CRT in congenital and paediatric heart disease

From immediate hemodynamic improvement to long-term benefit…

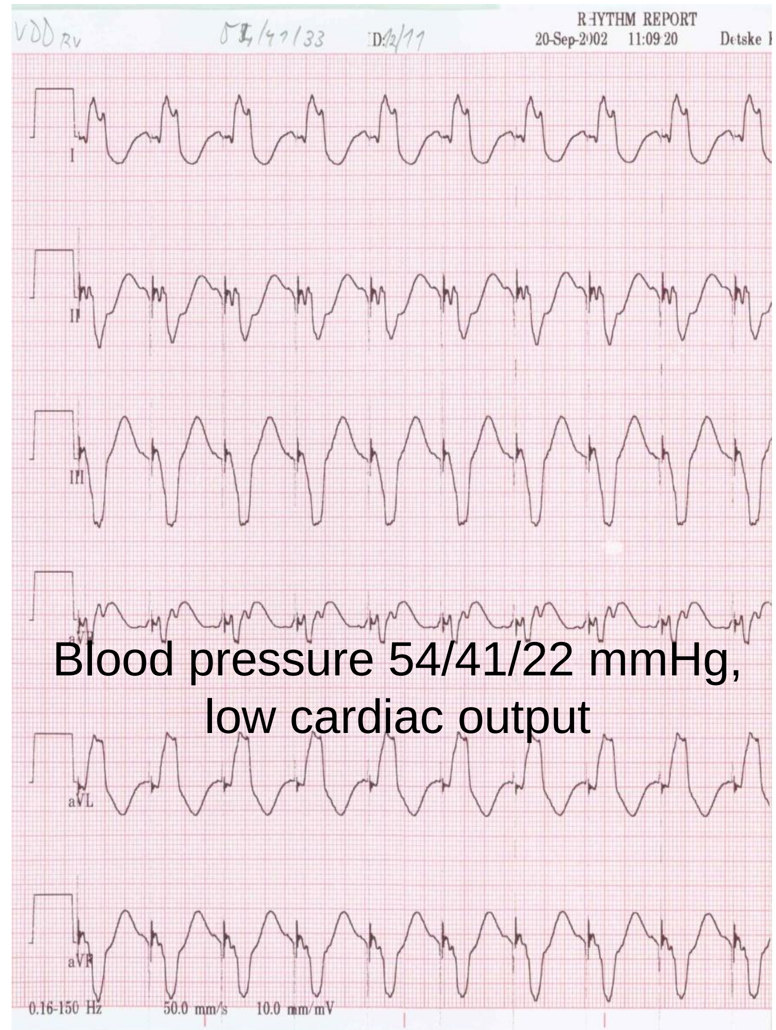
P. Kubuš, J. Janoušek

Children’s Heart Center

Univ. Hosp. Motol

Prague, Czech Republic

Acute resynchronization to improve cardiac output



Blood pressure 54/41/22 mmHg,
low cardiac output

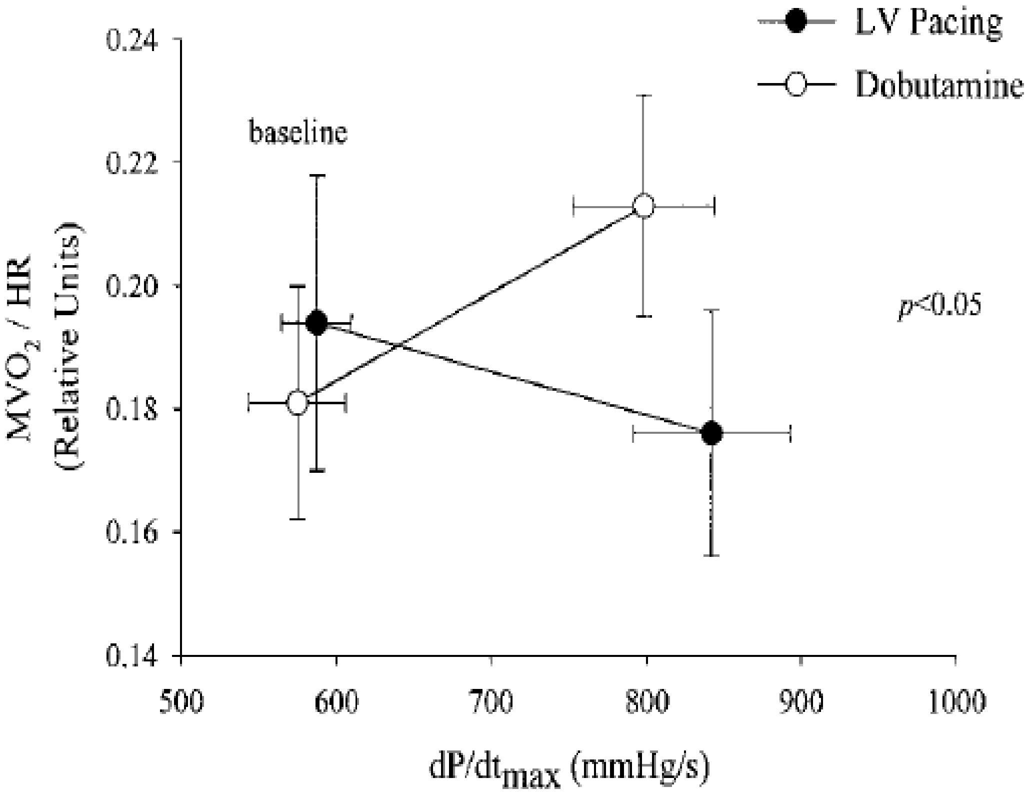
Components of cardiac output

- Heart rate
- Contractility
- Preload
- Afterload

AND

- Synchrony!

CRT - improved cardiac function at diminished energy cost

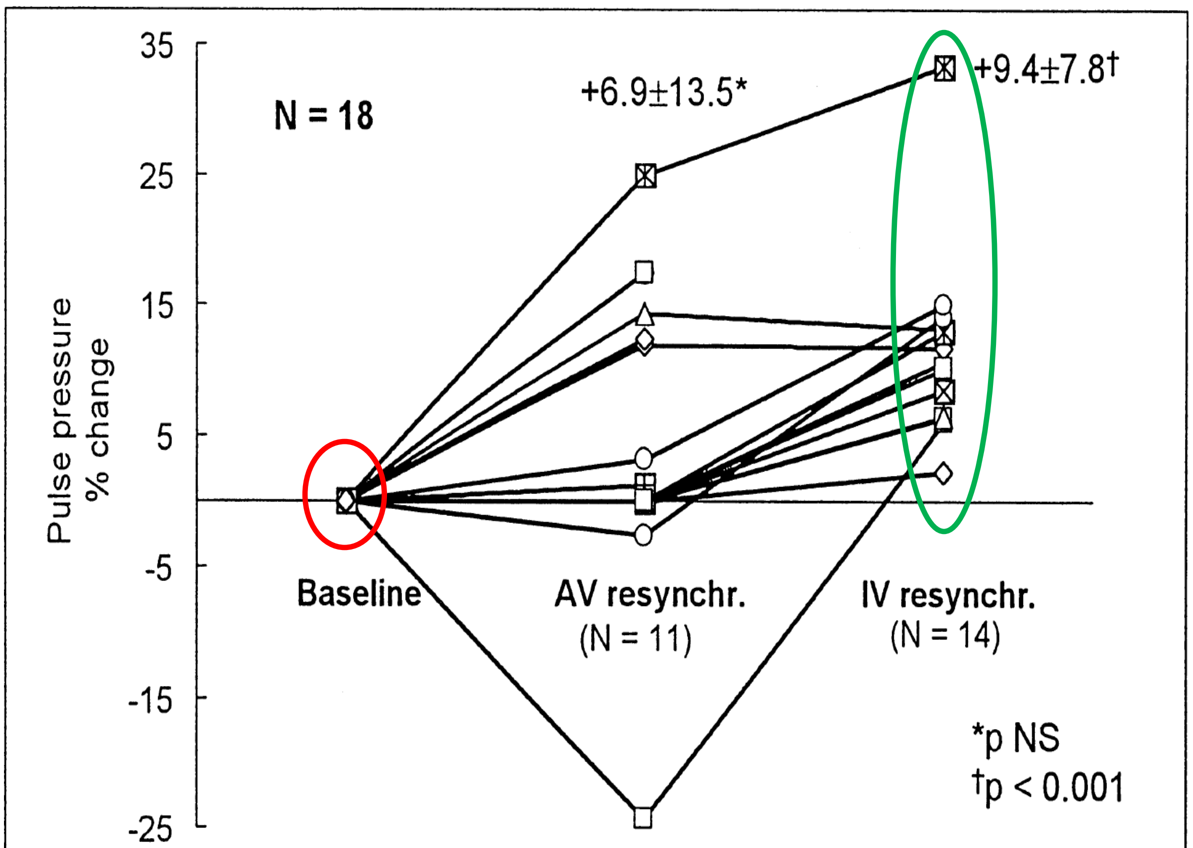


Nelson GS et al., Circulation 2000

Resynchronization Pacing Is a Useful Adjunct to the Management of Acute Heart Failure After Surgery for Congenital Heart Defects

Jan Janoušek, MD, Pavel Vojtovič, MD, Bohumil Hučín, MD, Tomáš Tláskal, MD, Roman Antonín Gebauer, MD, Roman Gebauer, MD, Tomáš Matějka, MD, Jan Marek, MD, and Oleg Reich, MD

(Am J Cardiol 2001;88:145–152)

