ΕΚΤΙΜΗΣΗ ΔΥΣΥΓΧΡΟΝΙΣΜΟΥ ΤΟ 2016

Ευαγγελία Χριστοφοράτου

Καρδιολόγος

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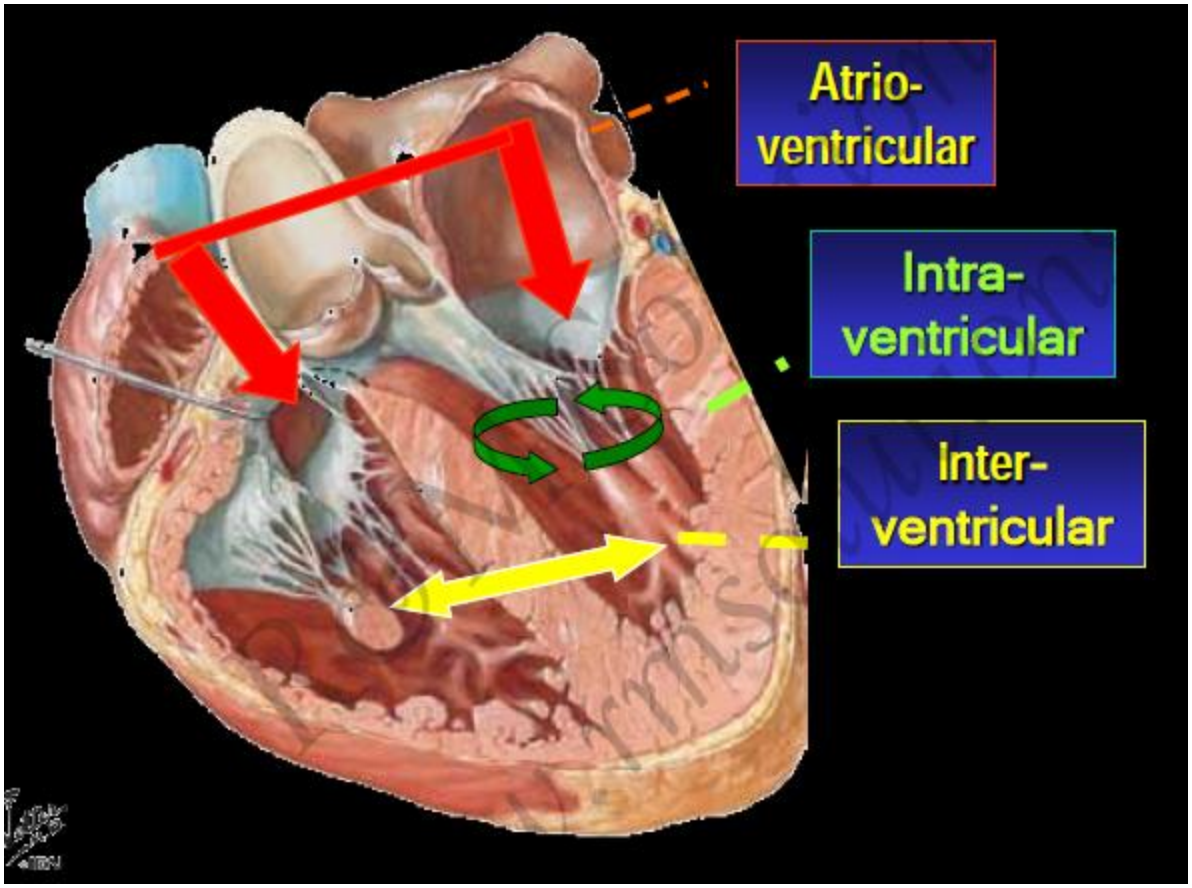
Definitions of Dyssynchrony

Electrical Vs Mechanical Dyssynchrony

Electrical Dyssynchrony refers to a prolonged conduction time in the ventricles resulting in a prolonged QRS duration

Mechanical Dyssynchrony→ is the mechanical discoordination , usually associated with simultaneous contraction and stretch in different regions of the LV as well as delays in the time to peak contraction from one segment to another


Atrio-
ventricular
Intra-
ventricular
Inter-
ventricular

AV dyssynchrony

There is a delay between atrial and ventricular contraction,

shortened ventricular filling time &

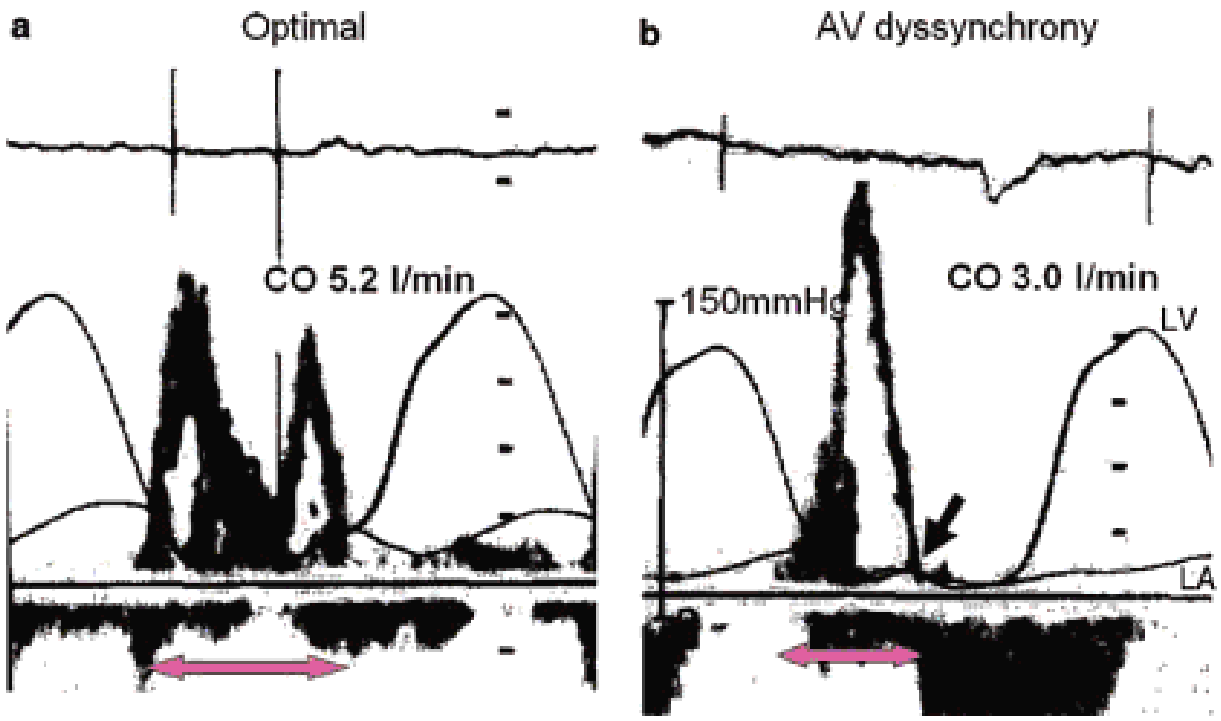
superimposition of atrial contraction on early passive filling,

→both of which reduce LV filling.

atrio-ventricular dyssynchrony : The ratio between diastolic filling time and duration of a complete cardiac cycle (A LV filling time of < 40% cardiac cycle is indicative of A-V dys.)

It can also be associated with late diastolic (presystolic) mitral regurgitation (MR).

Demonstration of AV dyssynchrony



Demonstration of AV dyssynchrony

*Inter*ventricular dyssynchrony

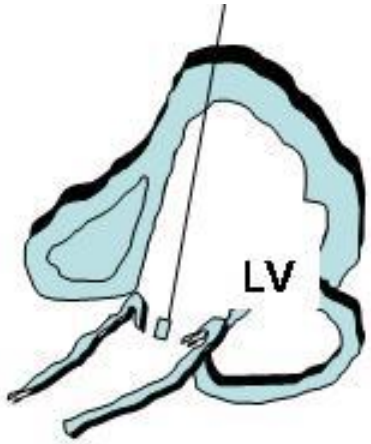
- Delay between RV and LV activation.

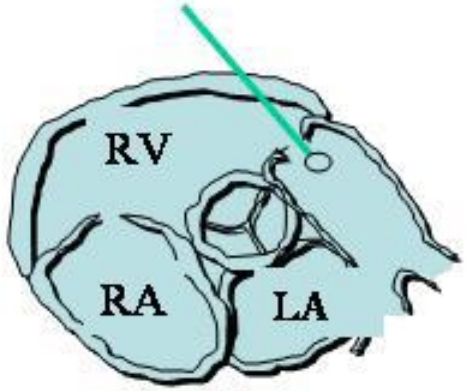
- Occurs mainly with left bundle branch block, in which RV contraction will precede LV contraction, leading to abnormal (partially paradoxical) septal motion, discoordinated LV contraction, and a decreased LV ejection fraction.

