

CRT in the RV Paced Patient – When to Upgrade?

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Disclosure

Conflict of Interest Statement:

I will follow standard conflict-of-interest guidelines and not advertise any commercial product during the presentation.

I have no a significant financial interest or other relationship with the manufacturer of a product or service to be discussed in my presentation.

CRT – State of the Art

- CRT, is an electrical intervention aimed at resolving the LV electrical dyssynchrony and alleviate HF.
- Although LV electrical dyssynchrony is assessed by QRSd and it is used as an indicator for choosing pts for CRT, recent data¹⁻⁴ show that additional evaluation of electrical and mechanical dyssynchrony⁵ may improve results of CRT.
- CRT has proved to be effective in selected pts (50 -70% of pts are responders).⁶
- However, little is known about CRT in RV paced pts with HF⁶, where frequently electrical dyssynchrony is not evident or cannot be assessed by native ECG .

1. Steffel J, et al. *Eur Heart J*. 2015 Aug;36:1983.

2. Cleland JGF, et al. *Eur Heart J* 2015 36: 1948.

3. Gold MR, et al. *Circulation* 2012;126:822.

4. Tereshchenko L, et al. *Heart Rhythm*. 2015;Sept

5. Risum N, et al. *JACC* 2015;66:631.

6. ESC Guidelines. *Eur Heart J* 2013;34:2281.

Scope of the Problem

Upgrading of RV Paced Patients to CRT Will be Discussed

- How many RV paced pts have LVEF \leq 35% with signs of HF?
- How of them can be candidates for CRT?
- How to assess the chance of RV paced patients with HF to respond to upgrading to CRT?



Characteristics of a large sample of candidates for permanent ventricular pacing included in the Biventricular Pacing for Atrio-ventricular Block to Prevent Cardiac Desynchronization Study (BioPace)

Reinhard C. Funck^{1*}, Hans-Helge Mueller², Maurizio Lunati³, Christopher Piorkowski⁴, Luc De Roy⁵, Vince Paul⁶, Michael Wittenberg⁷, David Wuensch⁸, and Jean-Jacques Blanc⁹ for the BioPace study group

Funck RC, et al. *Europace* 2014;16:354.

The BioPace trial used a sample (1800 RV paced pts) representing European pacing population (94 MCs, from 15 European countries):

- In 8.4% of European pacing population there is severe LV dysfunction, i.e. $LVEF \leq 35\%$.
- In U-Europe are implanted/year $\sim 470,000$ pacemakers¹⁻³ (500 million population and ~ 940 implants/million).¹⁻³
- Thus, in U-Europe expected 39,000 (i.e. 8.4%) RV paced pts with $LVEF \leq 35\%$; part of them are potential candidates for upgrading to CRT.

1. Medtronic Inc.

2. www.eucomed.org 2014

3. ESC Guidelines *Eur Heart J* 2013;34:2281.

Characteristics of a large sample of candidates for permanent ventricular pacing included in the Biventricular Pacing for Atrio-ventricular Block to Prevent Cardiac Desynchronization Study (BioPace)

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Europace 2014;16:354.

- Among pts with HF 5-10%/yr are candidates for CRT¹, i.e. 0.84% (10% from 8.4%) of RV paced pts are candidates for CRT or:
 - ✓ ~ 2000-4000 RV paced pts can be candidates for upgrading to CRT in U-Europe (0.42-0.84% from total number of PMs implants/year).
- About 25% (~ 500-1000) of candidates for CRT are pts with pacing induced cardiomyopathy and remaining with ischemic and dilated cardiomyopathy.²⁻⁵

1. ESC Guidelines *Eur Heart J* 2013;34:2281.
2. Thambo JB, et al. *Circulation* 2004;110:3766.
3. Dreger et al. *Europace* 2010;14:238
4. Sagar S, et al. *Circulation* 2010;121:1698.
5. Bordachar P, et al. *Heart Rhythm* 2013; 10:760

Scope of the Problem

Upgrading of RV Paced Patients to CRT

- In how many RV paced pts have LVEF $\leq 35\%$ with signs of HF?
- How of them can be candidates for CRT?
- How to assess the chance of RV paced patients with HF to respond to upgrading to CRT?