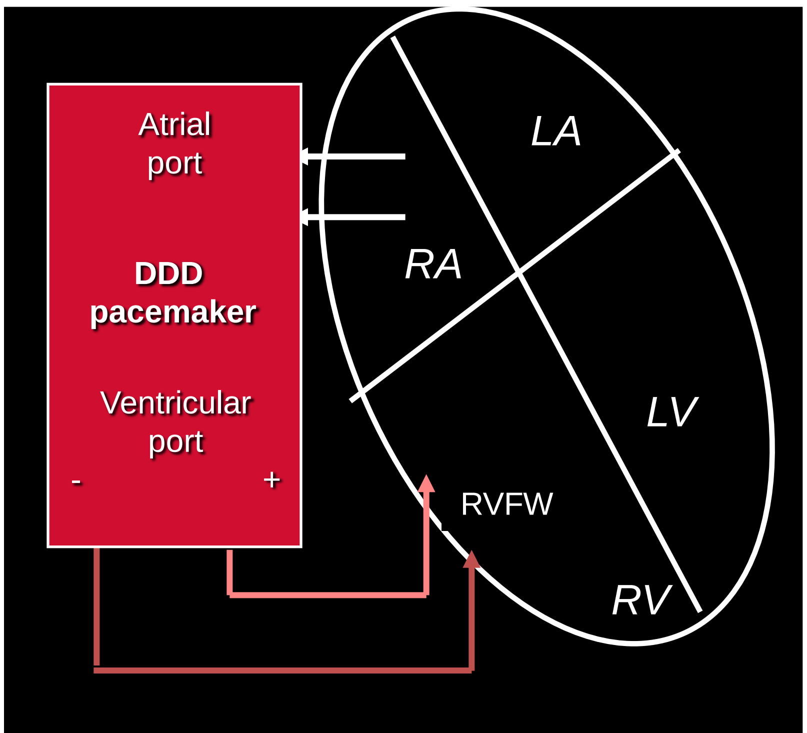


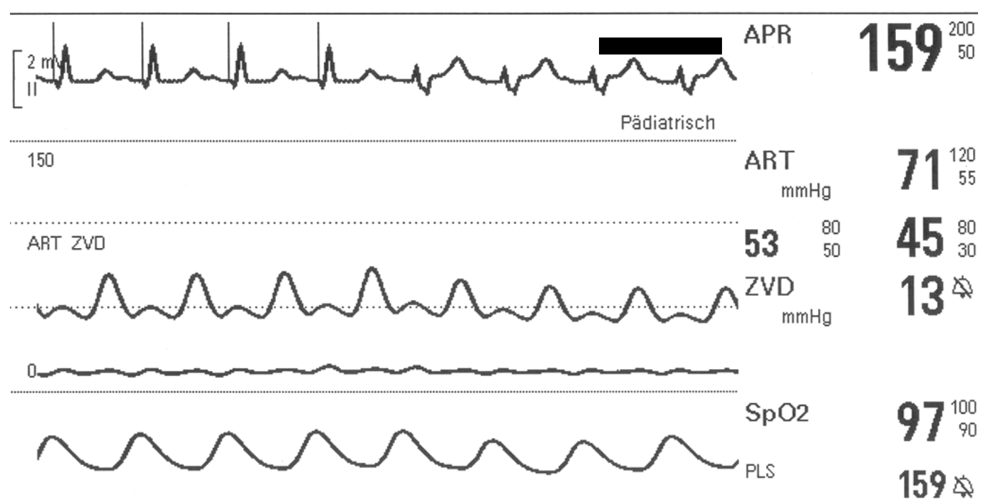
Acute right ventricular resynchronization improves haemodynamics in children after surgical repair of tetralogy of Fallot

Pavel Vojtovič*, Filip Kučera, Peter Kubuš, Roman Gebauer, Tomáš Matějka, Tomáš Tláskal, Miroslav Ložek, Jan Kovanda, and Jan Janoušek

Europace 2017

- Atrial-triggered RV free wall pacing (using temporary epicardial pacing leads) **in complete fusion** with spontaneous ventricular activation to achieve maximal QRS duration shortening (N=28)





Acute right ventricular resynchronization improves haemodynamics in children after surgical repair of tetralogy of Fallot

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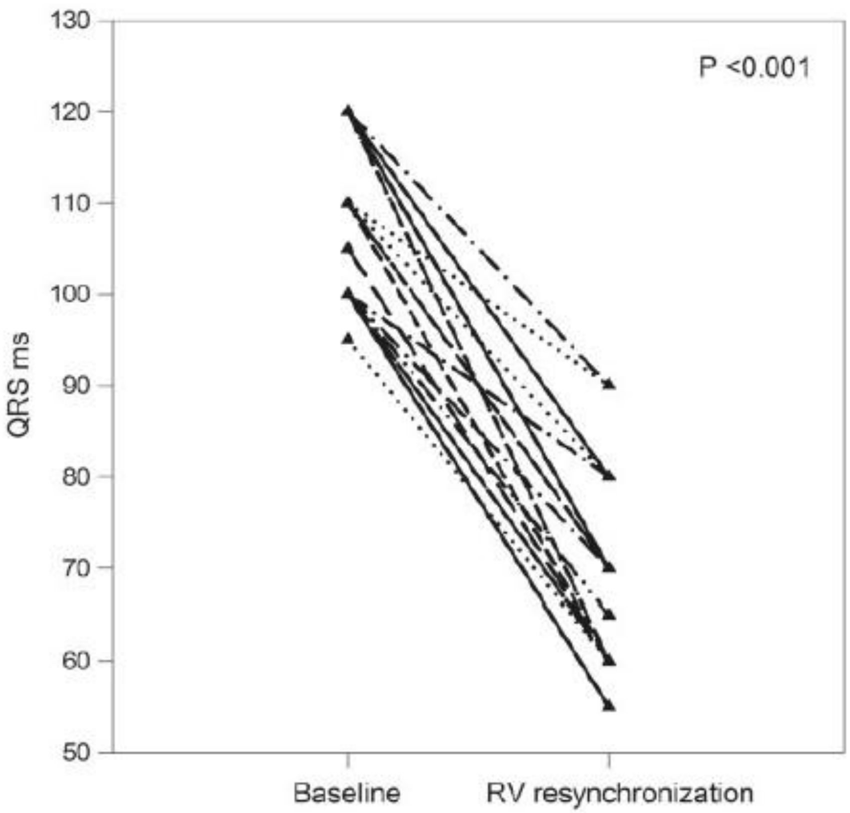
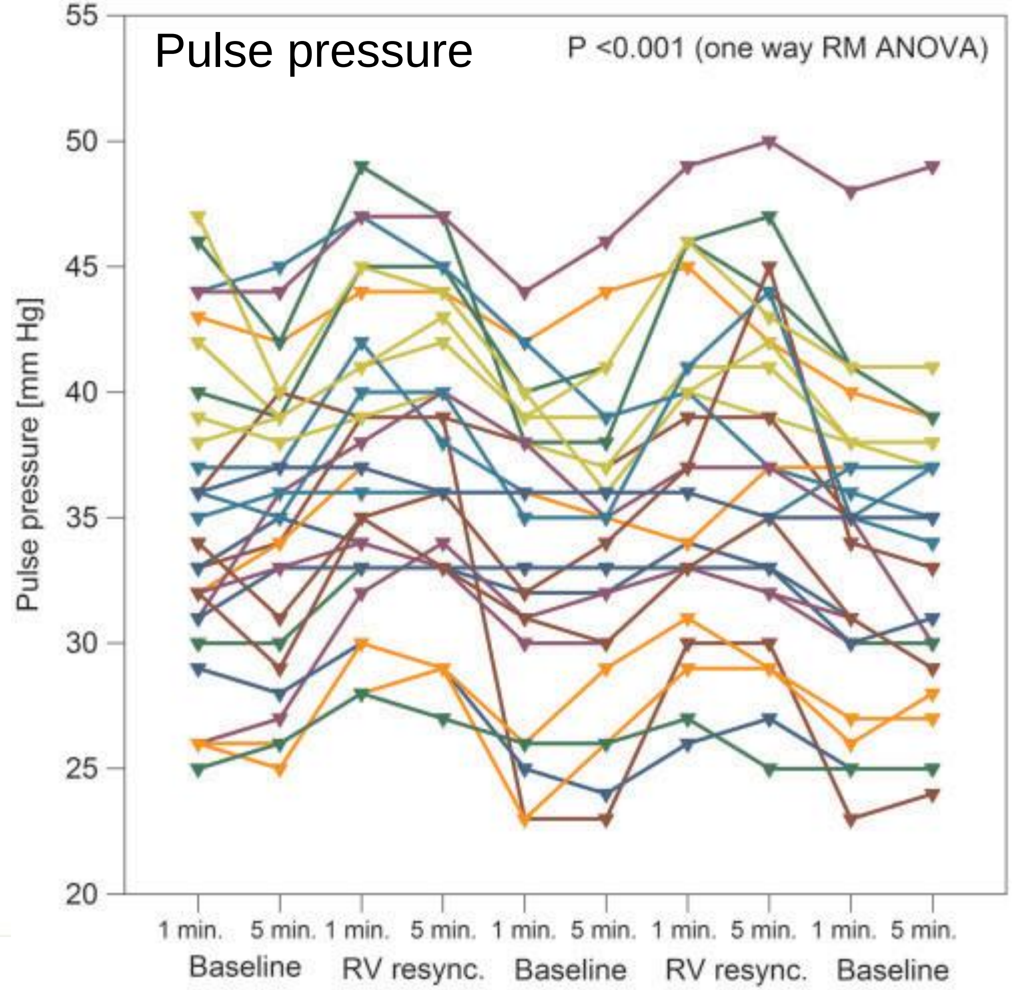
Europace 2017

QRS duration



Pulse pressure



CRT indications in children/congenital heart disease (CHD)