- With LBBB induced Dyssynchrony,
  - The LV septum shortens upto 10% prior to ejection, has minimal subsequent systolic shortening and undergoes late systolic strech

Interventricular Dyssynchrony

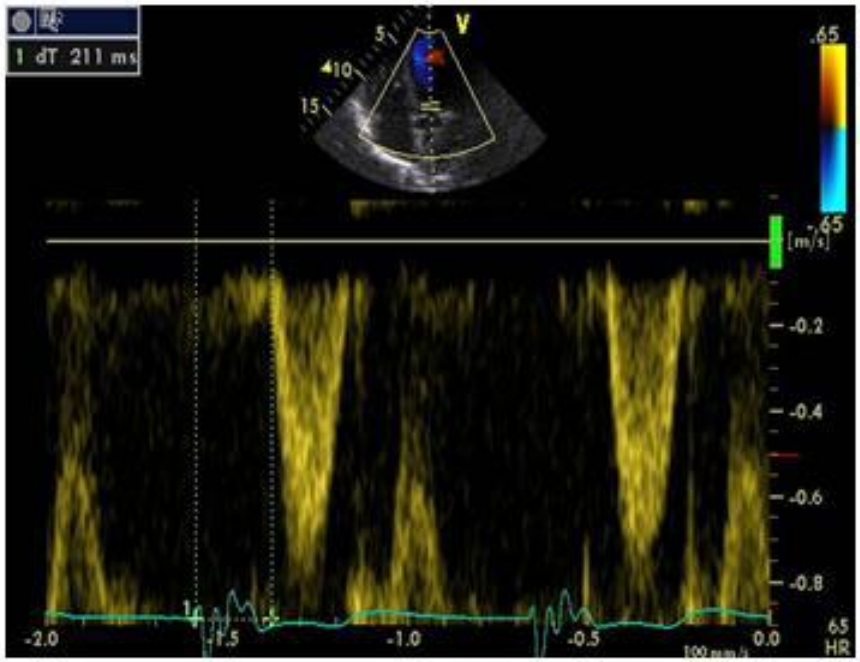
- ***Inter-ventricular mechanical delay (IVMD) is measured***
- PW aortic {LVOT - (apical 5-chamber view)} and and pulmonary (RV outflow tract-parasternal short-axis view) **flow velocities** are used.
- Then calculate the difference in time between ECG-derived **Q wave onset and the onset of LV outflow** and the time between the **onset of Q and the onset of RV outflow**

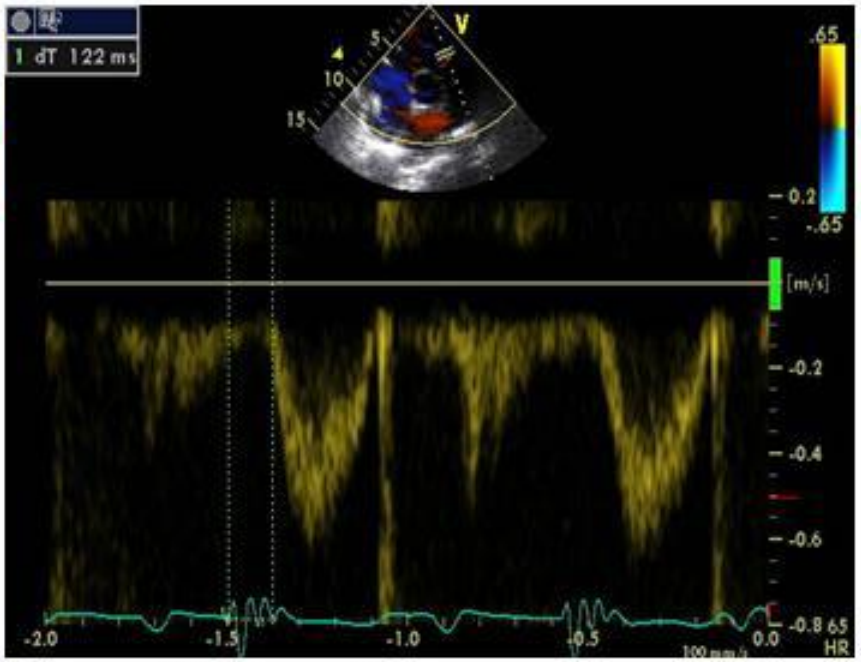




Aortic time to onset

Pulmonary time to onset





IVMD = 211 ms – 122 = 89 ms

- These values represent LV and RV pre-ejection period (PEP)

- IVMD values of > 40 ms and values of LV PEP of > 140 ms are considered pathological

Limitations

- Presence of pulmonary arterial hypertension and/or RV systolic dysfunction, which can prolong RV PEP
- Concomitantly impaired increase of LV pressure in very severe CHF.

Pulse tissue Doppler for IVMD

- The time from QRS onset to the peak myocardial systolic velocities (Sm) of the RV free wall (tricuspid annulus) versus the same time of LV lateral mitral annulus (apical 4-chamber view)

*Intra*ventricular dyssynchrony

- Here the normal ventricular activation sequence is disrupted, resulting in discoordinated contraction of the LV segments.

- The result is that those LV wall segments, which contract early, **do not contribute to the ejection of blood** from the left ventricle, and segments that contract late do so at a **higher wall stress**, causing the **early contracting segments to stretch**.

- Additionally, MR worsens in part because of LV remodeling, and presystolic regurgitation that may occur with ventricular dyssynchrony and delayed contraction of papillary muscle root attachments.

Intra-ventricular mechanical dyssynchrony

Intra-ventricular dyssynchrony is characterized by either premature or late contraction of LV wall segments due to delayed electrical Conduction

Methods:

- M-mode,
- pulsed Tissue Doppler,
- Colour Tissue Velocity Imaging
- 3-D echocardiography

M Mode

Septal-to-posterior wall motion delay

- It is the difference in timing of septal and posterior wall contraction

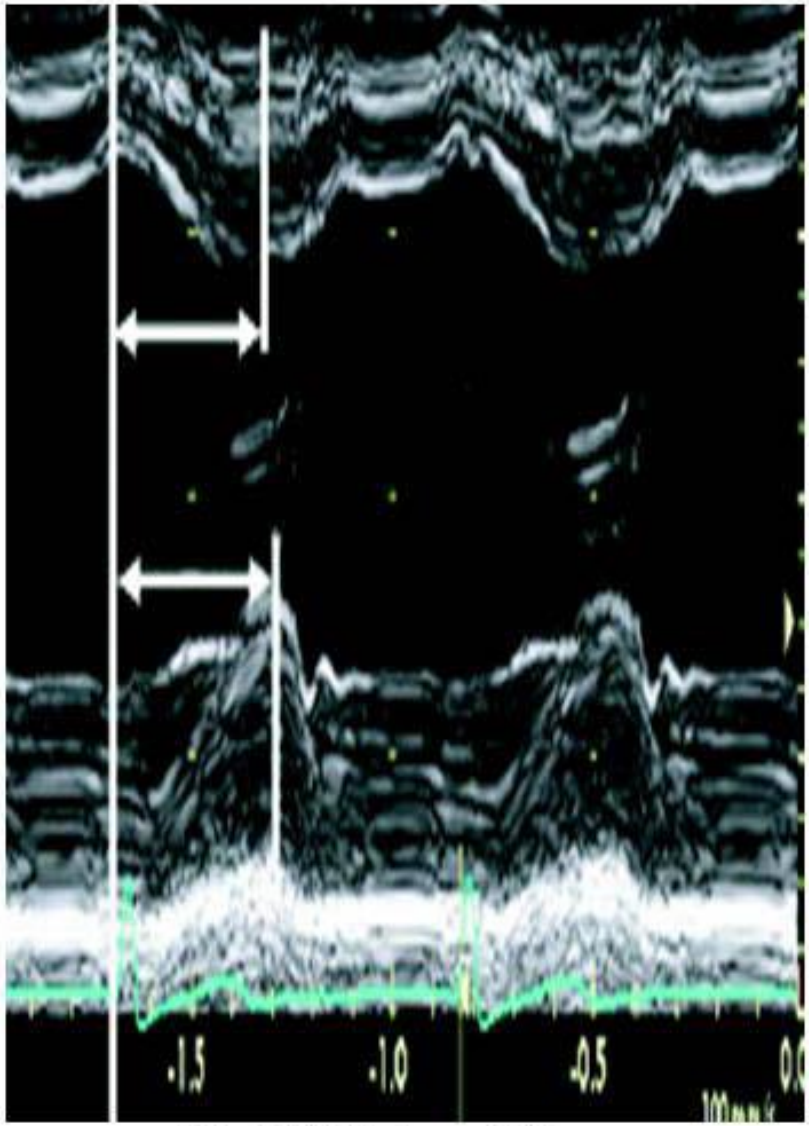
Place the M-mode cursor perpendicular to the septum

and posterior wall at the base of the left ventricle, in parasternal

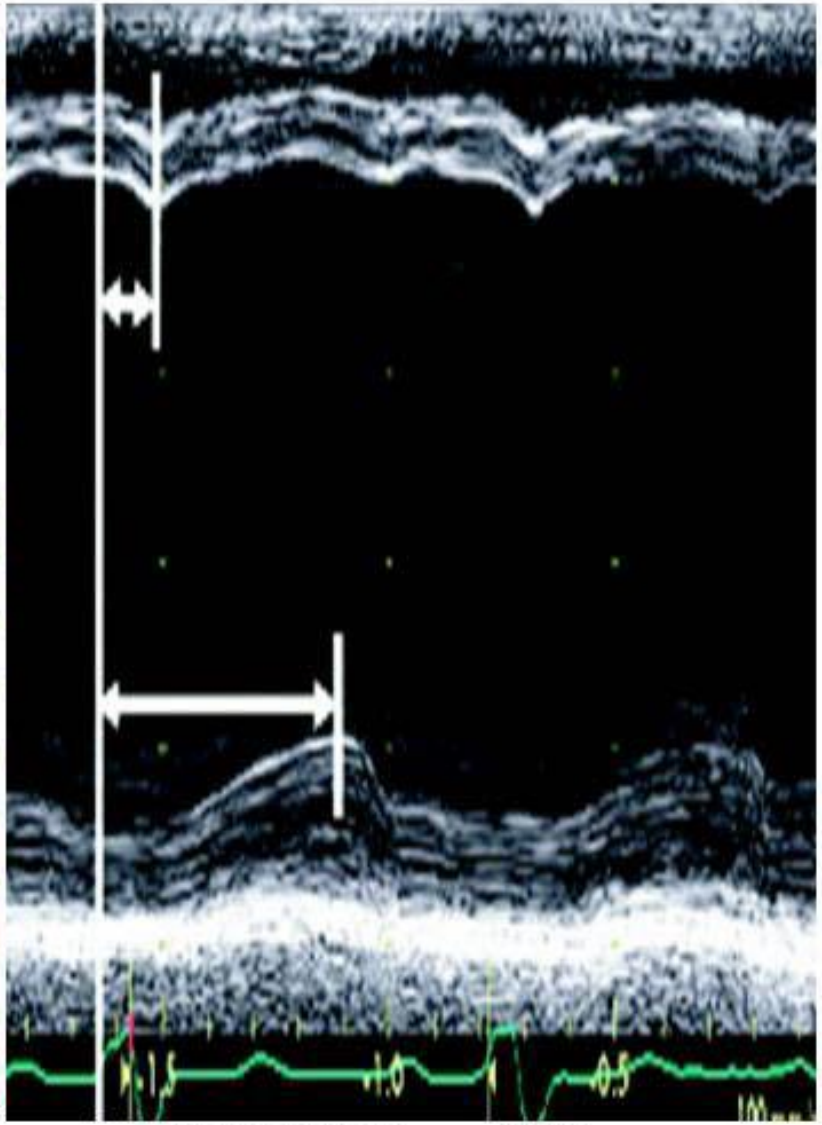
short- axis (or long-axis) view:

SPWMD is the difference between the time from the onset of ECG-derived Q wave to the initial peak posterior displacement of the septum, and the time from the onset of QRS to the peak systolic displacement of posterior wall

Sweep speed -100mm/s



SPWMD = 30 ms



SPWMD = 400 ms

Pitzalis et al , in an early study

SPWMD> 130 ms was considered pathological and also SPWMD predicted inverse LV remodeling and long-term clinical improvement after CRT, with 100% sensitivity, 63% specificity and 85% accuracy

Limitations

Impossibile to measure SPWMD in patients with a poor acoustic window, previous septal or posterior wall myocardial infarction, or abnormal septal motion secondary to RV pressure or volume overload.