LV Electrical Dyssynchrony as Main Sign for Choosing Candidates for CRT

- For CRT current guidelines recommend pts with LBBB and QRSd >150 ms by ECG alone, whereas the role of CRT in pts with QRSd ≤150 ms with LBBB, LBBB-like, or non-LBBB morphology is less well established.¹
- Response to CRT according to Randomized CT and registries occurs in 50-70% of pts.¹
- For the last several years new data has accumulated regarding CRT.²⁻⁶

1. ESC Guidelines *Eur Heart J* 2013;34:2281.
2. Ruschitzka F, et al. *NEJM* 2013;369:1395.
3. Steffel J, et al. *Eur Heart J* 2015; 36:1983.
4. Risum N, Sogaard P. *JACC* 2015;66:631.
5. Gold MR, et al. *Eur Heart J*. 2011;32:2516.
6. Tereshchenko LG, et al. *Heart Rhythm*. 2015 Epub ahead of print

Identification of Typical Left Bundle Branch Block Contraction by Strain Echocardiography Is Additive to Electrocardiography in Prediction of Long-Term Outcome After Cardiac Resynchronization Therapy



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Magnus T. Jensen, MD, PhD,|| Trine K. Lauridsen, MD,§ Samir Saba, MD,† Joseph Kisslo, MD,¶ John Gorcsan III, MD,†
Peter Sogaard, MD, DMSc|

JACC 2015;66:631

The main findings of the study¹ were:

- In 37% of pts with LBBB by ECG, at 2D strain Echo (2DSE) typical contraction pattern of LBBB was absent.
- Pts with typical LBBB had a wider QRSD (163 ± 23 vs. 153 ± 22 ; $p < 0.004$) and pts with atypical LBBB responded to CRT with a more than 3-fold increase in the risk of adverse events.
- These observations correlated well with previous data:² in LV endocardial mapping in one-third of pts with “typical” LBBB by ECG, recorded normal transseptal activation time and near-normal LV endocardial activation time.

1. Risum N, ...Sogaard P. *JACC* 2015;66:631.
2. Auricchio A, et al. *Circulation*. 2004;109:1133.

The effect of QRS duration on cardiac resynchronization therapy in patients with a narrow QRS complex: a subgroup analysis of the EchoCRT trial

Jan Steffel¹, Michele Robertson², Jagmeet P. Singh³, William T. Abraham⁴, Jeroen J. Bax⁵, Jeffrey S. Borer⁶, Kenneth Dickstein⁷, Ian Ford², John Gorcsan III⁸, Daniel Gras⁹, Henry Krum¹⁰, Peter Sogaard¹¹, Johannes Holzmeister¹, Josep Brugada¹², and Frank Ruschitzka^{1*}

- In subgroup analysis of EchoCRT Trial pts with QRSd ≤ 130 ms had no electrical dyssynchrony and no benefit from CRT. Moreover, CRT in these pts associated with higher all-cause mortality than in pts without CRT. *“These data further question the usefulness of CRT in this patient population.”*¹
- Of note, an ESC CRT Survey conducted in 13 countries, reported that 19% of CRT pts had QRSd < 130 ms, i.e. every fifth patient (!), who received CRT, *a priori* has no benefit and may even have harmful effects from CRT.²

1. Steffel J, et al. *Eur Heart J* 2015; 36:1983.

2. Dickstein K, et al. *Eur Heart J* 2009;30:2450.

LV Electrical Delay/Dyssynchrony and Respond to CRT

- Important data demonstrated regarding LV electrical delay and respond to CRT.
- Among LBBB pts LV electrical delay was 100 ± 35 ms compared with 73 ± 30 ms for non-LBBB pts ($P < 0.001$).
- For QRSd >150 ms, LV electrical delay was 113 ± 33 ms, compared with 78 ± 30 ms for QRS <150 ms ($P < 0.001$).
- The best outcomes were observed with LV electrical delay >95 ms with/without LBBB; this target is recommended when selecting LV lead position at the time of CRT implantation.

