Cardiac Resynchronization Therapy Optimization: Still Have a Role?!

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Cardiac Resynchronization Therapy Optimization: Still Have a Role?!

Yes

"Your Eyes See What Your Mind Knows"

Hippocrates (c. 460 BC – c. 370 BC)

Objectives of CRT

Table 2. The results from the CARE-HF (Cardiac Resynchronization in Heart Failure) program demonstrated that, in comparison with a control group, CRT had the following effects [7,8,21]. However, the analysis failed to identify any patient subgroup who did not respond.

Outcome	p value
Increased mean left ventricular ejection fraction by 6.9%	$p<0.001$
Improved symptoms and quality of life	$p<0.0001$
Reduced the rate of hospitalization for WHF by 52%	$p<0.0001$
Reduced the rate of all-cause mortality by 40%	$p<0.0001$
Reduced the rate of death due to WHF by 45%	$p=0.003$
Reduced the rate of sudden death by 46%	$p=0.006$

WHF: worsening heart failure.

CRT Optimization

- Device (PM/ ICD) Optimization
- CRT (HF therapy) Optimization
- Patient Optimization

CRT Follow Up

- **Device (PM/ ICD) Optimization**
- CRT (HF therapy) Optimization
- Patient Optimization

Device Optimization

- ✓ Rhythm
- ✓ Percent pacing
- ✓ Battery
- ✓ Lead status
- ✓ Sensing
- ✓ Threshold
- ✓ Events
- ✓ Diagnostics
- ✓ Programming

Look for Complications of CRT

The most common complication

- Inability to implant the LV pacing lead successfully in the coronary vein

Additional complications include

- Coronary sinus or coronary vein trauma
- Pneumothorax
- Diaphragmatic/phrenic nerve pacing
- Infection

CRT Follow Up

- Device (PM/ ICD) optimization
- **CRT (HF therapy) optimization**
- Patient Optimization

CRT Optimization

- CRT Promotion
- CRT Optimization

Promoting CRT

- Unlike conventional pacing (where the goal is to minimize unnecessary ventricular pacing), CRT should pace both ventricles as close to 100% of the time as possible.
- Percentage of LV pacing (as high as 90% or more) = Optimal CRT delivery
- **Lower pacing %**
  - LV lead dislocation
  - Paroxysmal or permanent atrial fibrillation
  - Frequent ventricular ectopic beats

Promoting CRT- MTR

- The Maximum Tracking Rate sets the highest rate at which the ventricles will be paced in response to intrinsic atrial activity
- If the patient has high intrinsic atrial rates >MTR with good conduction, it is possible that the ventricle will not be paced some of the time
- Make sure the MTR is high enough so that even in the presence of high intrinsic atrial rates, the patient will have V pacing as much as possible

CRT Optimization

- Why do we optimize CRT?
- How do we optimize CRT?
- When should we optimize CRT?
- Does optimizing CRT benefit patients?

Why Do We Optimize CRT?

- Proper CRT depends on precise timing of the ventricular contractions.
- Timing should allow:
  - Adequate time for the filling of the ventricles (i.e. diastolic optimization).
  - Proper contraction of the right and left ventricles with respect to each other (i.e. systolic optimization).

Who Should Be Optimized

Any CRT recipient should be optimized

Any CRT Patient who didn’t show:

- NYHA Class Improvement
- 6 Minutes walking distance Improvement
- BNP improvement
- Echocardiographic parameters Improvement
- Reduction of Hospitalization

CRT Non Responders 35%

Figure 1. The factors leading to poor, or no, CRT response.

LEADING ARTICLE

How Should Non-Responders to CRT be Managed?