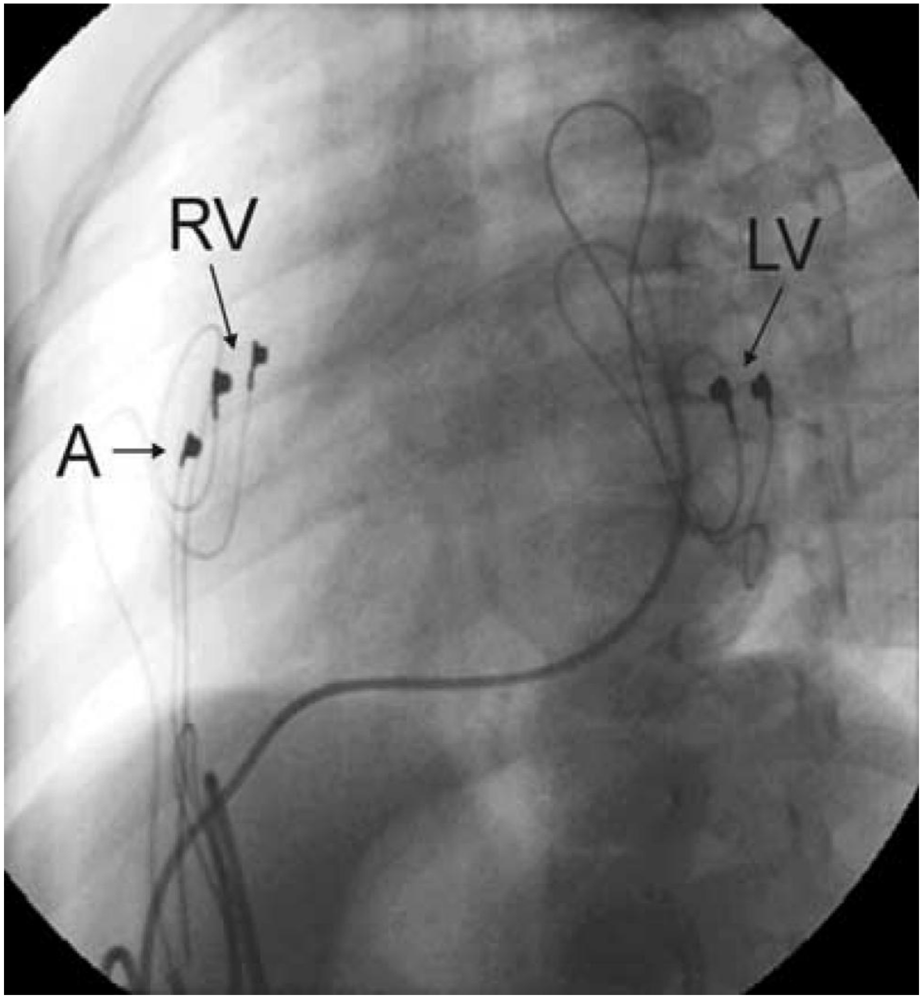
- Systemic LV
  - LBBB
  - RV pacing
- Systemic RV
  - RBBB
  - LV pacing
- Single ventricle
  - Any bundle branch block
  - „Single site“ pacing
- Subpulmonary RV?
  - RBBB

→ „classic“ CRT (Systemic LV)

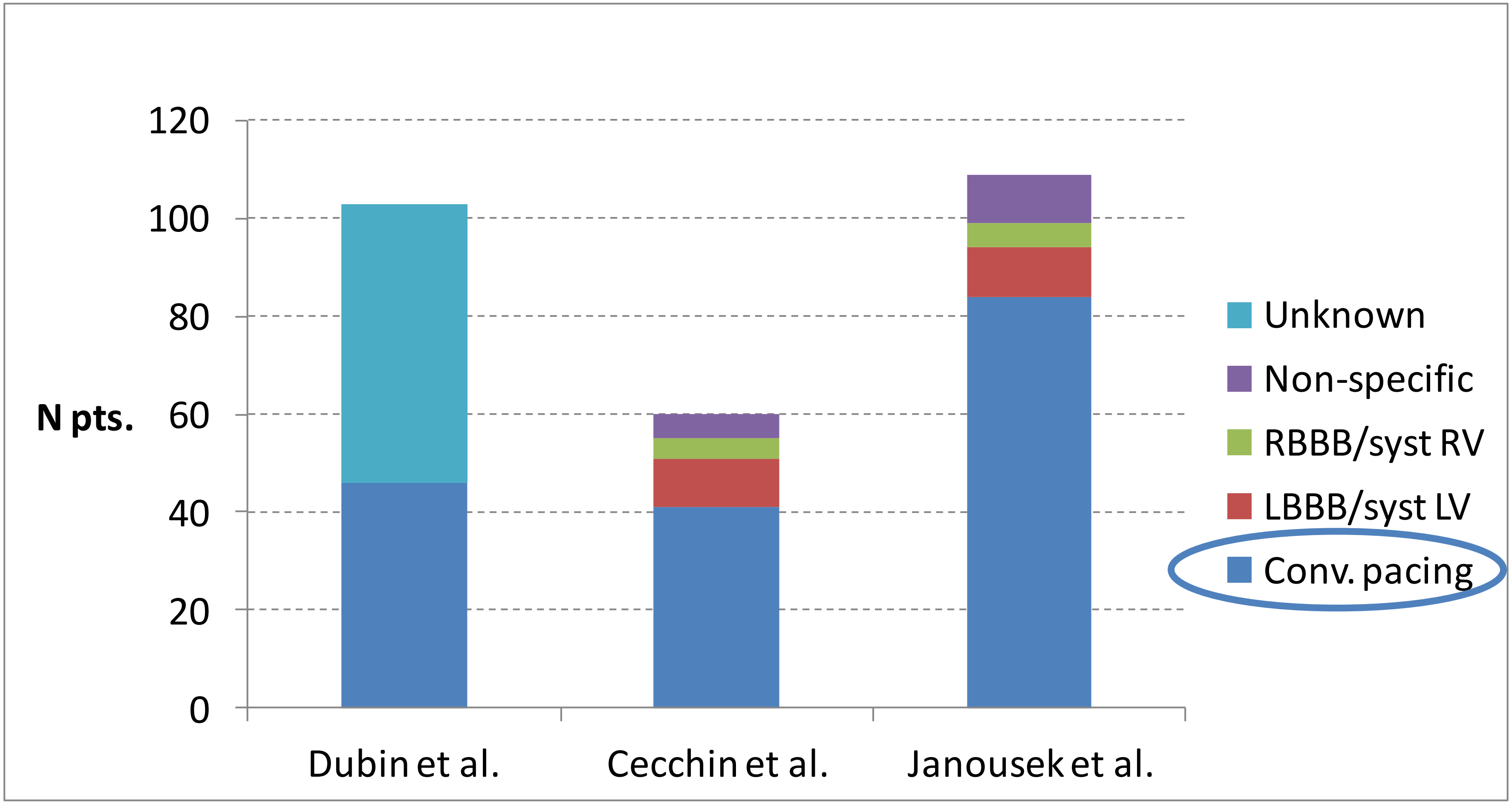
Specific for CHD (Systemic RV, Single ventricle, Subpulmonary RV?)

Electrical activation delay within failing ventricle required for CRT indication!

Permanent cardiac resynchronization therapy



Types of electrical dyssynchrony in pediatric/CHD CRT studies



Dubin AM et al. J Am Coll Cardiol 2005;46:2277-83

Cecchin F et al. JCE 2009;20:58-65

Janousek J et al. Heart 2009, 95:1165-71

Dilated Cardiomyopathy Associated with Dual-Chamber Pacing in Infants: Improvement Through Either Left Ventricular Cardiac Resynchronization or Programming the Pacemaker Off Allowing Intrinsic Normal Conduction

JAN JANOUŠEK, M.D., VIKTOR TOMEK, M.D., VÁCLAV CHALOUPECKÝ, M.D., PH.D., and ROMAN ANTONÍN GEBAUER, M.D.

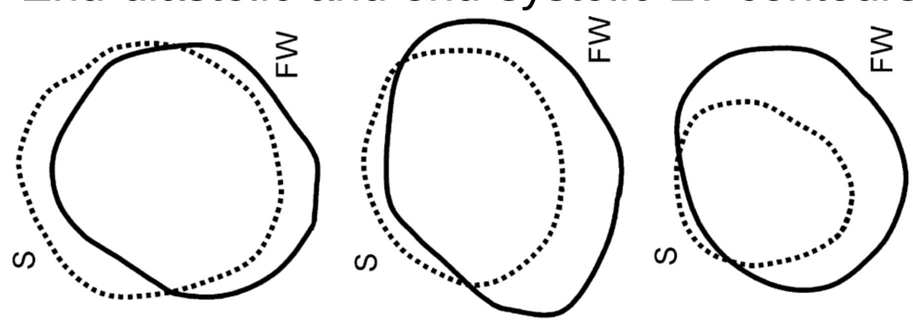
From Kardiocentrum, University Hospital Motol, Prague, Czech Republic

(J Cardiovasc Electrophysiol, Vol. 15, pp. 470-474, April 2004)

Left Ventricular Function and Reverse Remodeling

	LVEDD		LVESD					
	mm	**% Normal**	**mm**	**% Normal**	**LVEDV (mL)**	**LVESV (mL)**	**SF %**	**EF %**
Case 1								
At admission	57.1	182	52.5	260	110†	105	8	22
After 2 weeks of conventional heart failure therapy	58.2	186	52.1	258	98†	96	10	28
After 4 weeks of cardiac resynchronization therapy*	52.6	168	42.2	209	77†	57	20	48
Case 2								
At admission	49.0	184	43.2	253	53‡	47	12	32
After 4 weeks of pacemaker off*	34.8	131	21.6	126	37‡	20	38	76

End-diastolic and end-systolic LV contours



CRT off   CRT on   1 month of CRT

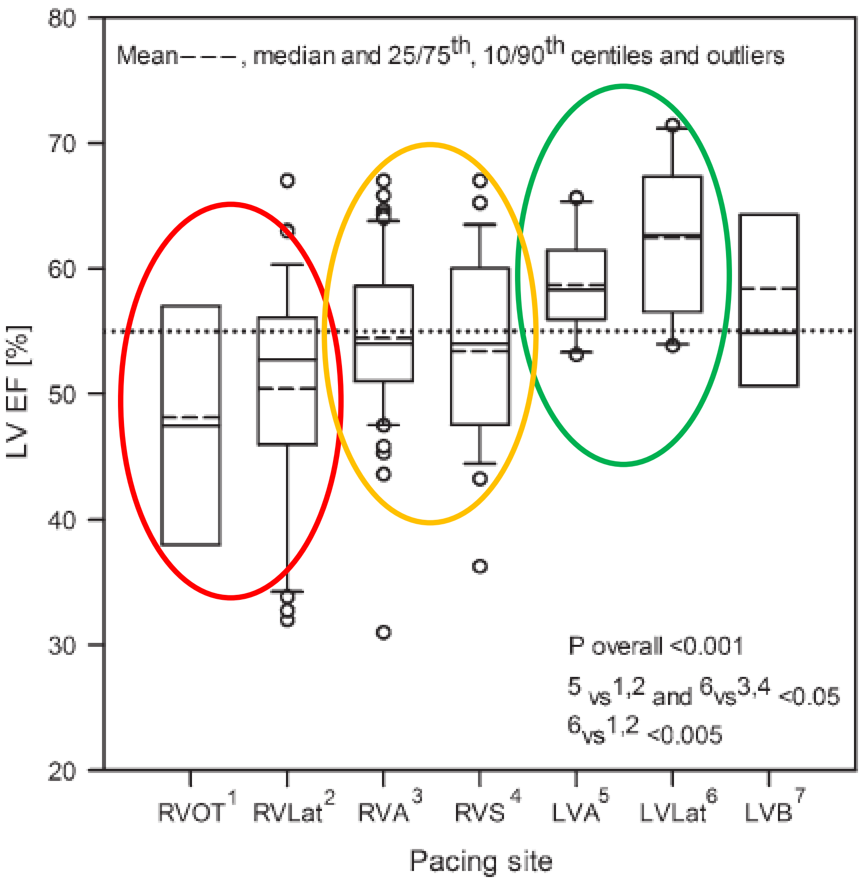
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