Gold MR, et al. *Eur Heart J.* 2011;32:2516.

Narrow/Wide QRS and LV Electrical Dyssynchrony

Putting all the available evidence together, it would appear that:

- CRT in pts with QRSd ≤ 130 ms increases HF mortality and HF hospitalization.¹⁻⁴
- Response to CRT among pts with QRS < 150 ms is low to moderate⁵ and can be facilitated by:
 - ✓ Exclusion of pts with QRSd ≤ 130 ms¹⁻⁴
 - ✓ Evaluation of pts with LBBB by 2DS Echo and exclusion atypical LBBB⁶
 - ✓ Evaluation LV electrical delay/dyssynchrony.^{7,8}

1. Steffel J, et al. *Eur Heart J* 2015; 36:1983.

2. Ruschitzka F, et al. *NEJM* 2013;369:1395.

3. Beshai JF, et al. *NEJM* 2007;357:2461.

4. Shah et al. *Europace* 2015;17:267.

5. ESC Guidelines *Eur Heart J* 2013;34:2281.

6. Risum N, Sogaard P. *JACC* 2015;66:631.

7. Gold MR, et al. *Eur Heart J*. 2011;32:2516.

8. Tereshchenko L, et al. *Heart Rhythm*. 2015;InPrint

Indication for Upgrading to CRT Patients with Conventional Pacemaker and HF

European Heart Journal Advance Access published June 24, 2013



European Heart Journal
doi:10.1093/eurheartj/ehs150

ESC GUIDELINES

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

The Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA).

Authors/Task Force Members: Michele Brignole (Chairperson) (Italy)*, Angelo Auricchio (Switzerland), Gonzalo Baron-Esquivias (Spain), Pierre Bordachar (France), Giuseppe Boriani (Italy), Ole-A Breithardt (Germany), John Cleland (UK), Jean-Claude Deharo (France), Victoria Delgado (Netherlands), Perry M. Elliott (UK), Bulent Gorenek (Turkey), Carsten W. Israel (Germany), Christophe Leclercq (France), Cecilia Linde (Sweden), Lluís Mont (Spain), Luigi Padeletti (Italy), Richard Sutton (UK), Panos E. Vardas (Greece)

Indication for Upgrading to CRT Patients with Conventional Pacemaker and HF

Recommendations	Class ^a	Level ^b	Ref. ^c
1) Upgrade from conventional PM or ICD. CRT is indicated in HF patients with LVEF <35% and <u>high percentage of ventricular pacing</u> who remain in NYHA class III and ambulatory IV despite adequate medical treatment. ^d	I	B	47, 108–122

ESC Guidelines. *Eur Heart J* 2013;34:2281.

CRT, is an electrical intervention aimed at resolving the LV electrical dyssynchrony and alleviate HF.

There are 4 small randomized studies (total number of 118 pts).

ESC Guidelines. *Eur Heart J* 2013;34:2281.

Studies	No. of patients	Echo, ESD (%)
RCT, cross-over design, upgraded CRT vs RV		
Holjer ¹¹⁰	10	-2
Leclercq ¹⁰⁸	32	-4
van Gerloep ¹¹¹	36	-9
Delnoy ¹⁰⁹	40	-31
Total	118	-6
Observational studies, post-CRT upgrading vs. pre-CRT		
Leon ¹¹⁵	20	-8
Baker ¹¹²	60	-
Valls ¹¹⁷	14	-8
Eldadah ¹¹³	12	-
Shimano ¹¹⁶	18	-
Laurenzi ¹¹⁴	38	-5
Vatankulu ¹¹⁸	26	-13
Total	188	-7

Response to CRT

- Response to CRT is defined as $\geq 15\%$ decrease in LV end-systolic volume (LVESV)¹, because LV end systolic volume is accepted as a predictor of mortality/morbidity in HF pts.²

1. ESC Guidelines *Eur Heart J* 2013;34:2281.
2. Braunwald E. *Circulation*. 1990;81:1161.

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There are 4 small randomized studies (total number of 118 pts). In these studies 77% of pts were non-responders to CRT upgrading. Worst results demonstrated in observational studies.