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CRT, applied according to existing guidelines, is an effective therapy for heart failure patients who are refractory to conventional medical treatment. No adequate definition of "response" or "non-response" to the therapy exists, and there is little evidence that electrocardiographic or cardiac imaging criteria are useful in selecting patients who are more or less likely to have a good clinical response to CRT. It is estimated from CRT studies that approximately one third of patients who receive the therapy do not exhibit an adequate response. Accordingly, it is important to develop strategies to enhance the effectiveness of CRT for patients who do not receive optimal benefit from the therapy. This review aims to discuss clinical approaches to managing heart failure patients who are labeled as non-responders. Ensuring that the CRT device is pacing and capturing both ventricles, and that the atrioventricular delay is optimal at rest and during exercise, is essential in all patients who have an inadequate response. The burden of atrial fibrillation, should it arise, requires quantification and management. Careful attention should also be paid to pharmacological therapy following the deployment of CRT. Finally, left ventricular lead re-positioning, or other cardiac procedures, will be occasionally required. *Device Therapy for Heart Failure* 2008;**2**(1):2–9.

What is a „responder“ ?

„soft“ end-point:

- NYHA improvement >1

„hard“ end-points:

- survival
- ↑ 6 MWD > 10 ... 25%
- ↑ EF > 5 ... 25%
- ↓ ED Volume > 15%
- ↓ ES Volume > 10 ...15%
- ↑ Stroke Volume > 15%

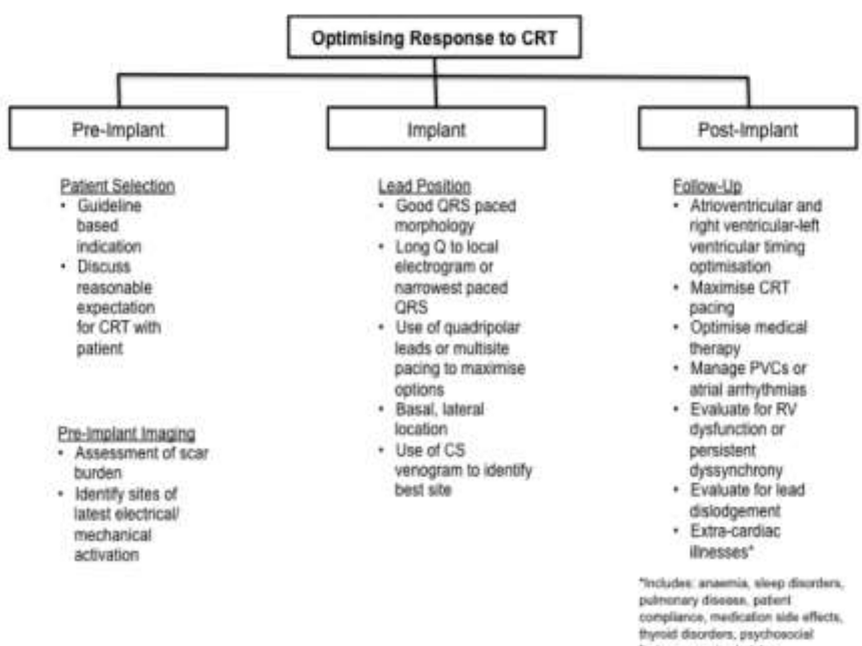
Table 4. Authors' summary of questions to be answered by the clinician before labeling an HF patient with a CRT device as a "non-responder".