Hence in later studies….

- Marcus et al

  - underlined the low feasibility of SPWMD (measured in parasternal long axis view), had a poor sensitivity (24%) and specificity (66%) in predicting the response to CRT of 79 heart failure patients

Lateral wall post-systolic displacement

- QRS onset to maximal systolic displacement of the basal LV lateral wall (assessed by M-mode in the apical 4-chamber view)

(Minus)

QRS onset to the beginning of transmitral E velocity (assessed by pulsed Doppler of mitral inflow)

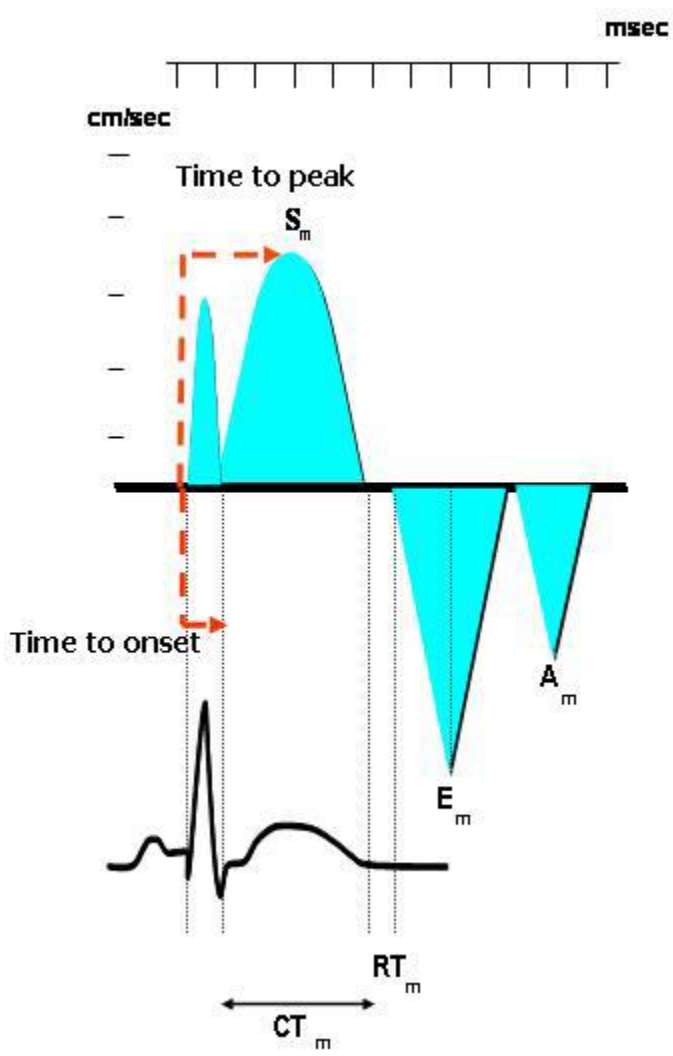
A positive LWPSD, i.e. a longer interval to maximal inward displacement of LV lateral wall than the interval to opening of the mitral valve, identifies a severe **post-systolic contraction**

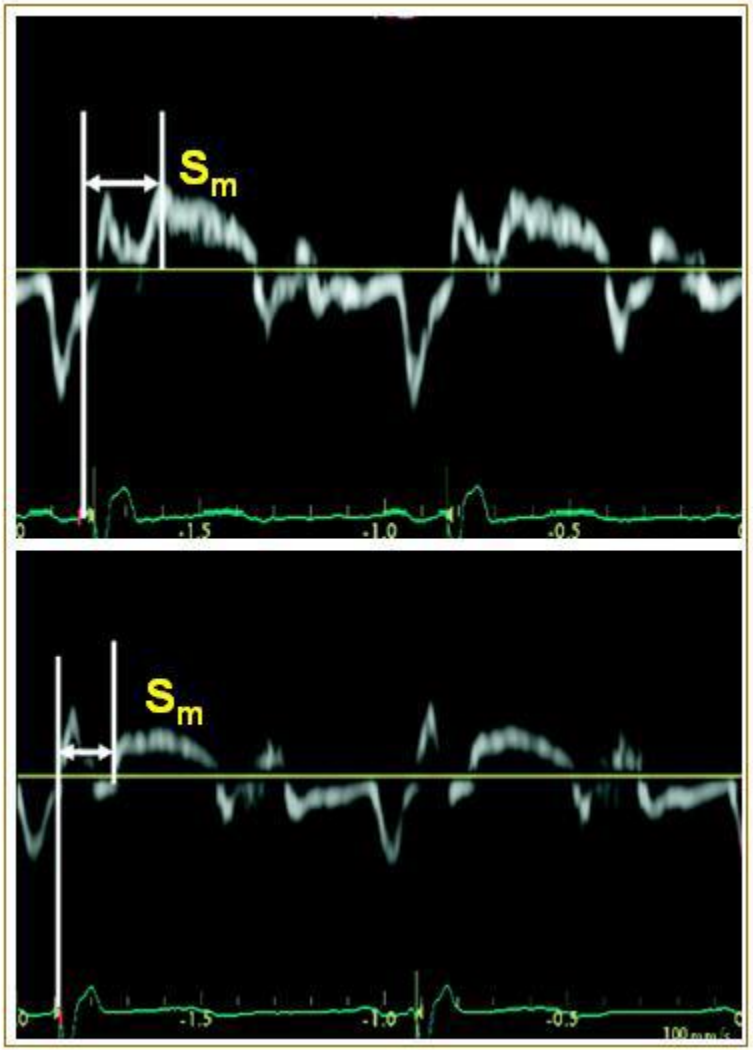
It has been demonstrated to be an independent predictor of CRT response in 48 patients with end-stage heart failure and left bundle branch block.

Pulsed Tissue Doppler

- Using PW TD, following are derived.
  - time interval between the onset of ECG derived QRS and the Sm peak (= ***time to Sm peak)***
  - time interval between the onset of QRS and the onset of Sm (= ***time to Sm onset), which correspond to LV PEP***

Intra-ventricular mechanical delay has been defined for differences of > 65 ms of time to Sm Peak between LV segments


msec
cm/sec
Time to peak
S_m
Time to onset
A_m
E_m
RT_m
CT_m


S_m
S_m

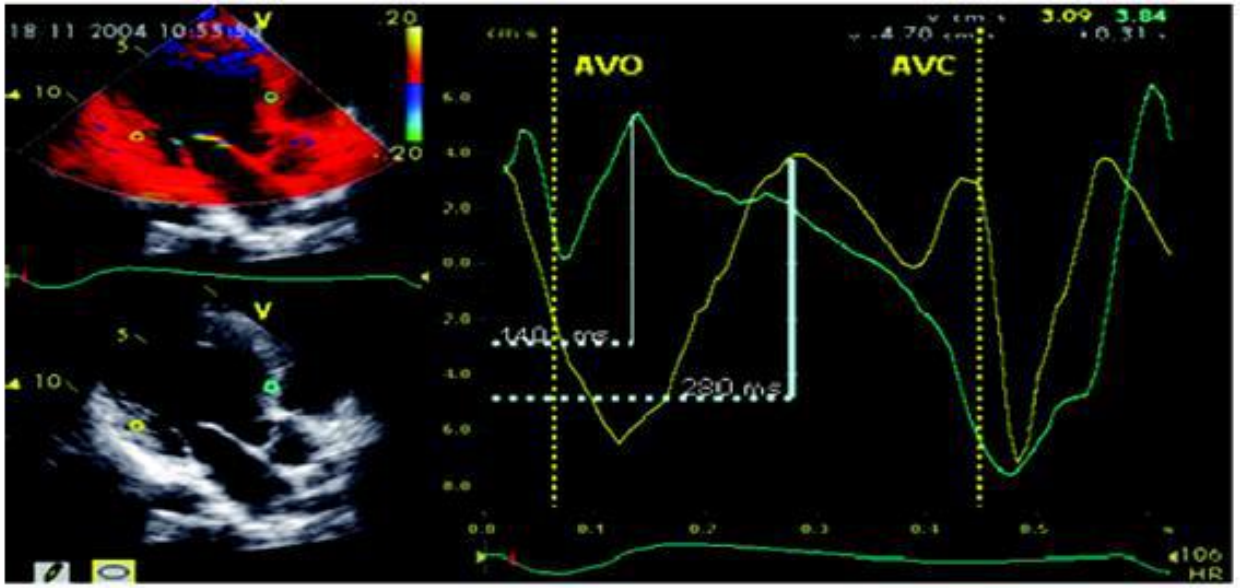
Colour Tissue Doppler

1. Off-line colour Tissue Doppler derived Tissue Velocity Imaging (TVI),
2. SRI

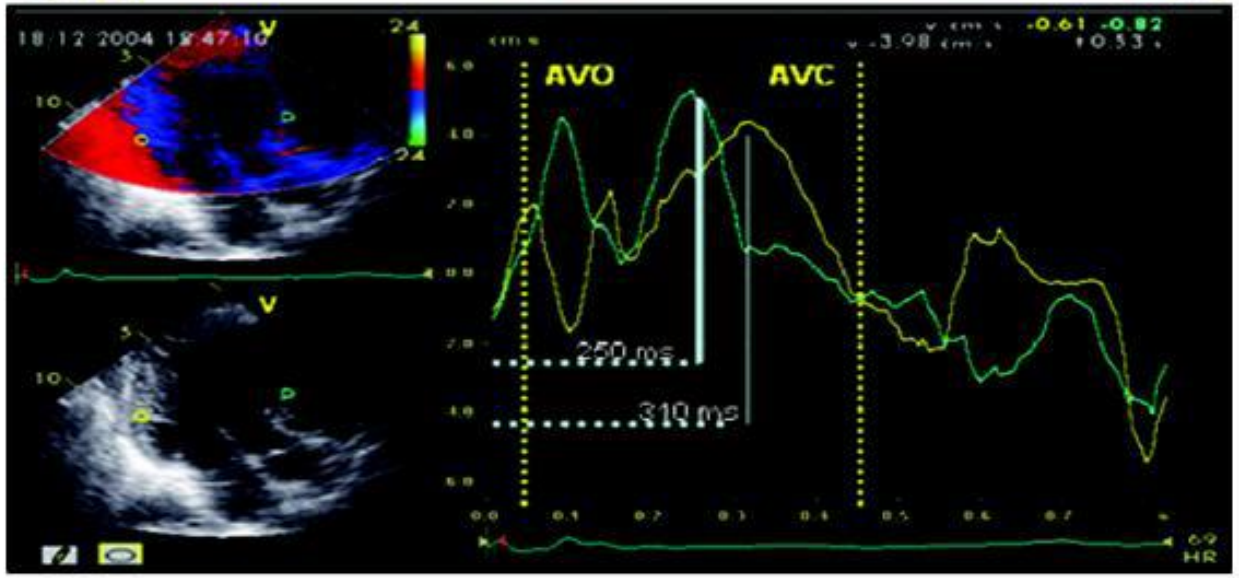
TVI measures the time to Sm peak (Ts) or the time to Sm onset in LV basal and middle segments of the three standard apical views