ESC Guidelines. *Eur Heart J* 2013;34:2281.

“upgrading to CRT pacing is likely to reduce hospitalization and improve their symptoms and cardiac performance. However, the quality of evidence is moderate and further research is likely to have an important impact on our confidence in the estimate of effect and might change the estimate. Upgrade to CRT is associated with a high complication rate, which was 18.7% in a recent large prospective trial.”^{w163}

^{w163}Poole JE. *Circulation* 2010;122:1553

Upgrading to CRT in RV Paced Patients with Conventional Pacemaker and HF

Summary of Current State

- According to theoretical speculations and common sense CRT for RV paced pts with HF and low LVEF should be effective.

"All true knowledge contradicts common sense."
Mandell Creighton, Cambridge professor of British history and a Bishop of the Church of England

- Upgrading of RV paced pts to CRT seems complicated and uncertain and warrants RCT with selection of pts for upgrading by criteria of electrical and mechanical dyssynchrony.

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Indication for Upgrading RV Paced Patients with HF to CRT- 1

There are two groups of pts with RV pacing and HF:

- Group I includes pts with visible native ECG. This group includes 2 subgroups:
 - ✓ Group IA are the pts with approved clinical signs of electrical dyssynchrony. These pts are candidates for upgrading to CRT when optimal medical therapy was noneffective. Expected response to CRT in such pts is similar to that in pts without RV pacing. *Class IIa, Level B*
 - ✓ Group IB are the pts without accepted signs of electrical dyssynchrony. For these pts CRT is not indicated and may be harmful. However, pacing from LV alone may be better than from RV, especially in pts with pacing induced CM. This approach warrants randomized study.

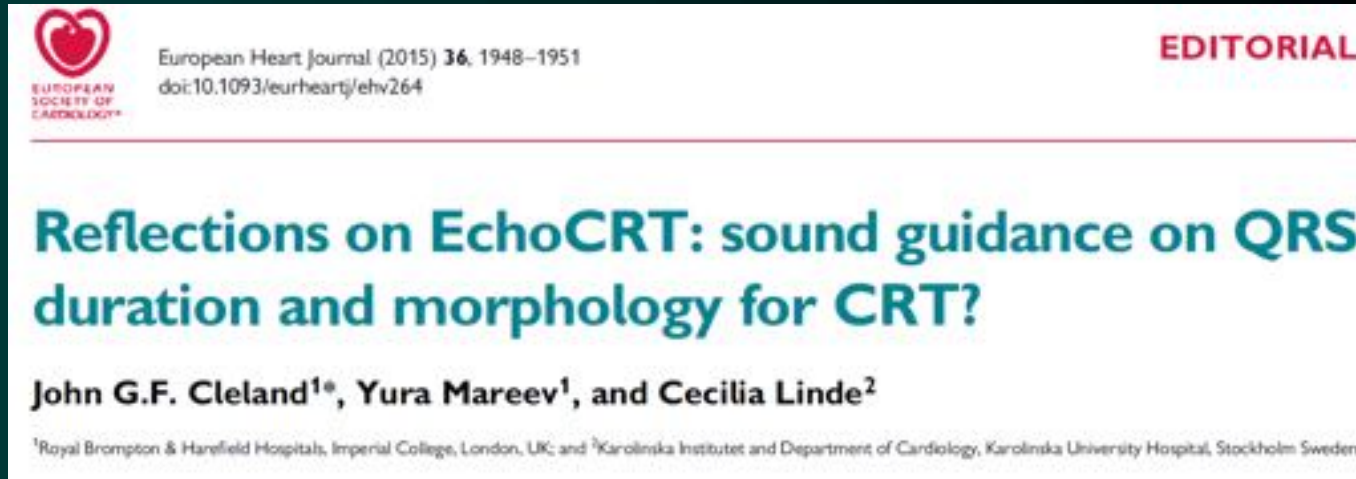
Indication for Upgrading to CRT Patients with Conventional Pacemaker and HF - 2