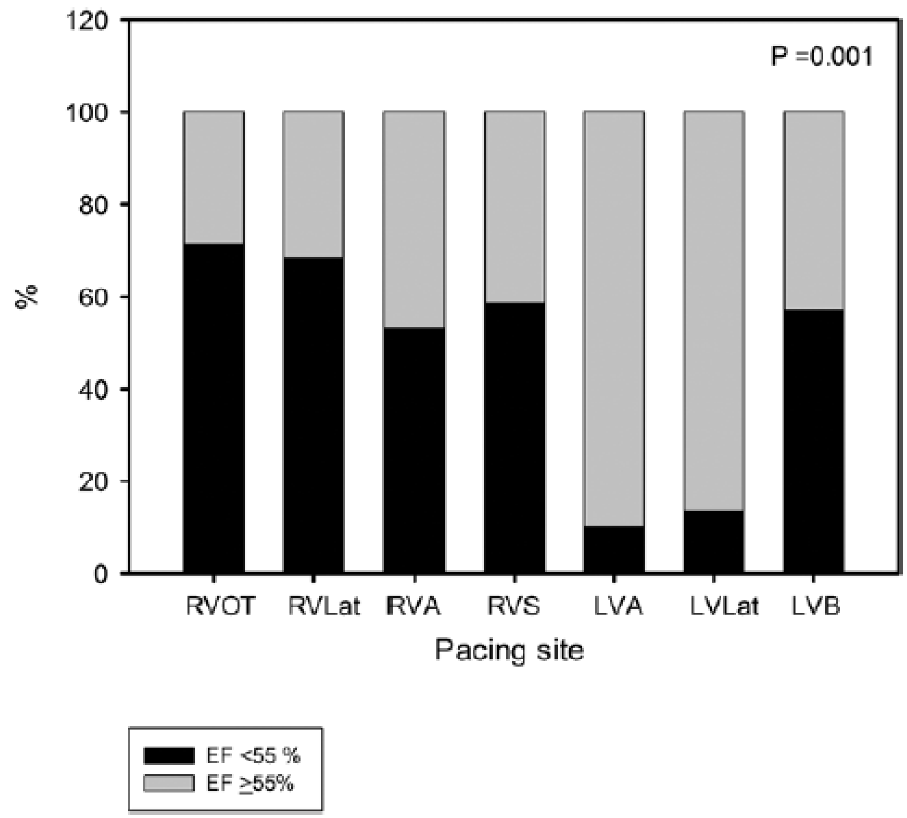
Janoušek J et al,
Circulation 2013;127:613-623

Permanent Cardiac Pacing in Children - Choosing the Optimal Pacing Site: A Multi-Center Study

LV ejection fraction at follow-up



Proportion of pts with LVEF<55 %



Systemic RV / Single-V

- More complex than just dyssynchrony
  - intrinsic myocardial dysfunction
  - AV valve regurgitation
  - Fontan physiology
- Do not expect full reverse remodeling

Presence of a systemic left ventricle was the strongest multivariable predictor of improvement in EF/fractional area of change ($p<0.001$).

Janousek J et al. Heart 2009

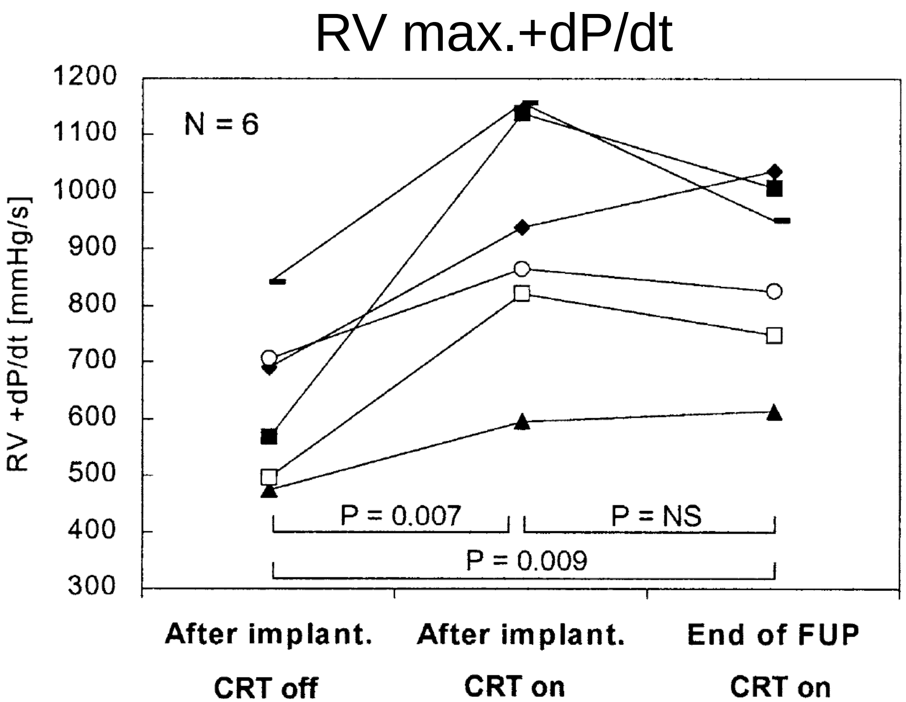
Journal of the American College of Cardiology
Vol. 44, No. 9, 2004
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.08.044

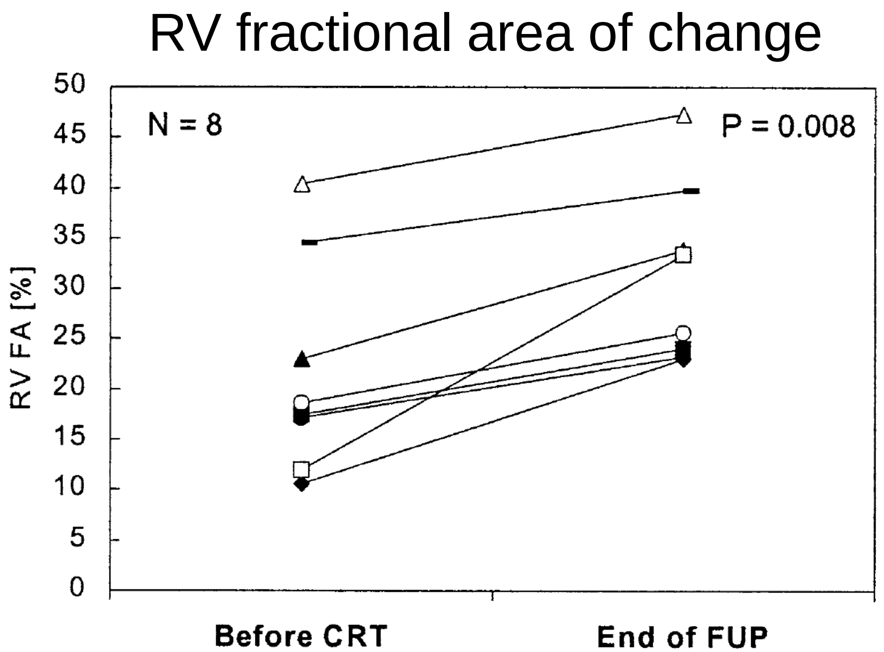
Published by Elsevier Inc.

EXPRESS PUBLICATION

Cardiac Resynchronization Therapy: A Novel Adjunct to the Treatment and Prevention of Systemic Right Ventricular Failure

Jan Janoušek, MD,* Viktor Tomek, MD,* Václav Chaloupecký, MD, PhD,* Oleg Reich, MD, PhD,* Roman A. Gebauer, MD,* Josef Kautzner, MD, PhD,† Bohumil Hučín, MD, PhD*





Cardiac Resynchronization Therapy for Pediatric Patients With Heart Failure and Congenital Heart Disease

A Reappraisal of Results

Kara S. Motonaga, MD; Anne M. Dubin, MD

(*Circulation*. 2014;129:1879-1891.)

Table 2. Multicenter Retrospective Studies of Permanent CRT in Pediatric and CHD-Related Heart Failure

	Dubin et al,[44] 2005	Janousek et al,[45] 2009
Total patients, n	103	109
Age (range), y	Median, 12.8 y (3 mo–55.4 y)	Median, 16.9 y (2.9 mo–73.8 y)
Follow-up duration (range)	Median, 4 mo (22 d–1 y)	Median, 7.5 mo
CHD population, n (%)	73 (70.9)	87 (79.8)
Systemic RV	17 (16.5)	36 (33)
Systemic LV	49 (47.6)	47 (43.1)
Single ventricle	7 (6.8)	4 (3.7)
Outcomes after CRT		
Change in QRSd, ms	↓ 37.7±30.7 (mean±SD)	↓ 40 (median)
Change in sysV EF units (mean±SD)	↑ 12.8±12.7	↑ 11.5±14.3
Change in sysV EDD (median *z* score)	N/A	↓ 1.1
NYHA improvement (median)	N/A	↓ 1
Removed from transplantation list, n (%)	3/18 (17)	4/10 (40)
Nonresponders, n (%)	11 (10.7)	15/81 (18.5)

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(*Circulation*. 2014;129:1879-1891.)