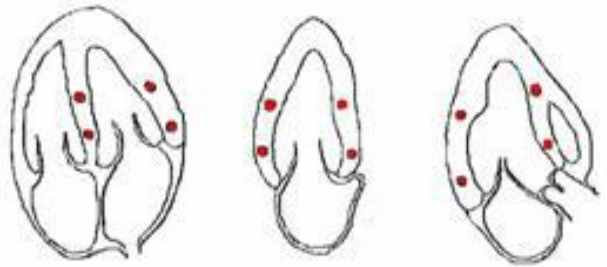
One or more difference of > 60 ms→ suggests significant intraventricular dysynchrony

Pre CRT



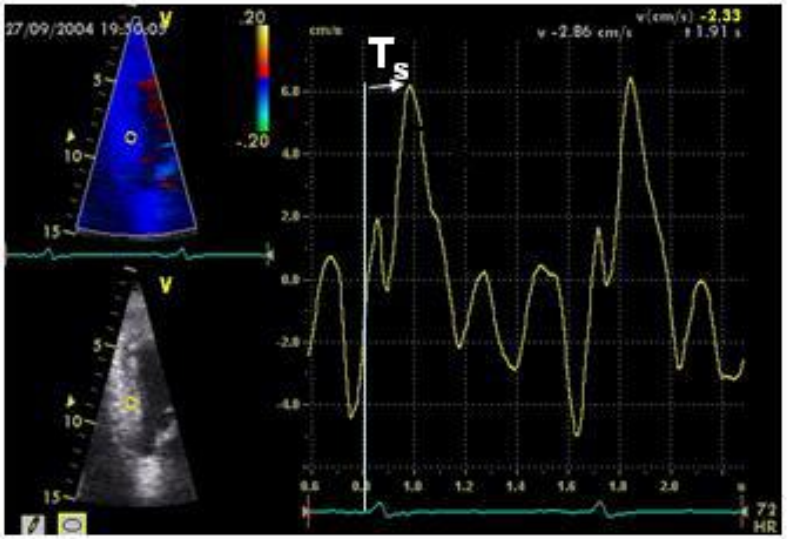
Post CRT

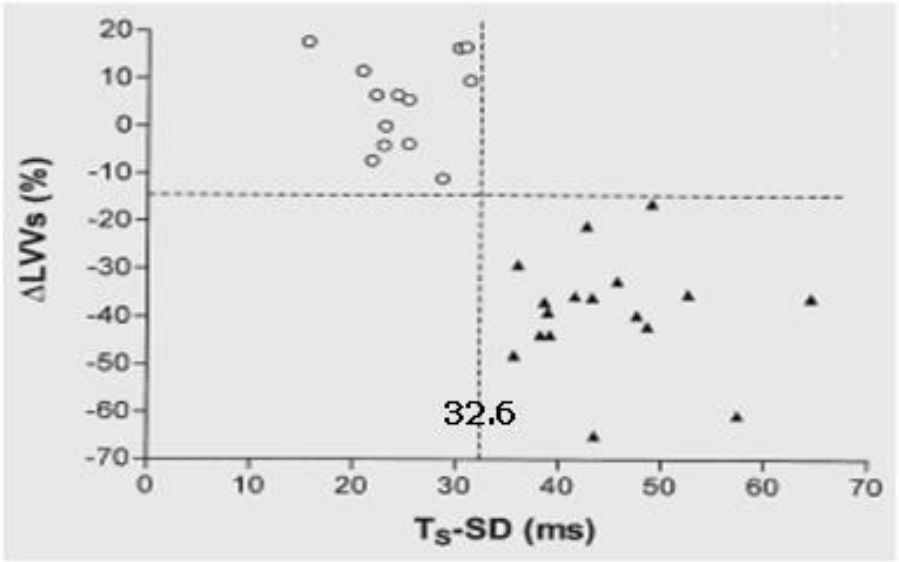




4-chamber 2-chamber 3-chamber

DI = Standard deviation of Ts of the 12 LV segments





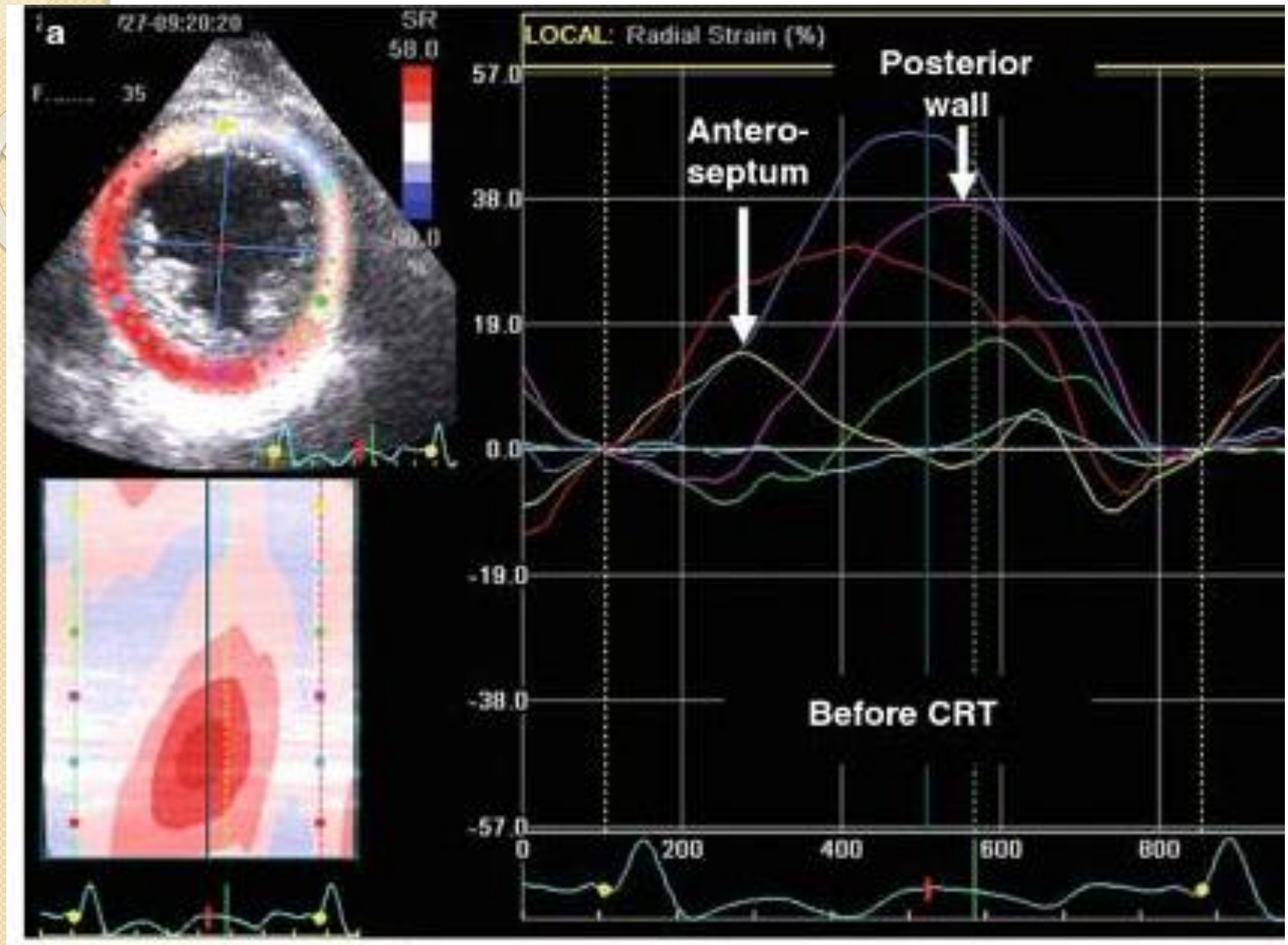
Using a LV 12-segment model,

A dyssynchrony index (DI) can be derived as the Standard deviation of the average values of Ts (Ts-SD)