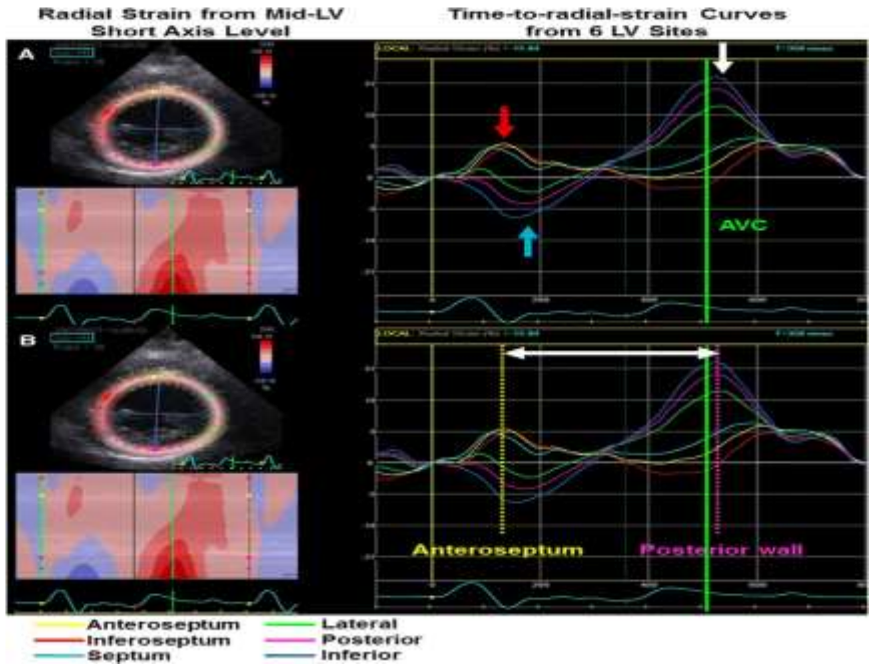
1.	Have all correctable cardiac causes of HF (including ischemia, valvular abnormalities, hypertension, or dysrhythmias) been identified and managed?
2.	Have all correctable non-cardiac abnormalities (including anemia, renal, thyroid, or other hormonal abnormalities) that cause or worsen HF been identified and managed?
3.	Have drugs that cause or worsen HF (including class I and III anti-arrhythmic agents, nonsteroidal anti-inflammatory drugs, or cancer chemotherapeutic agents) been stopped or substituted as appropriate?
4.	Has optimal medical management (including angiotensin-converting enzyme inhibitors, β-blockers, angiotensin receptor blockers, aldosterone antagonists, digoxin, and diuretics) been initiated at an optimal dose based on current evidence? Is the patient compliant with this regimen?
5.	Is the patient on an appropriate health education program (including salt intake restriction, avoidance of excessive alcohol consumption, regular exercise, and weight reduction)? Is he or she compliant with it?
6.	Is the CRT device functioning properly (for example, has optimal left ventricular lead position been ensured during CRT implantation? Have the atrioventricular and interventricular delay intervals been programmed to provide the best hemodynamic response?)

HF: heart failure.

CRT Optimization

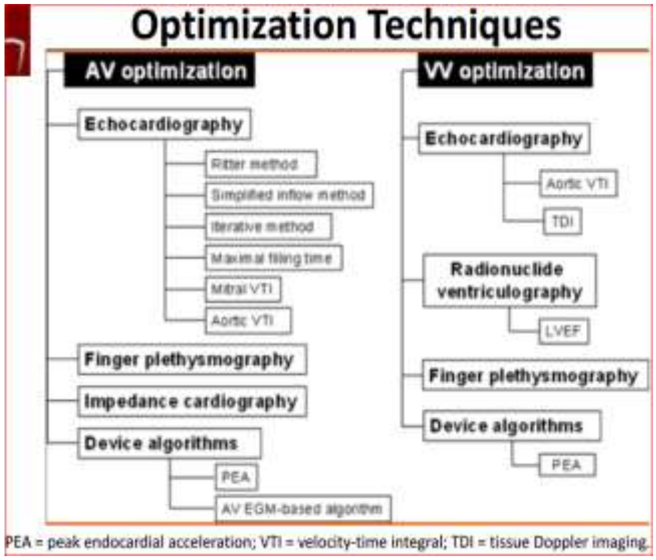
- Why do we optimize CRT?
- **How do we optimize CRT?**
- When should we optimize CRT?
- Does optimizing CRT benefit patients?