- Group II includes pts without native ECG – i.e., pts with complete AV Block and unavoidable/permanent RV pacing.
- Because assessment of LV dyssynchrony in these pts is impossible, response to CRT is unpredictable and may be harmful in some pts. Nevertheless, pacing from LV alone may be better than from RV. This approach warrants randomized study separated by subgroups according to paced QRSd.

Take Home Message - 1

- Any pacing is non-physiological, including CRT; if CRT is used in the heart where there is no dyssynchrony, CRT can induce it and decrease LV function or facilitate previous dysfunction.
- Before upgrading a patient with RV pacing to CRT:
 - ✓ Check exact place of RV lead and make sure that it is the optimal location (RV apical pacing is preferable).
 - ✓ Check LV dyssynchrony and electrical delay.
 - ✓ LBBB should be differentiated from LBBB-like.
- The decision to upgrade should be made after careful assessment of the risk–benefit ratio.

Take Home Message -2



"The efficacy of CRT relies on its benefits exceeding any harm that it might do. Identifying patients in whom CRT is harmful (QRSd \leq 130 ms) and ensuring they avoid CRT will increase the average effect and the proportion who respond amongst patients who remain indicated for CRT. This should increase appropriate and efficient use of medical resources and overall benefit."

Take Home Message -3



With CRT 
Live the pleasure
if it properly using!!!



Cardiac Arrhythmias 2016

The 13th International Dead Sea Symposium (IDSS)
on Innovations in Cardiac Arrhythmias and Device Therapy
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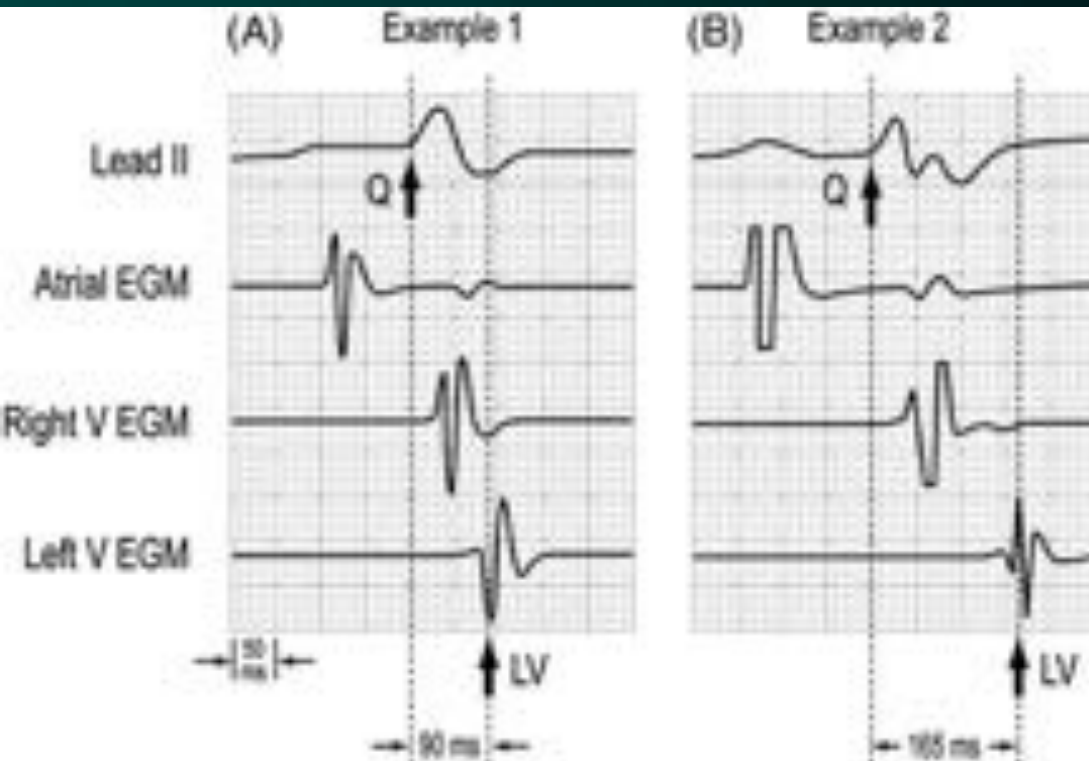
See You in
March 6-9, 2016
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IDSS Secretariat
Email: idss@idss-ep.com

