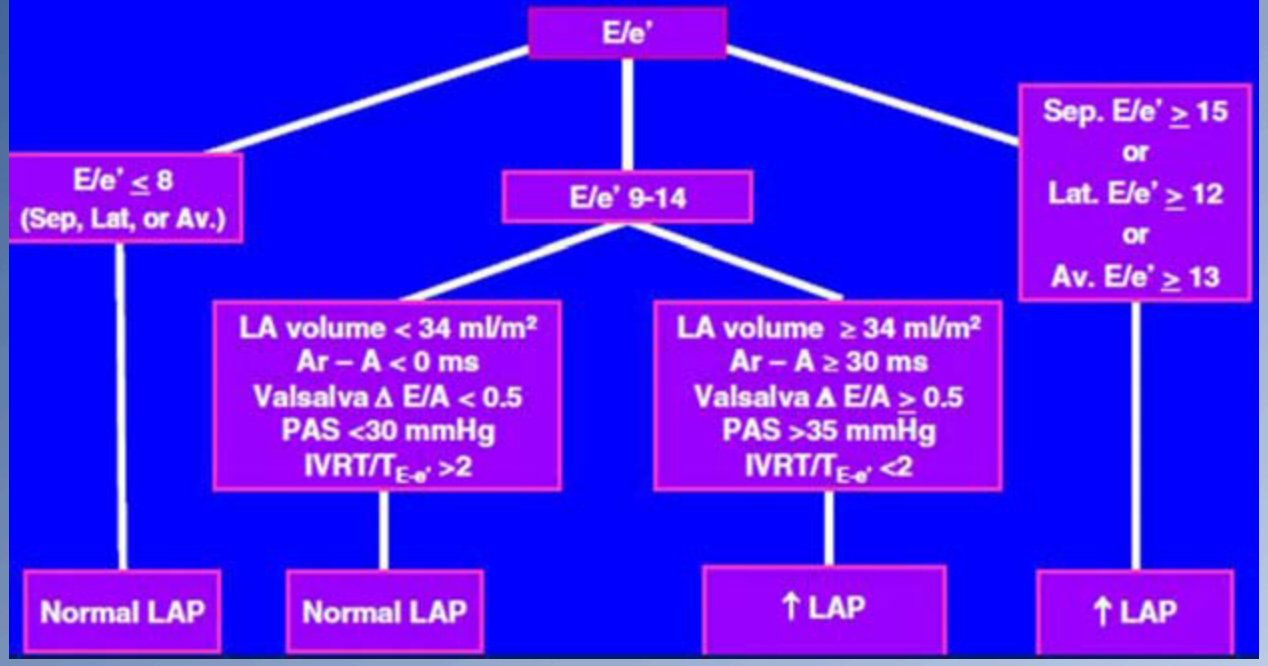
Differents modalities by Speckle Tracking approch

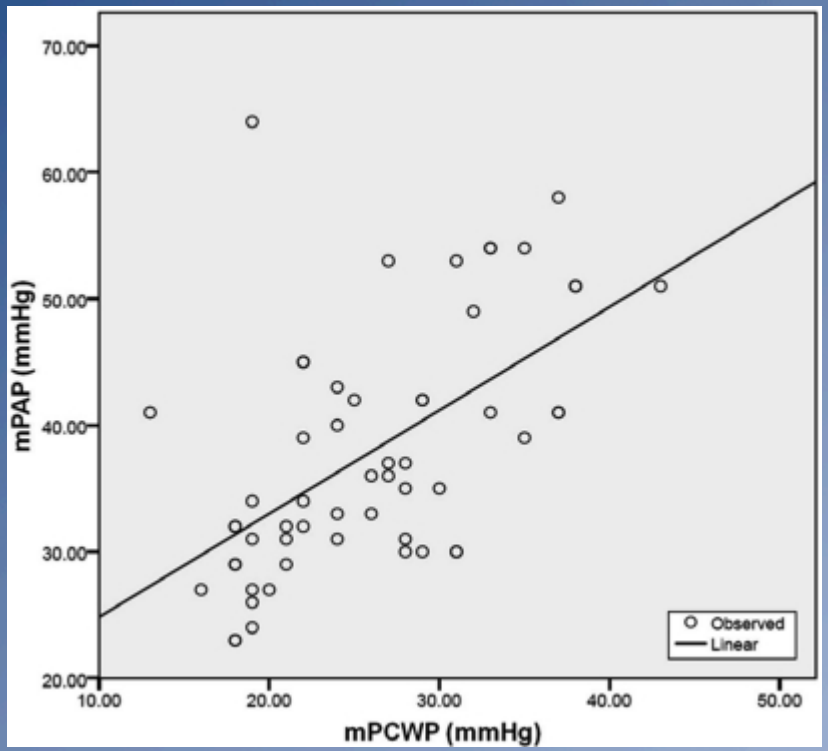
- Speckle tracking could be dedicated for diastolic function too and becomes complementary to Doppler assessment because they measure different physiologic phenomena and it is important to use both techniques, in the same time, so that to define better the clinical diastolic performance
- 3D offer much more robust data then 2D and not only for ventricular function…