Echocardiographic Parameters For Patient Selection and Response Prediction

Parameter	Description	View	Cutt-off	Advantages	Disadvantages
Apical rocking	Visual assessment of apical transverse motion	Apical 4-chamber view	Yes/No	Highly reproducible method, high specificity for response prediction	Affected by RV function
Septal flash	Visual assessment of short inward septal motion during beginning of systole	Apical 4-chamber view	Yes/No	Highly reproducible method, high specificity for response prediction	Translation of continuous process to on/off phenomenon, observer differences
IVMD	Interventricular mechanical delay, difference in onset of outflow of LV (LVPEP) and RV (RVPEP)	PW Doppler of LVOT and RVOT	40 msec	Highly reproducible method	Affected by both LV and RV function
Septal strain patterns	Strain pattern of the septum during systole	Apical 4-chamber view	3 types (1,2 responder/ 3 non-responder)	Prediction of volumetric response and outcome	Technically demanding
SD-TTP	Standard deviation of time to peak shortening (strain) or velocity (TDI) of all myocardial segments	Apical 4-chamber view, 2-chamber view, PLAX view	> 32 msec	Offline analysis	Requires high quality image, confounded by passive motion tethering
SL delay	Difference of time to peak velocity of septal and lateral view	Apical 4-chamber view	> 65 msec	Prediction of volumetric response and outcome	Confounded by passive motion tethering
SDI	Time to minimal systolic volume of 16 segments	3D	9.8%	High value for response prediction	Limited spatial and temporal resolution
SRSsept (Systolic rebound stretch of the septum)	All positive deflections after initial shortening of the septum during systole	Apical 4-chamber view	4.7%	Prediction of volumetric response and outcome	Technically demanding, observer differences



Summary of the various methods of AV and VV interval optimization.

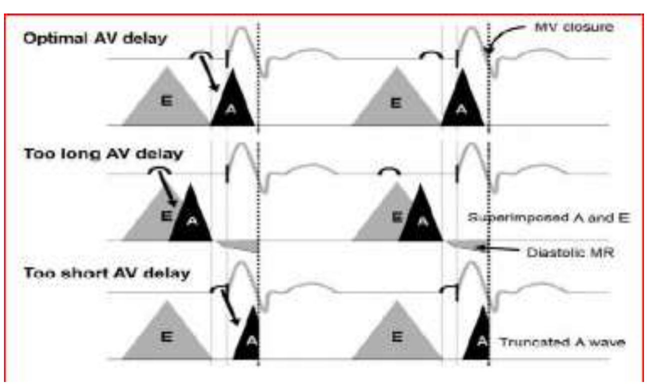
	AV optimization	VV optimization
Echocardiography	Mitral inflow (Ritter method, iterative method, "Fast and Simple") aortic VTI	LV M-mode (Septal-posterior wall motion delay), tissue Doppler imaging, aortic VTI
Alternative techniques	Impedance cardiography, finger photoplethysmography, acoustic cardiography, peak endocardial acceleration	Intracardiac echocardiography, electroanatomic mapping, radionuclide angiography, finger photoplethysmography, peak endocardial acceleration, surface ECG
Intracardiac electrogram-based algorithms	Boston Scientific SmartDelay™, St. Jude Medical QuickOpt™, Medtronic Adaptive Algorithm	Boston Scientific Expert Ease™, St. Jude Medical QuickOpt™, Medtronic Adaptive Algorithm

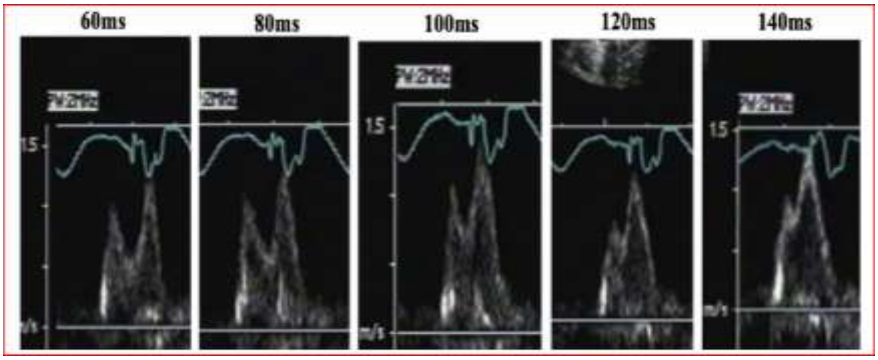
AV Optimization: Iterative Method

Objective: Identify the AV Delay that maximizes LV filling using mitral velocity echocardiographic measurements

Procedure

- Obtain transmitral Doppler echo at a "long" programmed AV Delay during ventricular pacing
- Shorten the programmed AV Delay by 10-20 ms until the echo Doppler A-wave becomes truncated (A wave is atrial contraction)
- Lengthen the programmed AV Delay back to the value where there is no A-wave cutoff. This timing should enable ventricular contraction to occur just at the end of atrial systole