Back-up slides

Evaluation of LV Electrical Delay/Dyssynchrony by Measurement of QLV Interval



- The QLV interval should be measured in sinus rhythm and without of pacing.
- It is the interval from the onset of QRS from the surface ECG to the first large positive or negative peak of the LV EGM during a cardiac cycle. (The amplitude of the first large peak needed to be >50% of the amplitude of the largest peak in the same cardiac cycle.)

Upgrading to CRT in Patients with Conventional Pacemaker and HF

- Additional argument for upgrading to CRT is based on the results of BLOCK-HF trial.^{1,2}
- This study was recently hardly criticized³; as well results of BioPace trial are rejected such approach.⁴

1. Curtis AB, et al. *NEJM* 2013;368:17;
2. St John Sutton M et al. *Circ HF*. 2015;8:510.
3. Arenas I, et al. *Circ Arrhythm EP*. 2015;8:730.
4. BIOPACE trial. ESC Congress Barcelona, 2014.

Circulation: Heart Failure

2015;8:510-518.



Left Ventricular Reverse Remodeling With Biventricular Versus Right Ventricular Pacing in Patients With Atrioventricular Block and Heart Failure in the BLOCK HF Trial

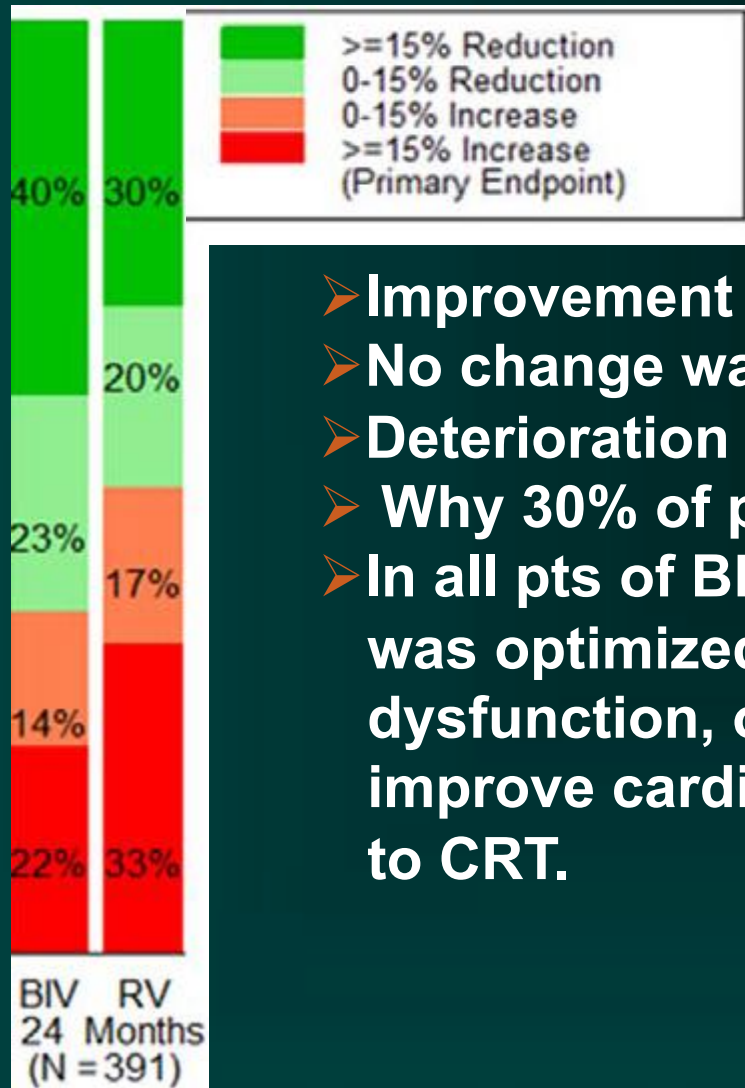
Martin St. John Sutton, MBBS; Ted Plappert, CVT; Philip B. Adamson, MD; Pei Li, PhD; Shelly A. Christman, PhD; Eugene S. Chung, MD; Anne B. Curtis, MD