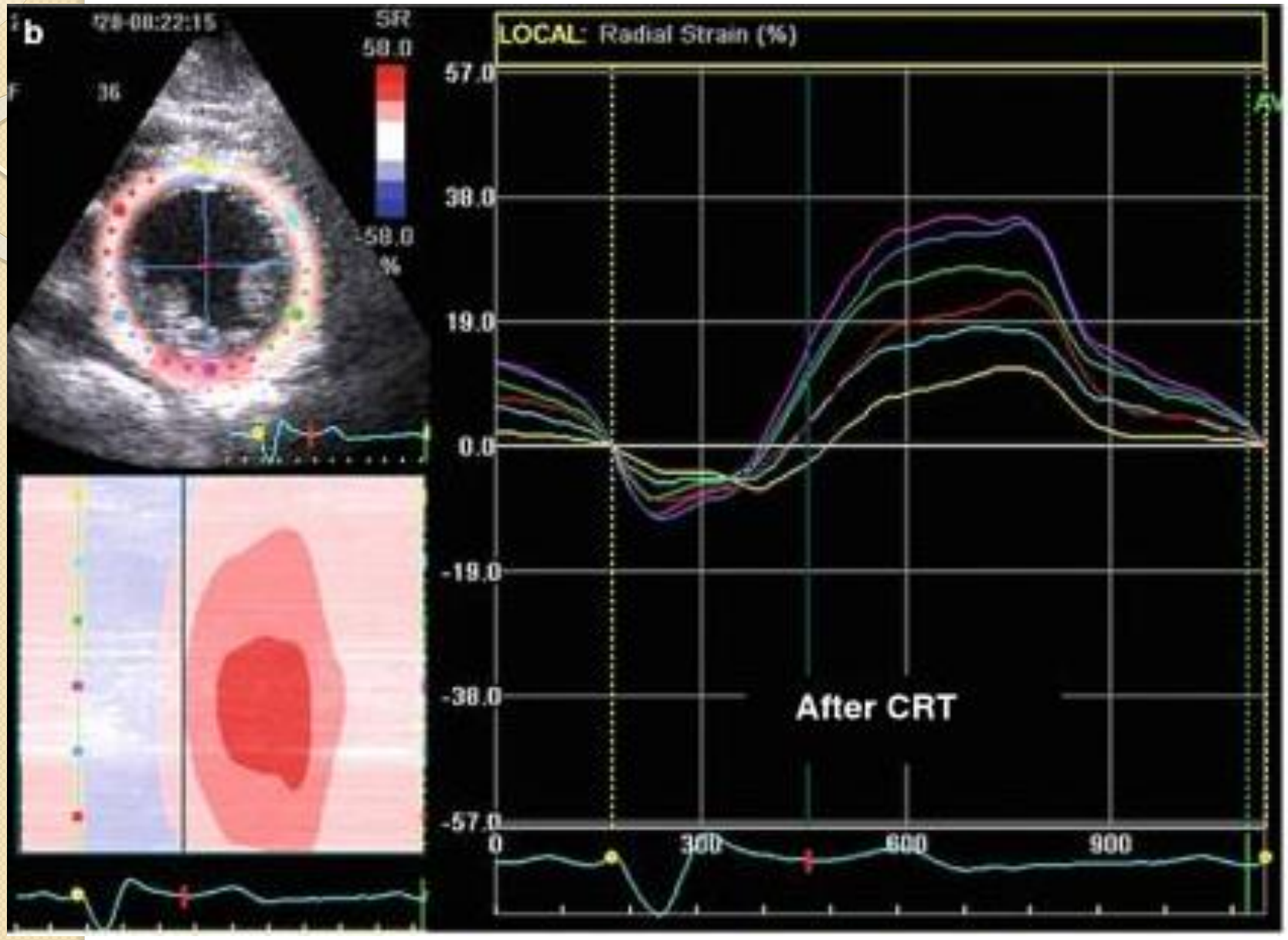
As per Yu et ala Ts-SD of > 32.6 ms predicts inverse LV remodeling after CRT with 100% sensitivity, 100% specificity and 100% accuracy in 30 candidates to CRT

Speckle tracking

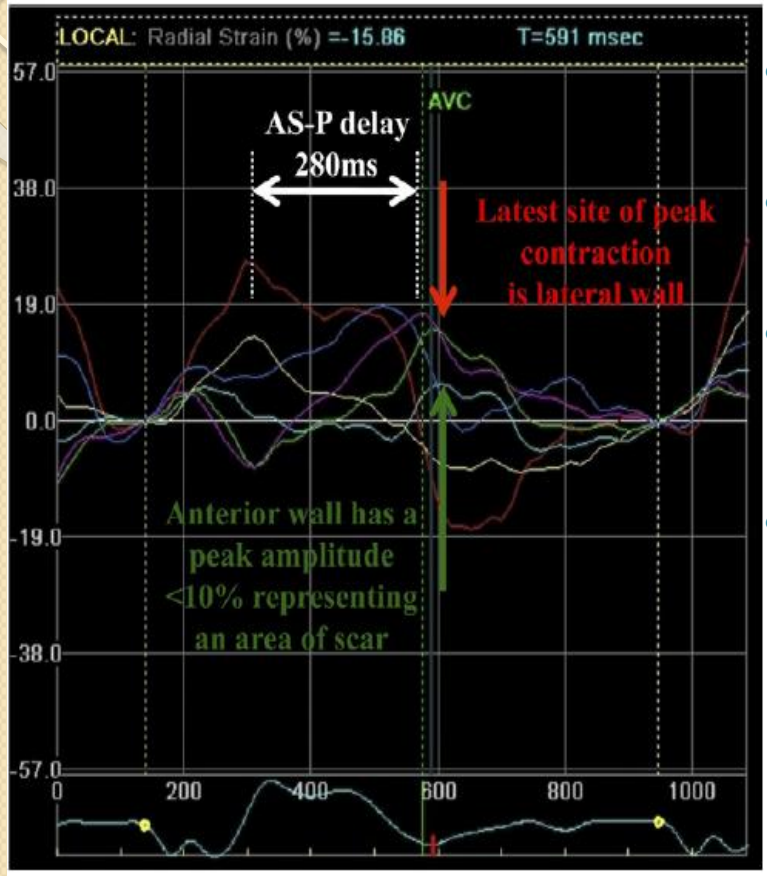
- This is a 2-D strain technique and has been used to assess radial dyssynchrony before/after CRT.
- Speckle tracking has been applied to routine mid-ventricular short-axis images to calculate radial strain from multiple circumferential points averaged to six standard segments.


a
SR
58.0
LOCAL: Radial Strain (%)
57.0
38.0
19.0
0.0
-19.0
-38.0
-57.0
Posterior wall
Antero-septum
Before CRT
0
200
400
600
800

- Dyssynchrony from timing of peak radial strain has been demonstrated to be correlated with Tissue Doppler measures
- A ***time difference ≥ 130 ms between the radial strain peak of LV posterior wall and anterior septum has shown to be highly predictive*** of an improved EF during follow-up, with 89% sensitivity and 83% specificity


b
SR
50.0
-50.0
%
LOCAL: Radial Strain (%)
57.0
38.0
19.0
0.0
-19.0
-38.0
-57.0
After CRT
0
300
600
900

The TARGET Study: A Randomized, Controlled Trial. Echo guided LV lead placement offers additional benefits



Echocardiographic speckle-tracking 2-D radial strain imaging

- 220 pts randomized 1:1 to Echo guided vs standard LV lead CRT implantation
- Segments with radial strain amplitude 10% were regarded as nonviable (scar)
- The LV pacing lead was placed in the most delayed segment in 63% of pts in TARGET Group vs 47% in control group.
- Compared with standard CRT treatment, the use of speckle-tracking echocardiography to the target LV lead placement yields significantly improved response and clinical status and lower rates of combined death and heart failure–related hospitalization

Khan F et al. J Am Coll Cardiol 2012;59:1509–1518

The TARGET Study: A Randomized, Controlled Trial. Echo guided LV lead placement offers additional benefits

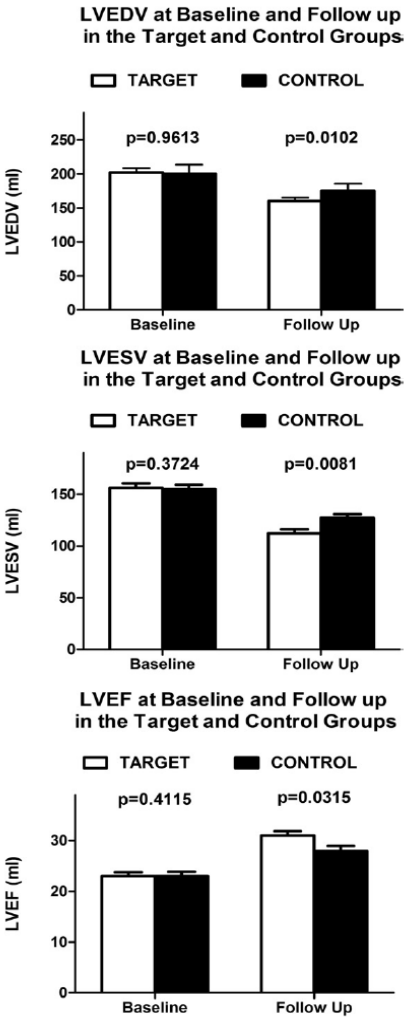


Figure 3 Comparison of LV Volumes and Function at Baseline and 6-Month Follow-up Between Both Groups

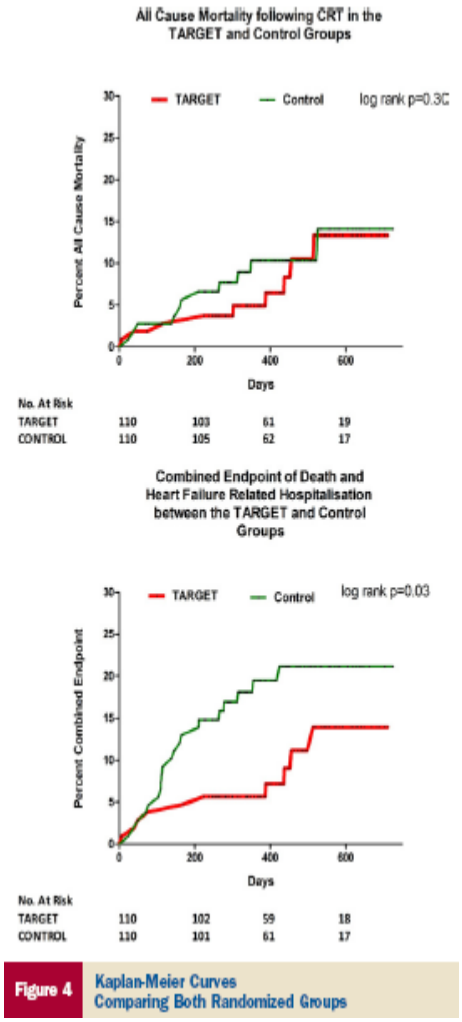


Figure 4 Kaplan-Meier Curves Comparing Both Randomized Groups

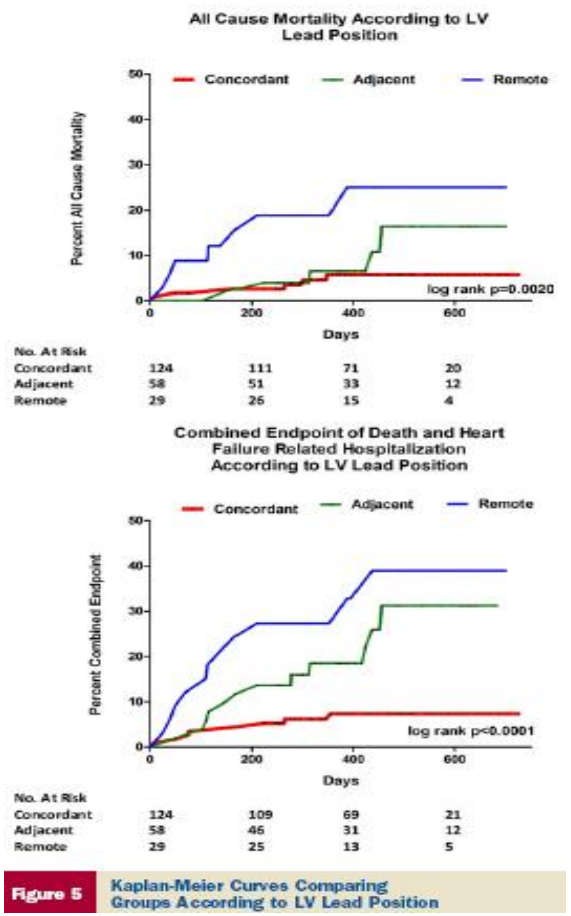


Figure 5 Kaplan-Meier Curves Comparing Groups According to LV Lead Position

The greatest benefit is demonstrated in pts with a concordant LV lead at sites free of scar