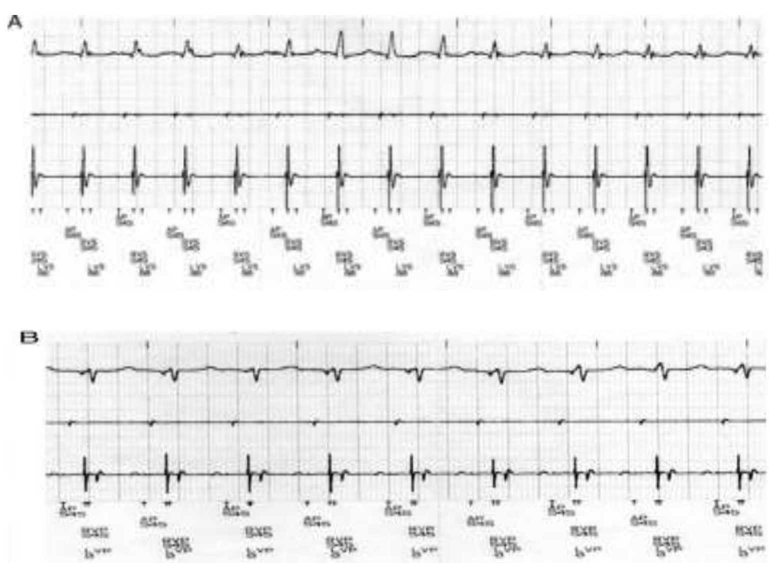




Optimal AV delay is

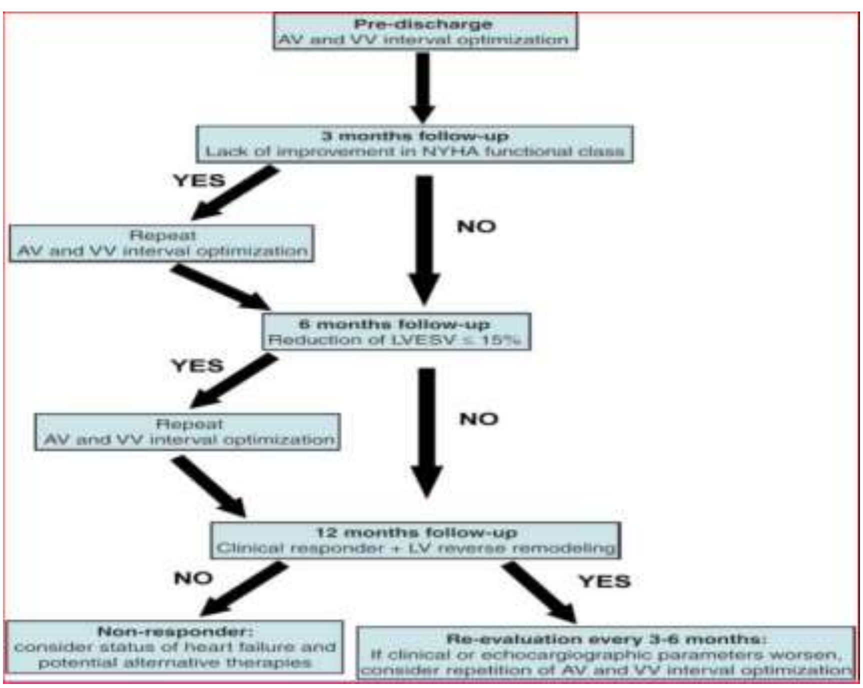
1. E and A wave separated.
2. Termination of the A wave at 40-60 msec before the onset of the QRS.
3. Stage I diastolic filling pattern i.e A > E pattern.

Optimize AV Delay to Permit 100% BiV Pacing During Exercise



Timing of Optimization

- **Best evidence-based practice is to follow the CARE-HF protocol and optimize AV delay using the iterative method at:**
  - Baseline(predischarge)
  - 3 months,
  - every 6 months thereafter.