- Methods: BLOCK HF trial randomized to BiV or RV pacing pts with AVB, NYHA classes I-III, QRSd ~125ms; LBBB and LVEF < 35% were in ~30% of pts; most of these pts already might benefit from CRT.
- The % of ventricular pacing was >97% for both pacing groups when 50% of participants were not in complete HB and could benefit minimization ventricular pacing.
- Results. LV end systolic volume index (LVESVI) was used as predictor of mortality/morbidity and HF hospitalization

Braunwald E. *Circulation*. 1990;81:1161.

Reverse Remodeling With BiV Pacing

Distribution of subjects by degree of change in LVESVI (LV end systolic volume index) from randomization



Results of Upgrading

At 24 mo. after upgrading pts with RV pacing and low EF, there were:

- Improvement in 10% more than in RV group
- No change was in 3% more than in RV group
- Deterioration was in 14% less than in RV group
- Why 30% of pts with RV pacing improved?
- In all pts of BLOCK-HF trial “HF medical therapy was optimized”, i.e. in 30% of RV pacing pts with LV dysfunction, optimization of medical treatment can improve cardiac state in same status as upgrading to CRT.

BLOCK HF Trial. *Circ Heart Fail.* 2015;8:510-518.

Circulation: Heart Failure

2015;8:510-518.



Left Ventricular Reverse Remodeling With Biventricular Versus Right Ventricular Pacing in Patients With Atrioventricular Block and Heart Failure in the BLOCK HF Trial

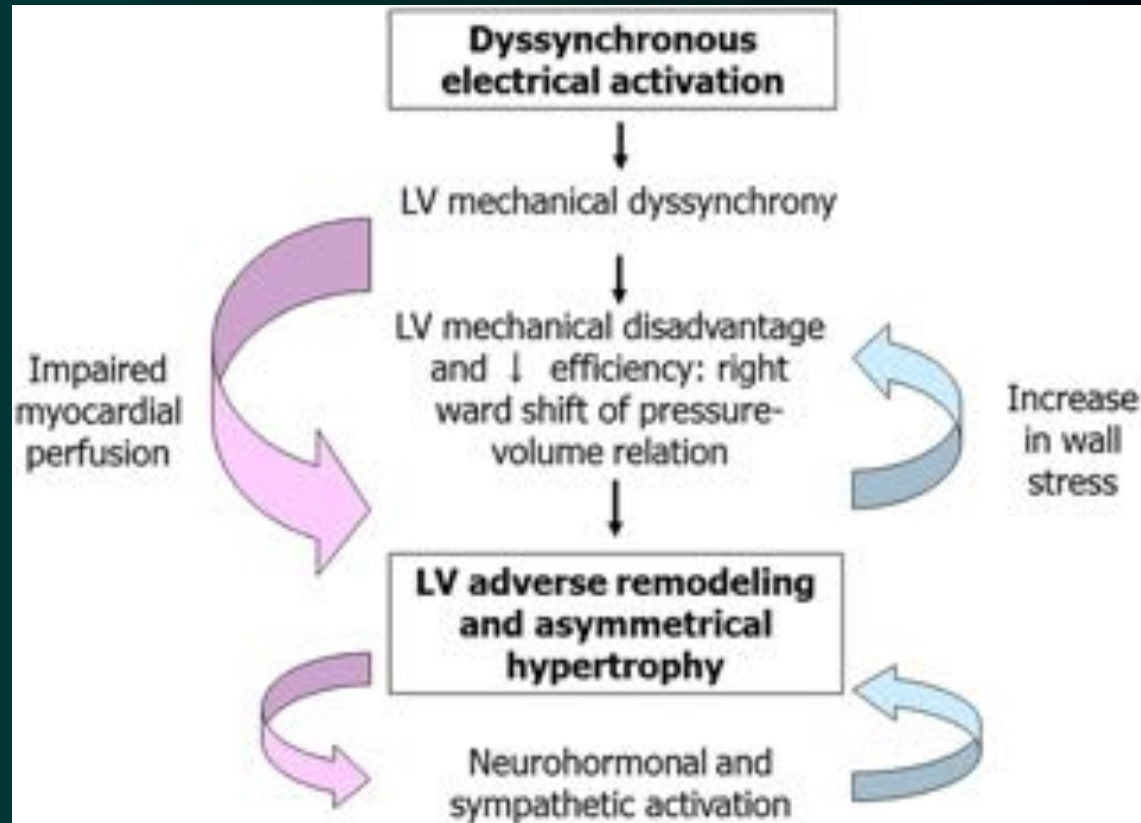
Martin St. John Sutton, MBBS; Ted Plappert, CVT; Philip B. Adamson, MD; Pei Li, PhD; Shelly A. Christman, PhD; Eugene S. Chung, MD; Anne B. Curtis, MD