Khan F et al. J Am Coll Cardiol 2012;59:1509–1518

3-D Echocardiography

Three-dimensional (3-D) echocardiography allows intraventricular dyssynchrony to be evaluated by analyzing LV wall motion in multiple apical planes during the same cardiac cycle.

It also offers better spatial resolution than a single plane.

The global LV volumetric dataset has been used to determine a dyssynchrony index that corresponds to the standard deviation of the average of the time intervals needed by multiple LV segments to reach minimal end-systolic volume.

This index is expressed as the percent value of the overall cardiac cycle, in order to be able to compare patients with different heart rates.

CRT responders show a significant reduction of this 3-D dyssynchrony index, which parallels the reduction of LV enddiastolic volume and the increase in EF

MRI for Dyssynchrony

Quantification of mechanical ventricular dyssynchrony: direct comparison of velocity-encodedand cine magnetic resonance imaging.

Rofo. 2011 Jun;183(6):554-60. Epub 2011 Apr 12.

VENC-MRI and cine-MRI were performed in 20 patients with heart failure NYHA class III and reduced ejection fraction before CRT device implantation.

The interventricular mechanical delay (IVMD) was assessed by VENC-MRI as the temporal difference between the onset of aortic and pulmonary flow.

Intraventricular dyssynchrony was quantified by cine-MRI, using the standard deviation of time to maximal wall thickening in sixteen left ventricular segments (SDt-16).

RESULTS

14 patients (70 %) clinically responded to CRT. A similar accuracy was found to predict the response to CRT by measurements of the IVMD and SDt-16

ALSO data analysis of the IVMD is significantly less time-consuming compared to data analysis of the SDt-16

Main ultrasound techniques, parameters and reference values for detection of intra-ventricular dyssynchrony and prediction of LV reverse remodeling

Technique	Parameter	Authors	Cut-off point
M-mode	SPWMD	Pitzalis et al, J Am Coll Cardiol 2002	> 130 ms
M-mode and PW Doppler	LWPSD	Sassone et al, Am J Cardiol 2007	> 1
PW Tissue Doppler	Diff. of T_s between LV segments	Bax JJ et al, J Am Coll Cardiol 2004	> 65 ms
TVI	T_s-SD	Yu et al, Am J Cardiol 2003	> 32.6 ms
TSI	T_s-SD	Yu et al, J Am Coll Cardiol 2005	> 34.4 ms
SRI	TPS-SD	Mele et al, Eur Heart J 2006	> 60 ms
SRI	ExcT	Porciani MC et al, Eur Heart J 2006	> 760 ms
2D radial strain	Time diff. in peak septal wall-to-posterior wall strain	Suffoletto et al, Circulation 2006	≥ 130 ms
3D echo	Triplane T_s-SD	Van der Veire NR et al, Am J Cardiol 2007	≥ 35.8 *

PROSPECT (Results of the Predictors of Response to CRT Trial)

Πολυκεντρική μελέτη (53): Europe, US, Hong Kong

- 467 ασθενείς , 54% ισχαιμική HF
- NYHA III ή IV
- QRS > 130ms, EF≤35%
- *Εκτίμηση δυσυγχρονισμού:*12 παράμετροι
- 5 +7 TDI
- *Response to CRT*: 0, 3, 6 months
- Κλινικά
- Επιβίωση
- NYHA CCS
- Νοσοκομειακή νοσηλεία
- Γενικότερη εκτίμηση ασθενούς
- Υπερηχογραφικά
- ↓LVESV ≥15%

SPWMD[10]	Septal-posterior wall motion delay; M mode measured by parasternal short-axis view	M mode
IVMD[14]	Interventricular mechanical delay defined as the difference between left and right ventricular preejection intervals	Pulsed Doppler
LVFT/RR[14]	Left ventricular filling time (LVFT) in relation to cardiac cycle length (RR) as measured by transmitral Doppler echo expressed as percentage	Pulsed Doppler
LPEI[14]	Left ventricular preejection interval defined as the time interval between the beginning of QRS and beginning of left ventricular ejection by Doppler	Pulsed Doppler
LLWC[14]	Intraventricular dyssynchrony left lateral wall contraction defined as the presence of overlap between the end of lateral wall contraction (via M mode) and onset of LV filling (by Doppler echocardiography)	M mode and pulsed Doppler
Ts-(lateral-septal)[15]	Delay between time to peak systolic velocity in ejection phase at basal septal and basal lateral segments	TDI
Ts-SD[11,12]	SD of time from QRS to peak systolic velocity in ejection phase for 12 left ventricular segments (6 basal and 6 middle)	TDI
PVD[16]	Peak velocity difference derived from subtracting the maximal from the minimal difference of time to peak velocity (excluding velocities occurring during isovolumic contraction time) for 6 segments at basal level	TDI
DLC[17,18]	Delayed longitudinal contraction measured in the 6 basal left ventricular segments with a systolic contraction component in early diastole by TDI and confirmed with strain rate imaging	TDI+SRI
Ts-peak displacement	Maximum difference of time to peak systolic displacement for 4 segments	TDI
Ts-peak (basal)	Maximum difference of time to peak systolic velocity for 6 segments at basal level	TDI
Ts-onset (basal)	Maximum difference of time to onset of systolic velocity for 6 segments at basal level	TDI

Chung et al Circulation 2008;117: 2608-2616

PROSPECT (Results of the Predictors of Response to CRT Trial)

Results

CCS end point

5 non-TDI parameters , 1 TDI έδειξαν *μέτρια* στατιστική συσχέτιση με το κλινικό αποτέλεσμα που θεωρείται επιτυχής ανταπόκριση στη CRT.

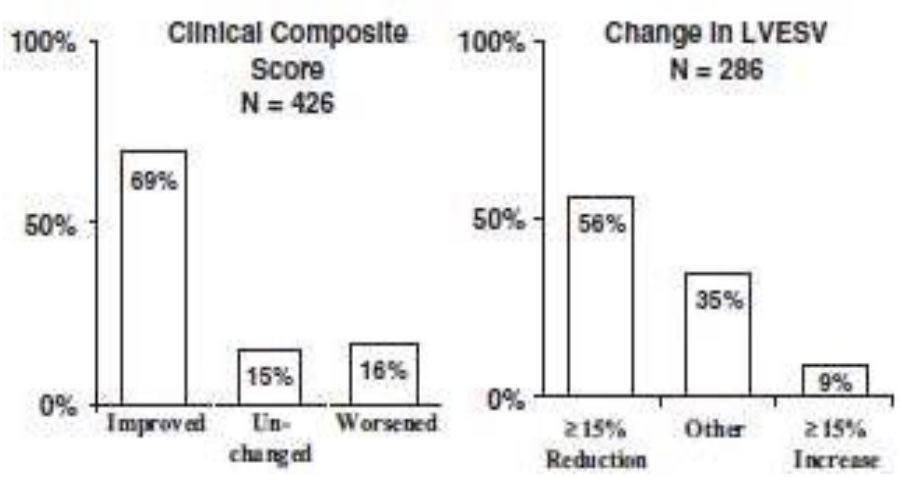
LVESV end point

4 non-TDI parameters, 1 TDI έδειξαν στατιστική συσχέτιση με το υπερηχογραφικό αποτέλεσμα που θεωρείται επιτυχής CRT.

Η ευαισθησία και ειδικότητα των μελετηθέντων παραμέτρων ήταν χαμηλή.

Η μελέτη δεν καταδεικνύει κάποιο από τους πολλούς υπερηχογραφικούς παράγοντες ως αξιόπιστο ώστε να χρησιμοποιηθεί στην κλινική πράξη για εκτίμηση του δυσυγχρονισμού.

Πιθανόν η κλινική βελτίωση να έρχεται γρηγορότερα από την ηχοκαρδιογραφική σε κάποιους ασθενείς.



Chung et al Circulation 2008;117: 2608-2616

PROSPECT (Results of the Predictors of Response to CRT Trial)

- Κριτικές *PROSPECT*
- Υψηλή μεταβλητότητα αποτελεσμάτων μεταξύτων εξεταστών.
- Βραχύς χρόνος εκπαίδευσης (1day)
- Κακή ποιότητα εικόνων (1/3 μη αναλυτές)
- Πολυκεντρικότητα → πρώιμη ένταξη κάποιωνασθενών (US) στη μελέτη.
- Cut off points για το δυσυγχρονισμό προέρχοντ από μικρές μελέτες μονοκεντρικές.
- Η ετερογένεια των ασθενών που ενταχθήκαν στη μελέτη (ισχαιμικοί που μπορεί να είχαν ουλώδες μυοκάρδιο).
- Η ύπαρξη παραμέτρων πέραν των υπερηχογραφικών όπως η θέση του ηλεκτροδίου για την αριστερή κοιλία που μπορεί να
- τροποποιήσει το αποτέλεσμα της βηματοδότησης.