V-V Optimization

- The best V-V setting is by measuring the RVOT & LVOT PW Doppler singnals
- V-V above 40 ms is considered abnormal
- Normally: the RV will contract after the LV by 20 ms

	Simultaneous BiV	Optimized V-V	% Improvement	P
VTI (mm)	122 ± 31	154 ± 42	26%	< .001
LVFT (ms)	404 ± 102	472 ± 110	17%	.001
LVFT/HR (ms/bpm)	6.0 ± 2.0	7.1 ± 2.2	18%	.001
IVD	35 ± 33	13 ± 25	63%	.013
VD	51 ± 34	34 ± 18	33%	.010
SUM dyssynchrony (ms)	86 ± 49	47 ± 31	45%	.002

Van Gelder BM, et al, Effect of optimizing the VV interval on left ventricular contractility in cardiac resynchronization therapy. Am J Cardiol. 2004;93:1500-1503.

CRT Optimization

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Table 5 **Optimization of atrioventricular (AV) delay in cardiac resynchronization therapy clinical trials**

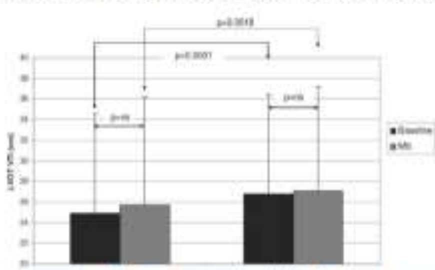
Study acronym	*n*	Echocardiographic optimization method	Alternative optimization method	Follow-up (months)	Timing of optimization after implant	Endpoints		
MUSTIC-SR[4]	48	Ritter's method	None	3	Time of implant	6MWT, +73 m, $P < 0.001$	MLHFQ, −13.6, $P < 0.001$	Peak VO_2, +1.2, $P = 0.029$
MUSTIC-AF[117]	37	None	None	3	None	6MWT, +32 m, $P = 0.05$	MLHFQ −4.3, $P = 0.11$	Peak VO_2 +1.7, $P = 0.04$
MIRACLE[3]	453	Ritter's method	None	6	Pre-discharge, 3 and 6 months	6MWT, +29 m, $P = 0.005$	MLHFQ, −9.0, $P = 0.001$	NYHA, $P < 0.001$
MIRACLE-ICD[5]	369	Ritter's method	None	6	Pre-discharge, 3 and 6 months	6MWT, +2 m, $P = 0.36$	MLHFQ, −6.5, $P = 0.02$	NYHA $P = 0.007$
MIRACLE-ICD II[6]	186	Ritter's method	None	6	Pre-discharge, 6 months	6MWT +5 m, $P = 0.59$	MLHFQ −2.6, $P = 0.49$	Peak VO_2, +0.3, $P = 0.87$
CONTAK-CD[118]	490	None	None	6	None	6MWT, +20 m, $P = 0.043$	MLHFQ, −2, $P = 0.39$	Peak VO_2, +0.8, $P = 0.03$
COMPANION[2]	1520	None	Device-based algorithm	16.2 (Median)	Time of implant	Death, Admission, HR 0.81, $P = 0.015$	Death, HR 0.76, $P = 0.06$	HF Death, Admission HR 0.66, $P = 0.002$
CARE-HF[1]	813	Iterative method	None	29.4 (Mean)	Pre-discharge 3, 9 and 18 months	Death or MACE HR 0.63, $P < 0.001$	Death, HR 0.64, $P = 0.002$	HF Admission, HR 0.48, $P < 0.001$

Major Randomized Trials of CRT AV/VV Optimization

Major trials of AV/VV delay optimization

	N	Technique	Result
Abraham et al. (FREEDOM)[74]	1525	Optimization at implant with standard of care vs. QuickOpt™ AV/VV optimization every 3 months	No difference in 12 month clinical composite score
Ellenbogen et al. (SMART-AV)[17]	980	Fixed AV delay (120 ms), iterative method, or SmartDelay™ AV optimization	No difference in 6 month change in LVESV, NYHA class, QOL, or 6 min walk
Martin et al. (adaptive CRT)[70]	522	Echo optimized AV/VV delays (iterative and aortic VTI) vs. Adaptive CRT algorithm	Adaptive CRT noninferior to echo optimization in clinical composite score (73.6 vs. 72.5% improved)
Ritter et al. (CLEAR)[30]	238	Standard of care optimization (mostly echo) vs. PEA AV/VV optimization algorithm	Significantly more improved in clinical composite score with PEA vs. standard of care (76 vs. 62%)