Table 3. Studies That Reported Response to CRT in Patients With Systemic Right Ventricles

	Janousek et al,[37] 2004	Dubin et al,[44] 2005	Cecchin et al,[42] 2009	Janousek et al,[45] 2009	Jauvert et al,[41] 2009
Total patients with systemic RVs, n	8	17	9	27	7
Age (range), y	Median, 12.5 (6.9–29.2)	Median,12.7 (4.9-50)	Median,27 (0.5-43)	Median,28.8	Mean, 24.6 (15–50)
Follow-up duration (range), mo	Median, 17.4	Median, 4	Median, 8.4	Median, 7.3	Median, 19.4
CRT pacing method, n	7 BiV 1 multisite RV	BiV	BiV	26 BiV 1 single-site RV	BiV
Pre-CRT QRSd, ms	161±21	…	Median, 165	Median, 160	160±31
Pre-CRT sysV EF, %	…	…	Median, 28	28.8±10	…
Pre-CRT NYHA FC	Mean, 2	…	…	Median, 2	Mean, 3
Outcomes after CRT					
Change in QRSd, ms	↓ 45 (mean)	↓ 38.2±29.4 (mean±SD)	↓ 15 (median)	↓ 21 (median)	120±28 (mean±SD)
Change in sysV EF units	↑ 4 (mean)	↑ 13.3±11.3 (mean±SD)	↑ 14 (median)	↑ 7.2±9.9 (mean±SD)	…
NYHA improvement	Mean, ↓ 0.7 FC	…	…	Median, ↓ 1 FC	Mean, ↓ 1.4 FC
Clinical improvement, n (%)	8/8 (100)	13/17 (76.5)	2/8 (25)	19 (86.4)	7 (100)
Nonresponders (%N)	…	4/17 (23.5)	6/8 (75)	3/22 (13.6)	…

BiV indicates biventricular; CRT, cardiac resynchronization therapy; EF, ejection fraction; FC, functional class; NYHA, New York Heart Association; QRSd, QRS duration; RV, right ventricle; and sysV, systemic ventricle.

Cardiac Resynchronization Therapy for Pediatric Patients With Heart Failure and Congenital Heart Disease

A Reappraisal of Results

Kara S. Motonaga, MD; Anne M. Dubin, MD

(*Circulation*. 2014;129:1879-1891.)

Table 4. Studies That Reported Response to CRT in Patients With Single Ventricles

	Dubin et al,[44] 2005	Cecchin et al,[42] 2009	Janousek et al,[45] 2009
Total patients single ventricles, n	7	13 but only 11 with >3 mo of follow-up	4
Median age (range)	3.1 y (5 mo–23.7 y)	17.3 y (0.5–42.5 y)	10.3 y (3.7–30.3 y)
Conventional pacing before CRT, n (%)	…	8 (61.5)	3 (75)
Median pre-CRT QRSd, ms	…	129	…
Median pre-CRT EF, %	…	37	…
Outcomes after CRT			
Change in QRSd, ms	↓ 44.8±26.2 (mean)	↓ 13 (median)	…
Change in EF units	No change	↑ 11 (median)	…
Clinical improvement, n (%)	2 (28.6)	10 (90.9)	3 (75)
Nonresponders, n (%)	5 (71.4)	1 (9.1)	1 (25)

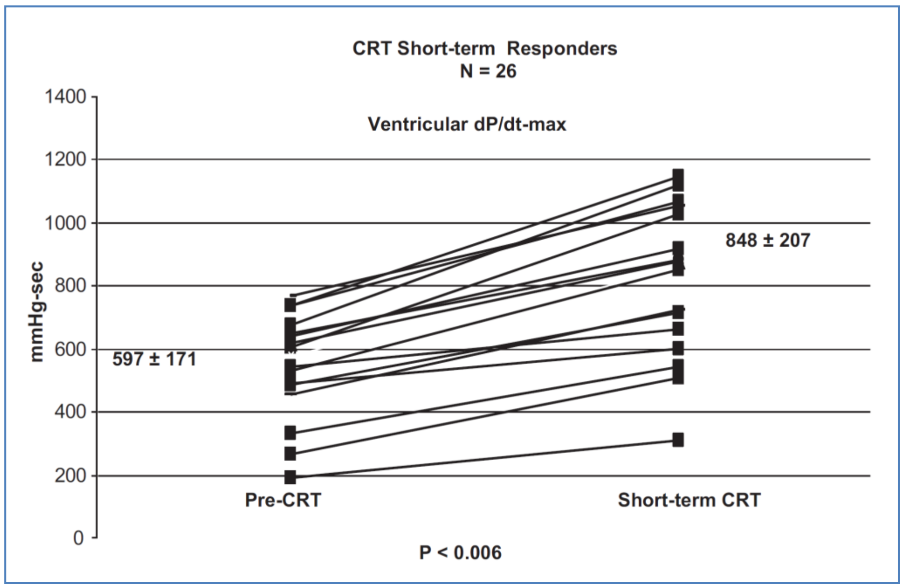
CRT indicates cardiac resynchronization therapy; EF, ejection fraction; and QRSd, QRS duration.

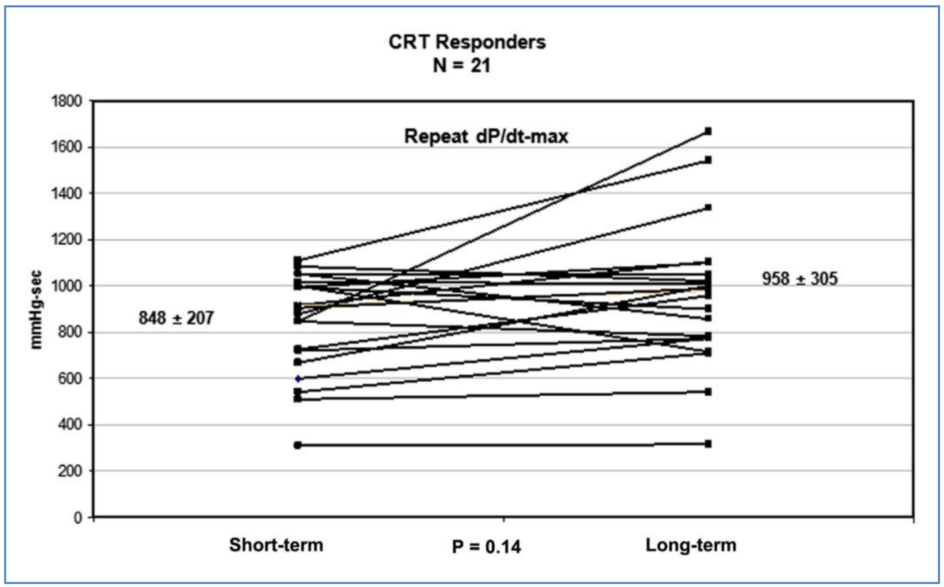
16 Years of Cardiac Resynchronization Pacing Among Congenital Heart Disease Patients

J Am Coll Cardiol EP 2017

Direct Contractility (dP/dt-max) Screening When the Guidelines Do Not Apply

Peter P. Karpawich, MSc, MD, Neha Bansal, MD, Sharmeen Samuel, MD, Yamuna Sanil, MD, Kathleen Zelin, MSN, CPNP





Europace (2017) 0, 1–8
doi:10.1093/europace/euw386

CLINICAL RESEARCH

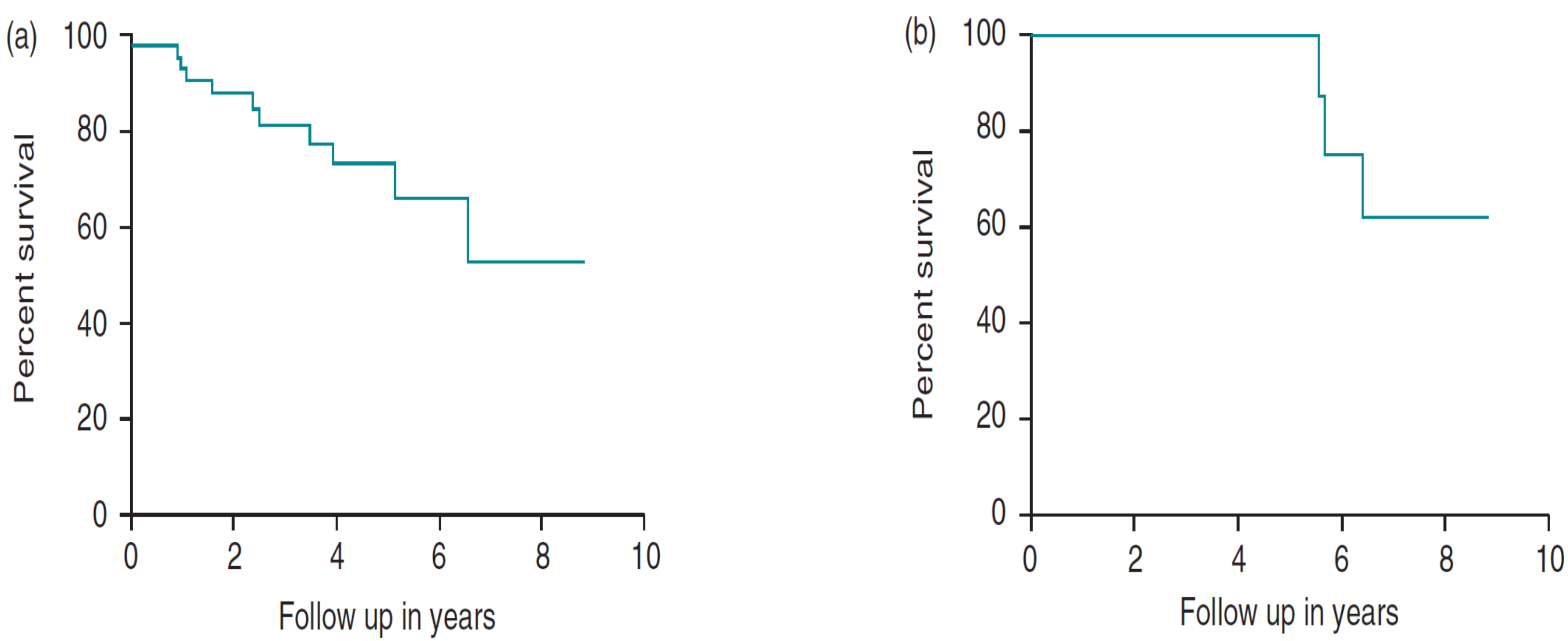
Cardiac resynchronization therapy in adults with congenital heart disease