Echocardiographic Measure	Intraobserver CV, %	Interobserver CV, %	Interobserver κ Coefficient*
LVESV	3.8	14.5	NA
LPEI	3.7	6.5	0.67
SPWMD	24.3	72.1	0.35
Ts-SD	11.4	33.7	0.15
Ts-peak (basal)	15.8	31.9	0.25

Cardiac-Resynchronization Therapy in Heart Failure with a Narrow QRS Complex

Frank Ruschitzka, M.D., William T. Abraham, M.D., Jagmeet P. Singh, M.D., Ph.D., Jeroen J. Bax, M.D., Ph.D., Jeffrey S. Borer, M.D., Josep Brugada, M.D., Ph.D., Kenneth Dickstein, M.D., Ph.D., Ian Ford, M.D., Ph.D., John Gorcsan III, M.D., Daniel Gras, M.D., Henry Krum, M.B., B.S., Ph.D., Peter Sogaard, M.D., D.M.Sc., and Johannes Holzmeister, M.D., for the EchoCRT Study Group*

BACKGROUND

Cardiac-resynchronization therapy (CRT) reduces morbidity and mortality in chronic systolic heart failure with a wide QRS complex. Mechanical dyssynchrony also occurs in patients with a narrow QRS complex, which suggests the potential usefulness of CRT in such patients.

METHODS

We conducted a randomized trial involving 115 centers to evaluate the effect of CRT in patients with New York Heart Association class III or IV heart failure, a left ventricular ejection fraction of 35% or less, a QRS duration of less than 130 msec, and echocardiographic evidence of left ventricular dyssynchrony. All patients underwent device implantation and were randomly assigned to have CRT capability turned on or off. The primary efficacy outcome was the composite of death from any cause or first hospitalization for worsening heart failure.

RESULTS

On March 13, 2013, the study was stopped for futility on the recommendation of the data and safety monitoring board. At study closure, the 809 patients who had undergone randomization had been followed for a mean of 19.4 months. The primary outcome occurred in 116 of 404 patients in the CRT group, as compared with 102 of 405 in the control group (28.7% vs. 25.2%; hazard ratio, 1.20; 95% confidence interval [CI], 0.92 to 1.57; P=0.15). There were 45 deaths in the CRT group and 26 in the control group (11.1% vs. 6.4%; hazard ratio, 1.81; 95% CI, 1.11 to 2.93; P=0.02).

CONCLUSIONS

In patients with systolic heart failure and a QRS duration of less than 130 msec, CRT does not reduce the rate of death or hospitalization for heart failure and may increase mortality. (Funded by Biotronik and GE Healthcare; EchoCRT ClinicalTrials.gov number, NCT00683696.)

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Cardiac-Resynchronization Therapy in Heart Failure with a Narrow QRS Complex

Frank Ruschitzka, M.D., William T. Abraham, M.D., Jagm

Table 2. Protocol-Specified Cardiovascular Outcomes.*

Outcome	Control Group (N=405)	CRT Group (N=404)	Adjusted Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)			
Primary composite outcome				
Death from any cause or hospitalization for heart failure	102 (25.2)	116 (28.7)	1.20 (0.92–1.57)	0.15
Components of primary outcome				
Hospitalization for heart failure	90 (22.2)	99 (24.5)	1.16 (0.87–1.55)	0.25
Death from any cause	26 (6.4)	45 (11.1)	1.81 (1.11–2.93)	0.02
Other cardiovascular outcomes				
Hospitalization for cardiovascular event	137 (33.8)	147 (36.4)	1.11 (0.88–1.40)	0.36
Death				
Cardiovascular event	17 (4.2)	37 (9.2)	2.26 (1.27–4.01)	0.004
Heart failure	10 (2.5)	17 (4.2)	1.74 (0.80–3.81)	0.15
Follow-up data censored				
Owing to LVAD implantation	10 (2.5)	7 (1.7)	—	—
Owing to heart transplantation	5 (1.2)	3 (0.7)	—	—
Death after data were censored owing to LVAD implantation or heart transplantation†	4 (1.0)	1 (0.2)	—	—

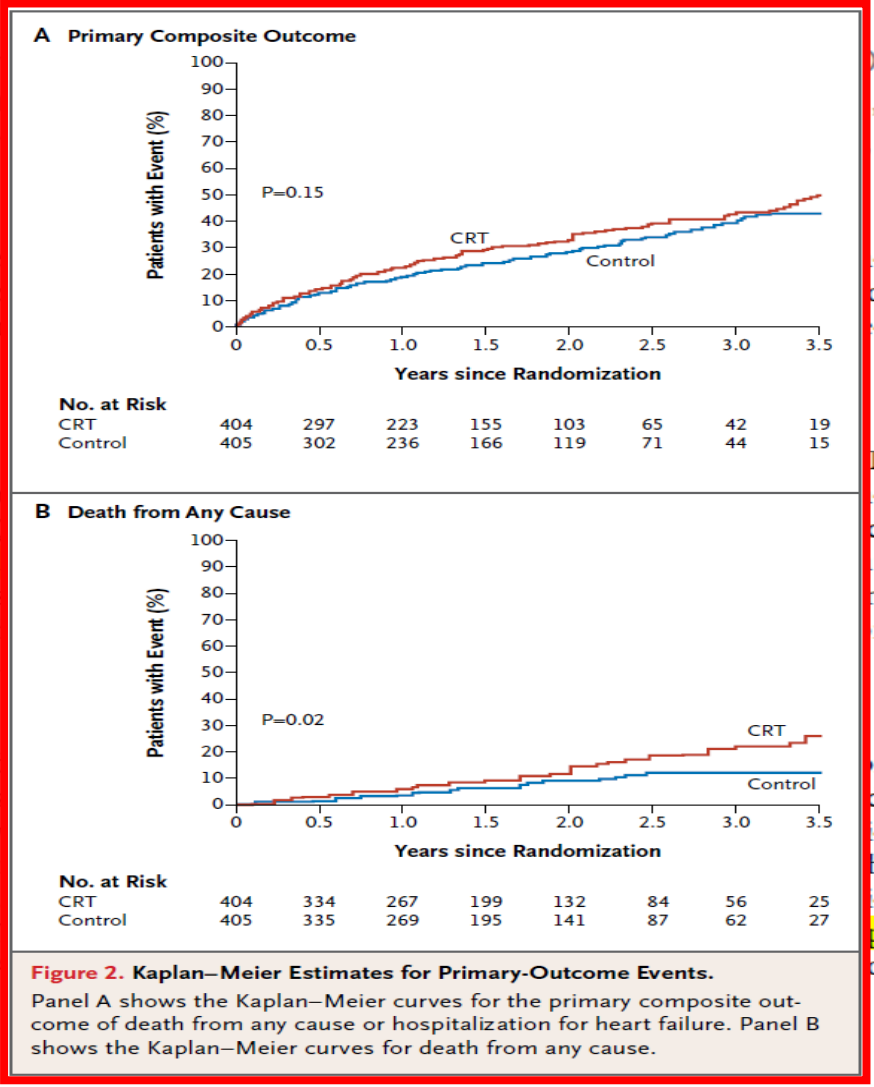

Figure 2. Kaplan–Meier Estimates for Primary-Outcome Events.
Panel A shows the Kaplan–Meier curves for the primary composite outcome of death from any cause or hospitalization for heart failure. Panel B shows the Kaplan–Meier curves for death from any cause.

CONCLUSIONS

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Death after data were censored owing to LVAD implantation or heart transplantation†	4 (1.0)	1 (0.2)	—	—

Reason of Death	Control Group, number (%) with event N=405	CRT Group, number (%) with event N=404
Any reason	26 (6.4%)	45 (11.1%)*
Cardiovascular	17 (4.2%)	37 (9.2%)**
Death due to heart failure	10 (2.5%)	17 (4.2%)
Death due to arrhythmic events	4 (1.0%)	14 (3.5%)*
Death due to non-ischemic dysrhythmia	0	2 (0.5%)
Death due to symptomatic heart block/bradycardia/ PEA	0	4 (1.0%)
Sudden cardiac death	4 (1.0%)	8 (2.0%)
Presumed cardiovascular death	1 (0.3%)	5 (1.2%)
Fatal stroke	1 (0.3%)	1 (0.3%)
Other vascular death	1 (0.3%)	0
Non-Cardiovascular	9 (2.2%)	8 (2.0%)
Cancer	4 (1.0%)	1 (0.3%)
Infection-pneumonia	0	2 (0.5%)
Infection-sepsis	1 (0.3%)	3 (0.7%)
Other non-cardiovascular	1 (0.3%)	0
Respiratory-exacerbation of COPD	2 (0.5%)	0
Traumatic injury	1 (0.3%)	2 (0.5%)
Death after crossover	7 (1.7%)	1 (0.3%)

Statistically significant difference of *p<0.05, **p<0.01

CONCLUSIONS

In patients with systolic heart failure and a QRS duration of less than 130 msec, CRT does not reduce the rate of death or hospitalization for heart failure and may increase mortality. (Funded by Biotronik and GE Healthcare; EchoCRT ClinicalTrials.gov number, NCT00683696.)