Conclusions

In BLOCK-HF trial demonstrated:

- In 30% of RV pts with AVB and LV dysfunction, LVESVI can be improved and in 20% of these pts progress in LV dysfunction can be prevent by optimal medical therapy.
- At least 10% of RV pts with AVB may have significant advantage in LV remodeling from CRT.
- In 40% of RV pacing pts with AVB, CRT can be considered only after evaluation of electrical conduction delay and demonstrating ventricular desynchronization.

Pathophysiological Mechanism of RV Pacing – Induced Electric Dyssynchrony



CRT can help only to patient who has both electrical and mechanical dyssynchrony

Disadvantages of Upgrading to CRT

In the decision-making process concerning upgrade to CRT RV paced patient, should take into account:

- Complication rate (up to 18.7%), related to the more complex BiV system (the rate of complications may be significantly higher in clinical practice)
- Requires the use of contrast agents
- Longer fluoroscopic time
- The shorter service life of CRT devices
- The additional costs.

RV Pacing Induced Cardiomyopathy

- In non-selected pts with complete AV block the prevalence of RV pacing induced cardiomyopathy is ~1% per year.
- Probability of RV pacing inducing cardiomyopathy in pts with SND, appropriately treated, close to zero.
- The risk of PICM and HF after pacemaker implantation is not solely the result of abnormal ventricular activation, but instead an interaction between pacing and abnormal cardiac substrate (myocardial as well as electrical) and anterior-free wall position of RV lead.
- In pts without heart disease, RV pacing in any position, does not appear to have a significant detrimental effect on heart size or performance at least for 1st decade of pacing.

Summary-5

- Any RV-pacing is not ideal, but it is the best modality that we currently have for treatment brady-arrhythmias.
- RV-apical pacing is not a disease but a therapeutic modality with potentially harmful side effects which can be prevented or treated.

Electrical Dyssynchrony and QRS Duration

- Electrical dyssynchrony was observed in:
 - ✓ 23.3% of pts with HF and QRSd \leq 100ms
 - ✓ 86.7% pts with QRSd \geq 120ms.
- Conclusions: To identify the potential responders for CRT, both QRS duration and electrical synchrony should be assessed.

Niu H¹, Hua W, Zhang S, Sun X, Wang F, Chen K, Chen X. *Echocardiography*. 2007;24(4):348-52