Zeliha Koyak[1,2], Joris R. de Groot[1], Ahmed Krimly[3], Tara M. Mackay[1], Berto J. Bouma[1], Candice K. Silversides[3], Erwin N. Oechslin[3], Ulas Hoke[4], Lieselot van Erven[4], Werner Budts[5], Isabelle C. Van Gelder[6], Barbara J. M. Mulder[1,2]*, and Louise Harris[3]

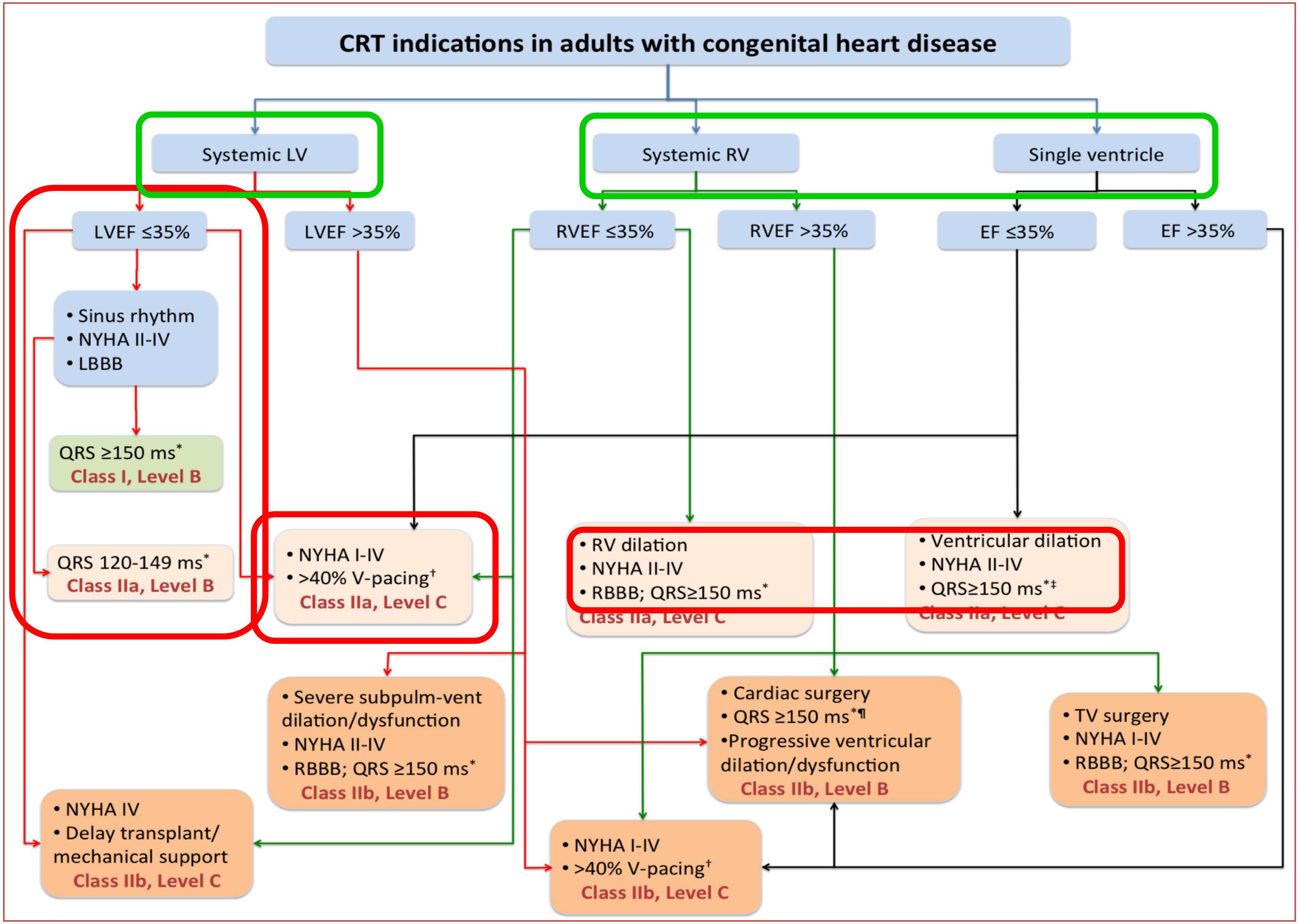
N = 48, median age/FUP: 47.0/2.6 yrs

Freedom from death/heart transplantation

Freedom from CRT system dysfunction



Improvement in NYHA and/or EF in ¾ of pts



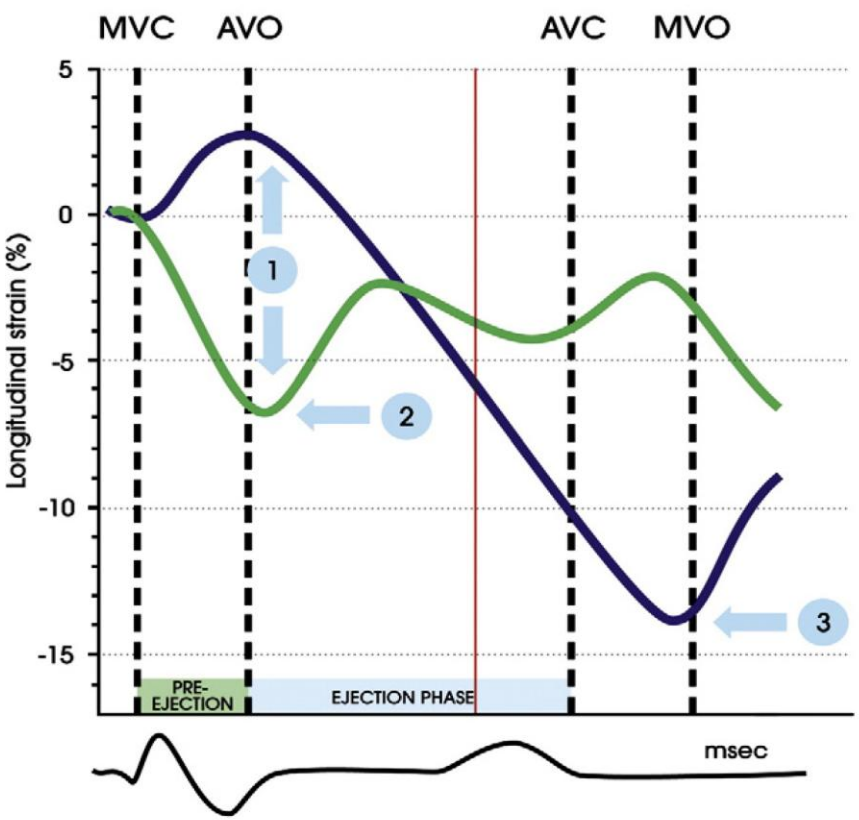
Khairy P et al. PACES/HRS Expert Consensus Statement on the Recognition and Management of Arrhythmias in Adult Congenital Heart Disease. *HeartRhythm Journal 2014*

Future trends

Simple regional strain pattern analysis to predict response to cardiac resynchronization therapy: Rationale, initial results, and advantages

Niels Risum, MD,[a] Christian Jons, MD, PhD,[a] Niels T. Olsen, MD, PhD,[a] Thomas Fritz-Hansen, MD,[a] Niels E. Bruun, MD, DMSc,[a] Michael V. Hojgaard, MD, PhD,[a] Nana Valeur, MD, PhD,[a] Mads B. Kronborg, MD, PhD,[b] Joseph Kisslo, MD,[c] and Peter Sogaard, MD, PhD[a] *Skejby, Denmark; and Durham, NC*

(Am Heart J 2012;163:697-704.)



Classic-pattern dyssynchrony

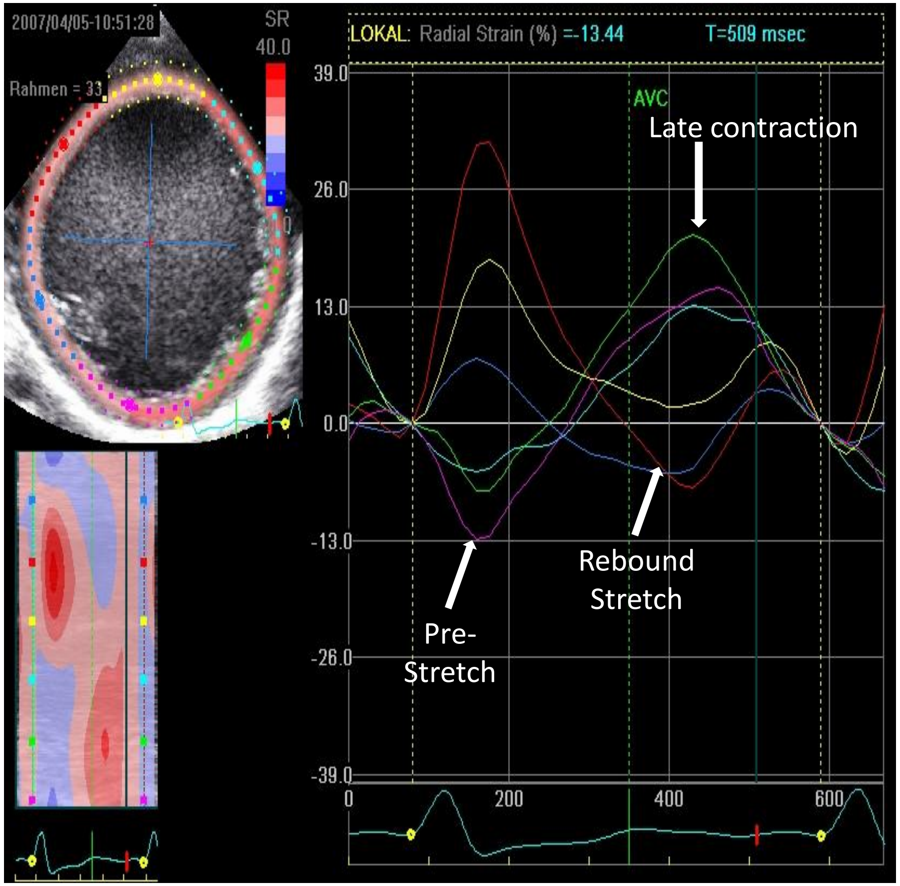
1. Early septal contraction and *early lateral wall stretching*
2. Peak septal contraction <70 % of ejection phase followed by *rebound stretch*
3. Peak lateral wall contraction after AVC