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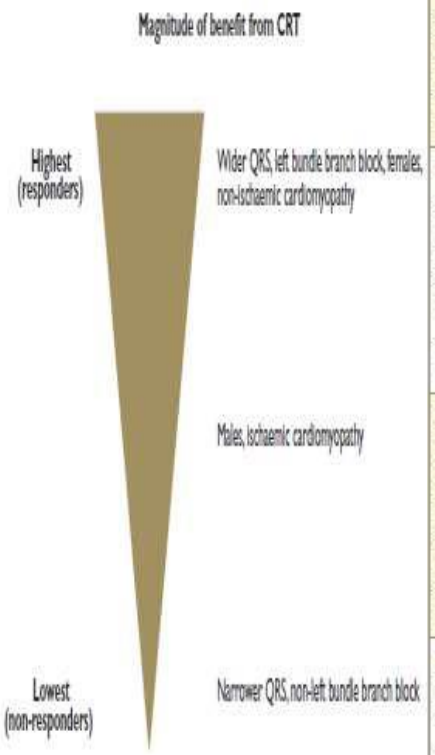
2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

EUROPEAN SOCIETY OF CARDIOLOGY®

Trial (ref)	No.	Design	NYHA	LVEF	QRS	Primary endpoint	Secondary endpoints	Main Findings
MUSTIC-SR[C]	58	Single-blinded, crossover, randomized CRT vs. OMT, 6 months	III	<35%	≥150	6MWD	NYHA class, QoL, peak VO_2,LV volumes, MR hospitalizations, mortality	CRT-P improved 6MWD, NYHA class, QoL, peak VO_2, reduced LV volumes and MR and reduced hospitalizations
PATH-CHF[I]	41	Single-blinded, crossover, randomized AV vs. LV vs. BiV, 12 months	III–IV	NA	≥150	Peak VO_2, 6MWD	NYHA class, QoL hospitalizations	CRT-P improved NYHA class, QoL and 6MWD and reduced hospitalizations
MIRACLE[M]	453	Double-blinded, randomized CRT vs. OMT, 6 months	III–IV	≤35%	≥130	NYHA class, 6MWD , QoL	Peak VO_2, LVEDD, LVEF, MR clinical composite response	CRT-P improved NYHA class, QoL and 6MWD and reduced LVEDD, MR and increased LVEF
MIRACLE-ICD[M]	369	Double-blinded, randomized CRT-D vs. ICD, 6 months	III–IV	≤35%	≥130	NYHA class, 6MWD , QoL	Peak VO_2, LVEDD, LVEF, MR clinical composite response	CRT-D improved NYHA class, QoL, peak VO_2
CONTAK-CD[R]	490	Double-blinded randomized CRT-D vs. ICD, 6 months	II–III–IV	≤35%	≥120	NYHA class, 6MWD , QoL	LV volume, LVEF composite of mortality, VT/VF, hospitalizations	CRT-D improved 6MWD, NYHA class, QoL, reduced LV volume and increased LVEF
MIRACLE-ICD II[R]	186	Double-blinded, randomized CRT-D vs. ICD, 6 months	II	≤35%	≥130	Peak VO_2	VE/VCO_2, NYHA, QoL, 6MWD, LV volumes and EF, composite clinical endpoint	CRT-D improved NYHA, VE/CO_2 and reduced LV volumes and improved LVEF
COMPANION[R]	1520	Double-blinded randomized OMT vs. CRT-P / or vs. CRT-D, 15 months	III–IV	≤35%	≥120	All-cause mortality or hospitalization	All-cause mortality, cardiac mortality	CRT-P and CRT-D reduced all-cause mortality or hospitalization
CARE-HF[M]	813	Double-blinded randomized OMT vs. CRT-P 29.4 months	III–IV	≤35%	≥120	All-cause mortality or hospitalization	All-cause mortality, NYHA class, QoL	CRT-P reduced all-cause mortality and hospitalization and improved NYHA class and QoL
REVERSE[I]	610	Double-blinded, randomized CRT-ON vs. CRT-OFF, 12 months	I–II	≥40%	≥120	% worsened by clinical composite endpoint	LVESV index, heart failure hospitalizations and all-cause mortality	CRT-P/CRT-D did not change the primary endpoint and did not reduce all-cause mortality but reduced LVESV index and heart failure hospitalizations
MADIT-CRT[M]	1820	Single-blinded, randomized CRT-D vs. ICD, 12 months	I–II	≤30%	≥130	All-cause mortality or heart failure hospitalizations	All-cause mortality and LVESV	CRT-D reduced the endpoint heart failure hospitalizations or all-cause mortality and LVESV. CRT-D did not reduced all-cause mortality
RAFT[M]	1798	Double-blinded, randomized CRT-D vs. ICD 40 months	II–III	≤30%	≥120	All-cause mortality or heart failure hospitalizations	All-cause mortality and cardiovascular death	CRT-D reduced the endpoint all-cause mortality or heart failure hospitalizations. In NYHA III, CRT-D only reduced significantly all-cause mortality



Recommendations	Class [a]	Level [b]	Ref. [c]
1) LBBB with QRS duration >150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment.[d]	I	A	48–64
2) LBBB with QRS duration 120–150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment.[d]	I	B	48–64
3) Non-LBBB with QRS duration >150 ms. CRT should be considered in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment.[d]	IIa	B	48–64
4) Non-LBBB with QRS duration 120–150 ms. CRT may be considered in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment.[d]	IIb	B	48–64
5) CRT in patients with chronic HF with QRS duration <120 ms is not recommended.	III	B	65, 66

Συμπεράσματα

- Η υπερηχογραφία αποτελεί βασικό εργαλείο στη εκτίμηση των αποτελεσμάτων της θεραπείας επανασυγχρονισμού.
- *Προς το παρόν* η επιλογή ασθενών για θεραπεία δυσυγχρονισμού βάσει υπερηχογραφήματος *δεν* είναι τεκμηριωμένη.
- Στοιχεία από μελέτες καθιστούν υπερηχογραφικές παραμέτρους προ και μετά τη CRT ανεξάρτητους προγνωστικούς παράγοντες επιτυχίας της θεραπειας.
- Η πιο σημαντικη συνιστώσα είναι ο διακοιλιακός δυσυγχρονισμός-οσο πιο μεγάλος τόσο πιο μεγάλη η πιθανότητα για ανάστροφη αναδιαμόρφωση.
- Νεώτερες τεχνικές όπως το speckle tracking και η 3D υπερηχοκαρδιογραφία υποσχονται πολλα στην επιλογή των ασθενών που θα ανταποκριθούν τα μέγιστα μετα τον επανασυγχρονισμό και στην μειωση των non-Responders(30%).

THANK YOU

- When applied to the left ventricle, left ventricular deformation is defined by the three normal strains (longitudinal, circumferential, and radial) and three shear strains (circumferential-longitudinal, circumferential-radial, and longitudinal-radial).
- The principal benefit of LV shear strains is amplification of the 15% shortening of myocytes into 40% radial LV wall thickening, which ultimately translates into a >60% change in LV ejection fraction.
- Left ventricular shearing increases towards the subendoardium, resulting in a subepicardial to subendocardial thickening strain gradient.

Strain

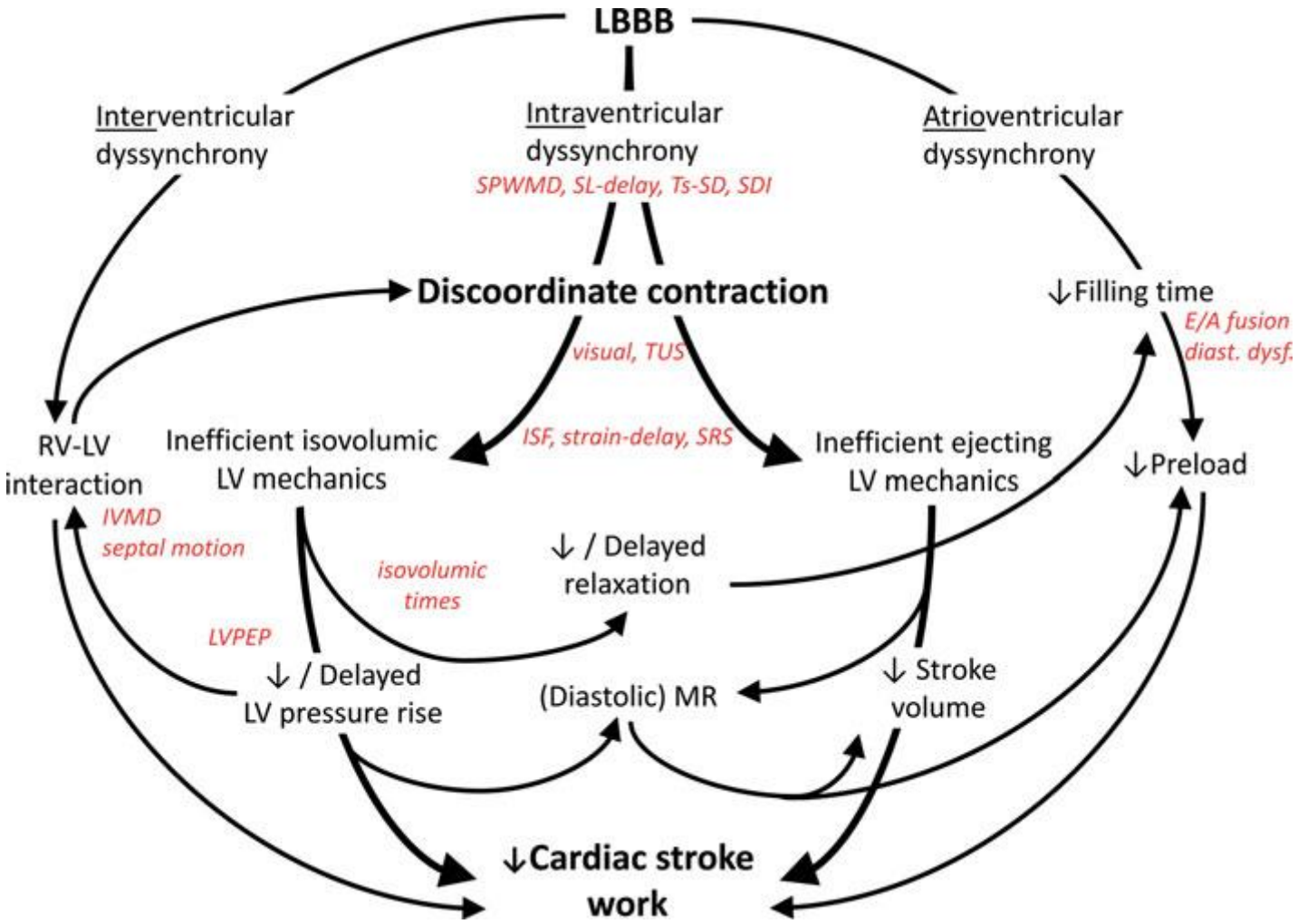
- Strain is defined as the fractional or percentage change in an objects dimension in comparison to the object's original dimension.

- Similarly, strain rate can be defined as the speed at which deformation occurs.

In Conclusion

- There are several techniques for determining LV dyssynchrony
- The most important clinical application is for assessment of patient planned for CRT(with or without prolonged QRS duration)
- Intraventricular Dyssynchrony seems to be the most important
- Greater the intraventricular dyssynchrony, the higher the possibility of significant inverse LV remodeling
- 3D echo has great potential

The common advantages of these techniques is the possibility of measuring the dyssynchrony of opposite LV walls (horizontal dyssynchrony) and of different segments of the same LV wall (vertical dyssynchrony) in a given view, from the same cardiac cycle



Mechanical dyssynchrony in left bundle branch block.