A Prospective Randomized Evaluation of VV Delay Optimization in CRT-D Recipients: Echocardiographic Observations from the RHYTHM II ICD Study



V-V delay optimization was associated

-with better immediate hemodynamic function than simultaneous biventricular stimulation,

-did not promote additional reverse remodeling at 6 Mos

-did not increase the proportion of echocardiographic responders to CRT

PACE 2009; 32:S120–S125

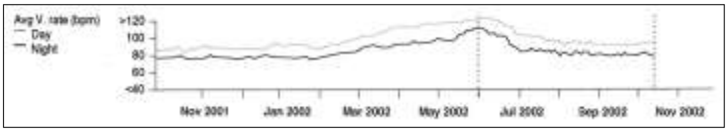
CRT Optimization

- Device (PM/ ICD) optimization
- CRT (HF therapy) optimization
- **Patient Optimization**

Patient Optimization

- Device Interrogation
- NYHA Class
- 6 minute walking test
- BNP
- Echocardiography
- Responder status
- Overall wellbeing and Activity

Patient Follow-up: HR trend



- With worsening of HF, HR increases during the day and night.
- This is indicative of increased SNS activity

– Patients with increased average HR need to be seen more frequently until HR return to baseline/normal

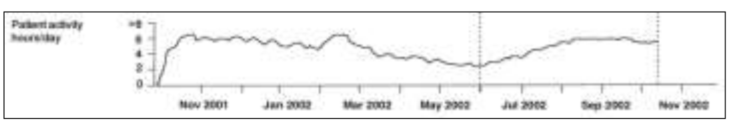
– Assess for signs/symptoms of decompensation

– Verify adherence to low sodium diet and medication regimen

– BNP levels may be useful in diagnosing decompensation

- Correlate with HRV and activity for more insight into overall status

Patient Follow-up: Activity



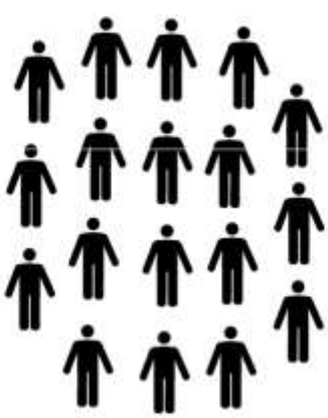
- Goal: 30 minutes 5x/week
- Patient physically active -> Encourage continued or increased activity
- Activity levels decreased -> Correlate with symptoms, clinical exam, and other trend data to identify possible cause, e.g. decompensation, arrhythmias
- Patient remains inactive and is clinically stable -> encourage increased activity

CRT OPTIMIZATION IN THE GUIDELINES

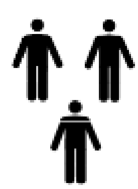
- 2013 ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR CRT guidelines:
- Posterolateral LV lead position, the target of latest activated area and avoidance of apical position.
- A shortest AV delay without truncation of the A-wave (Ritter's method) or change in LV systolic function
- The largest stroke volume by Echo Doppler is recommended as CRT optimization about VV delay
- The 2016 ESC guidelines suggest that echocardiography may be considered for patients who have had a disappointing response to CRT

CONCLUSIONS

Who wants to implant CRT?



Who wants to Optimize CRT?



Conclusion

- CRT could be implanted by a cardiologist who has good invasive skills
- However, only few who could precisely follow-up their patients post implantation to maximize & optimize their benefits from CRT
- CRT Optimization aims to increase the likelihood of being a good, or even super, responder to this impotent HF therapy
- It should be tailored to the patient
- This includes: Device, CRT, and Patient HF status Optimization

Cardiac Resynchronization Therapy Optimization: Still Have a Role?!

Yes


Thank You!
Ahmed Tageldien