A
Prevalence of diastolic dysfunction (any grade)
100
80
60
40
20
0
%
P=NS
P=NS
P<0.01
HT−/DM−
HT
DM
HT+DM
B
Prevalence of E/E' > 15
25
20
15
10
5
0
%
P<0.01
P<0.05
P<0.01
P=NS
HT−/DM−
HT
DM
HT+DM

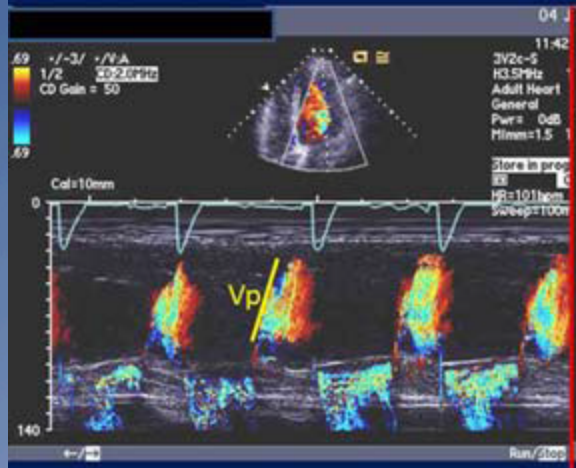

A
BMI > 25
P<0.01
P<0.05
12
11.5
11
10.5
10
9.5
9
8.5
8
E/E'
8.9
9.6
10.0
11.0
HT−/DM−
(n=70)
HT
(n=77)
DM
(n=9)
HT+DM
(n=28)
B
BMI < 25
All P<0.01 vs. HT+DM
12
11.5
11
10.5
10
9.5
9
8.5
8
E/E'
9.7
10.6
9.9
11.6
HT−/DM−
(n=108)
HT
(n=249)
DM
(n=25)
HT+DM
(n=142)

Estimation of Filling Pressures in Patients with Normal EF

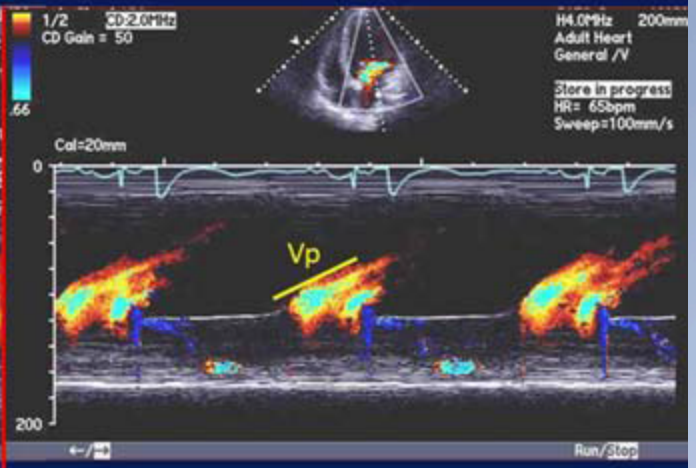



70.00
60.00
50.00
40.00
30.00
20.00
mPAP (mmHg)
10.00
20.00
30.00
40.00
50.00
mPCWP (mmHg)
Observed
Linear

Diastolic Assessment: Transmitral Flow Propagation Velocity (Vp)



Normal ventricular diastolic function with vertical (rapid) Vp slope



Severe diastolic dysfunction with nearly flat (delayed) Vp slope

Tricuspid Regurgitation Velocity for Pulmonary Artery Systolic Pressure Estimation in Diastolic Dysfunction