Correlates wit CRT efficacy in adult patients with LBBB

Sensitivity 95 %, specificity 91 %

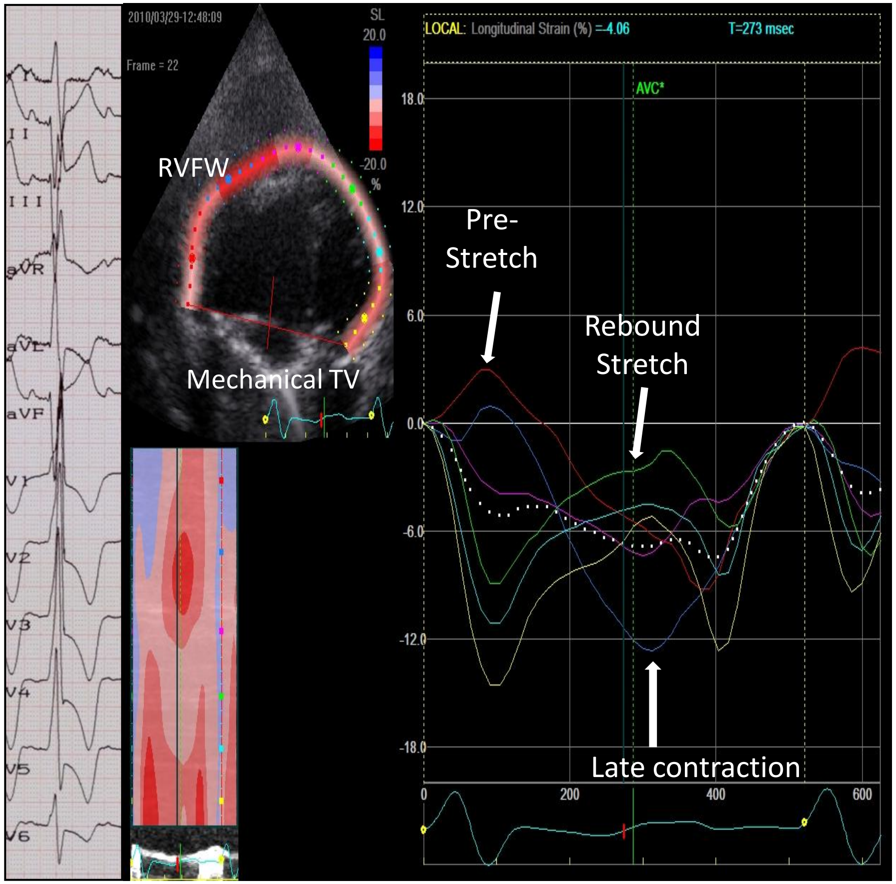
Classic-pattern dyssynchrony in pediatric heart disease

Systemic left ventricle, LBBB



Gonzales MB, PACE 2009

Single (double inlet right) ventricle, RBBB



Materna O, HeartRhythm J 2014

We are able to evaluate mechanical dyssynchrony to support CRT indication!

Pulmonary RV-CRT

RBBB is by far the most frequent dyssychrony pattern in CHD and RV dysfunction/failure is common!

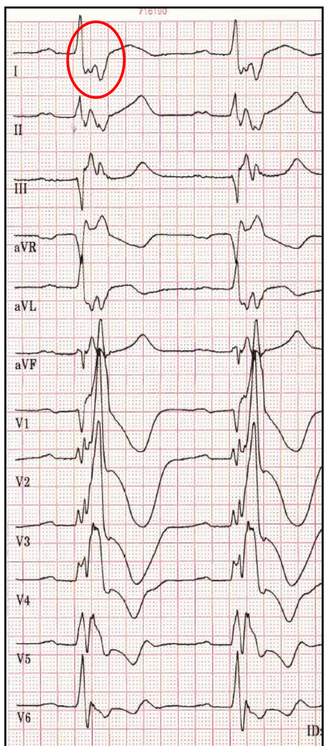
- Postoperative tetralogy of Fallot
  - Chronic RV failure model (RV volume overload due to PR)
- Decreased probability of RV reverse remodeling after pulmonary valve replacement
  - RVEDV >150 to 170 mL/m2 or RVESV > 82 to 90 mL/m2
  - RV EF ≤45%
  - **QRS ≥160 ms!**
- PVR alone may not lead to RV myocardial performance normalization
  - Myocardial fibrosis?
  - Dyssynchronopathy?

Therrien J, Am J Cardiol 2005
Oosterhof T, Circulation 2007
Henkens IR, Ann Thorac Surg 2007
Baumgartner H et al. EHJ 2010
Kutty S et al. J Am Soc Echocardiogr 2008
Geva T et al. Circulation 2010

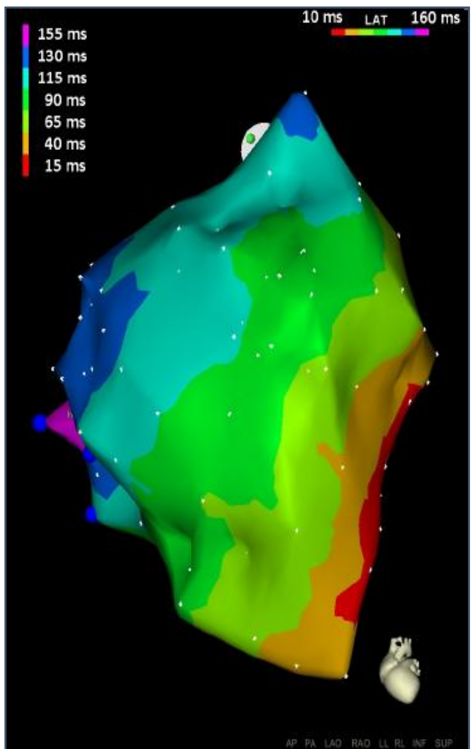
Dyssynchronopathy of the pulmonary right ventricle in congenital heart disease

From ECG to mechanical activation

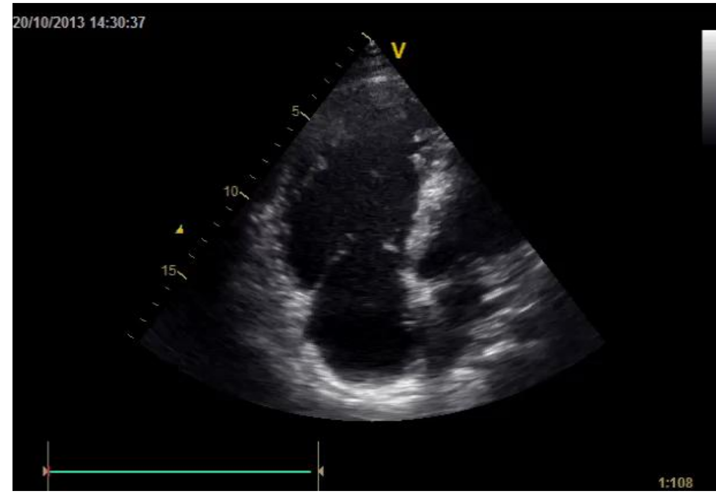
RBBB, QRS 200 ms



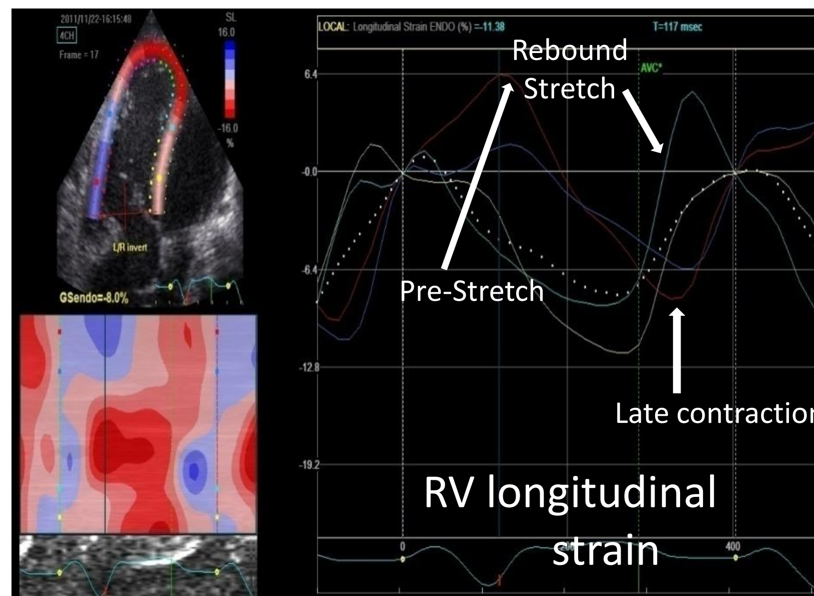
RV activation map



RV motion



Classic-pattern dyssynchrony



Kubuš P et al. Circulation 2014

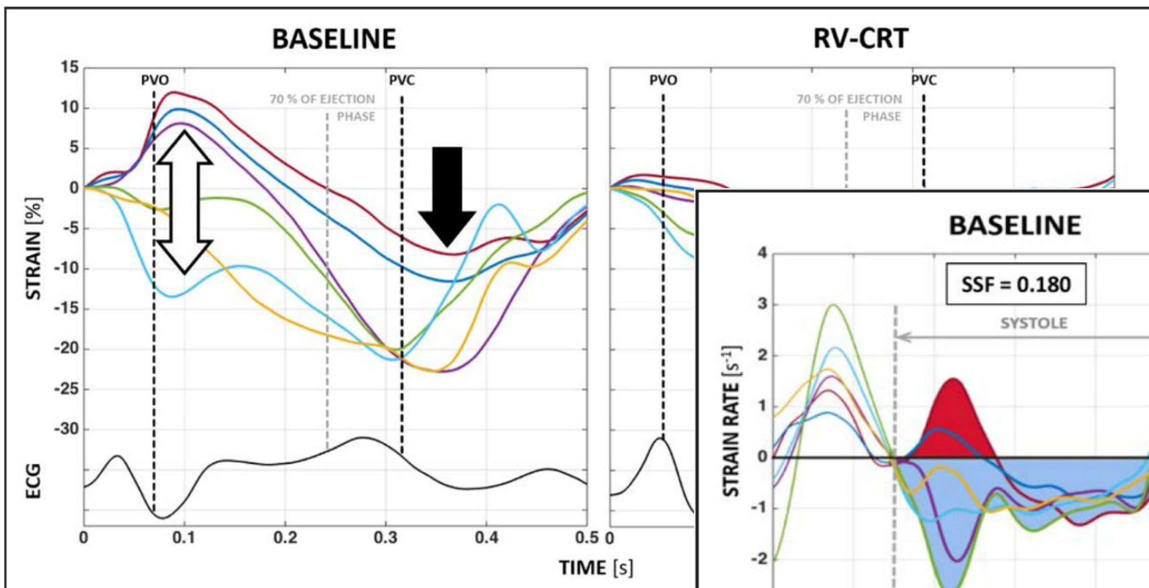
CLINICAL PERSPECTIVE

In patients with congenital heart disease, right ventricular (RV) dyssynchrony caused by right bundle block has been associ-

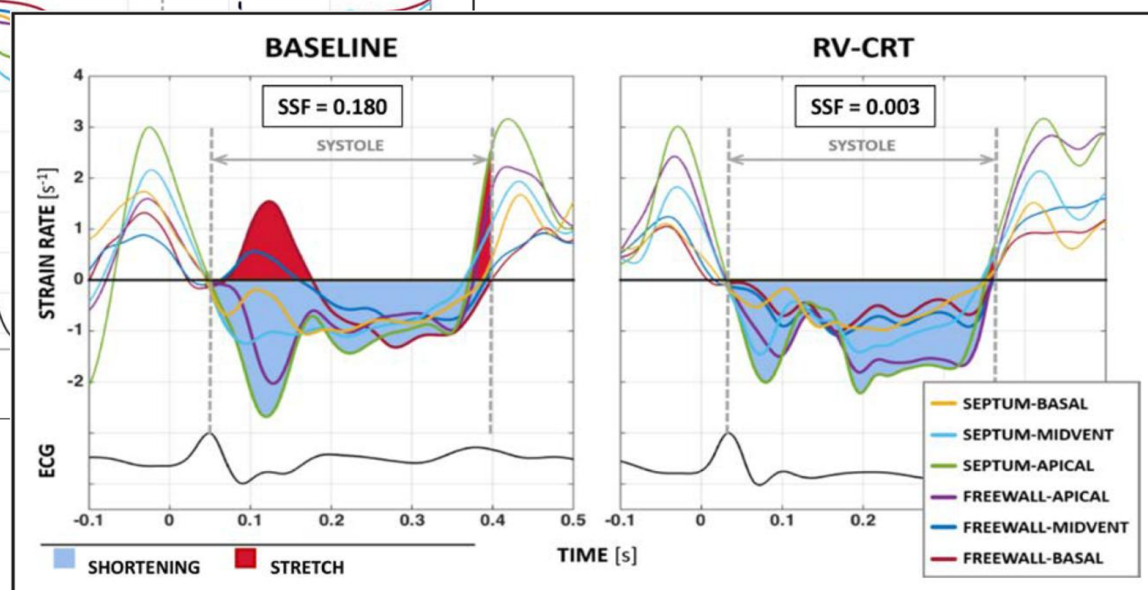
RV-CRT may be beneficial for patients with tetralogy of Fallot and similar lesions who do not show reverse RV remodeling after PVR

in patients late after repair of tetralogy of Fallot undergoing pulmonary valve replacement to observe chronic RV functional parameters, exercise capacity, and clinical outcome.

RV mechanics



RV contraction efficiency



adapted according to: Kirn et al., AJP Heart and Circ. Phys. 2008; 10.1152/ajpheart.00106.2008

Circulation: Arrhythmia and Electrophysiology

SPECIAL REPORT

Janousek J et al., 2019

Cardiac Resynchronization Therapy for Treatment of Chronic Subpulmonary Right Ventricular Dysfunction in Congenital Heart Disease

Chronic Response	Baseline	Last Follow-Up	*P* Value
QRS duration, ms	158 (29) [200, 180, 150]	113 (20) [140, 120, 90]	0.002
NYHA class ≥2 [n]	6/6 [3/3]	1/6 [0/3]	0.015
NT-proBNP, ng/L	842 (756) [N/A, 361, 556]	233 (175) [81, 123, 460]	0.156
RV fractional area change, %	17.5 (9.2) [18, 32, 24]	35.0 (3.3) [36, 34, 36]	0.006
RV end-diastolic area index, cm^2/m^2 BSA	28.1 (11.4) [32.0, 18.8, 18.2]	20.1 (3.6) [24.3, 17.5, 20.6]	0.198
RV end-systolic area index, cm^2/m^2 BSA	23.7 (11.2) [26.4, 12.8, 13.8]	13.1 (2.1) [15.5, 11.5, 13.2]	0.086
RV dP/dt_{max}, mm Hg/s	316 (153) [113, 301, 374]	444 (161) [305, 386, 409]	0.051
Late systolic right to left septal flash [n]	6/6 [3/3]	1/6 [0/3]	0.015
RV septal to lateral mechanical delay, ms	150 (80) [131, 88, 83]	1 (22) [−62, 81, 49]	0.044
RV systolic stretch fraction, %	28.4 (22.3) [22.5, 15.7, 7.5]	11.7 (4.8) [13.0, 11.0, 4.0]	0.092
LV ejection fraction, %	62 (19) [59, 29, 66]	62 (13) [72, 43, 71]	0.910

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

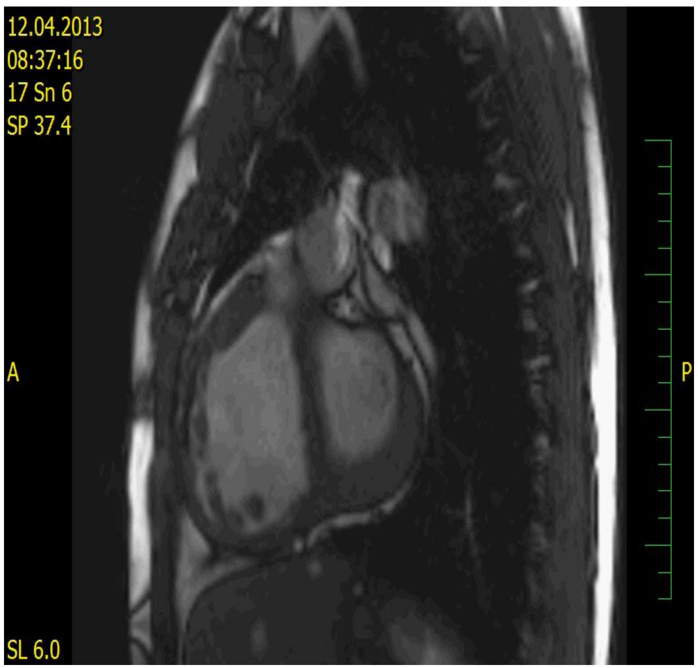
Circulation. 2014;130:e186-e190

Successful Permanent Resynchronization for Failing Right Ventricle After Repair of Tetralogy of Fallot

Peter Kubus, Ondrej Materna, Petr Tax, Viktor Tomek and Jan Janousek

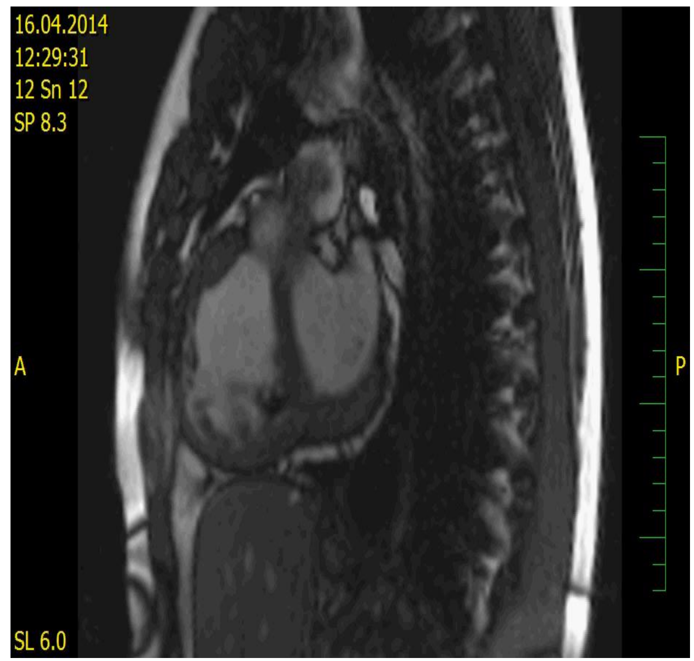
Before

- RV: EDV/ESV 212/172 ml/m2, EF 19 %
- LV: EDV/ESV 80/46 ml/m2, EF 41 %



6 months after RV CRT

- RV: EDV/ESV 141/87 ml/m2, EF 38 %
- LV: EDV/ESV 63/28 ml/m2, EF 56 %



Exercise stress testing - $V0_2$ max: 21,0 (before) ➡ 30,4 ml/kg/min. (6 mos of CRT)

NYHA II ➡ I

Conclusion

- CRT is a powerful tool for
  - acute management of low cardiac output in the postoperative setting
  - treatment of chronic dyssynchronous heart failure in congenital heart disease
- Basic principles similar to CRT in adults with idiopathic/ischemic heart disease
  - structural heterogeneity and patient size requires specific approaches
- Pulmonary RV resynchronization may be an additional strategy for treatment of chronic RV dysfunction