Les Indications "borderline" de la CRT

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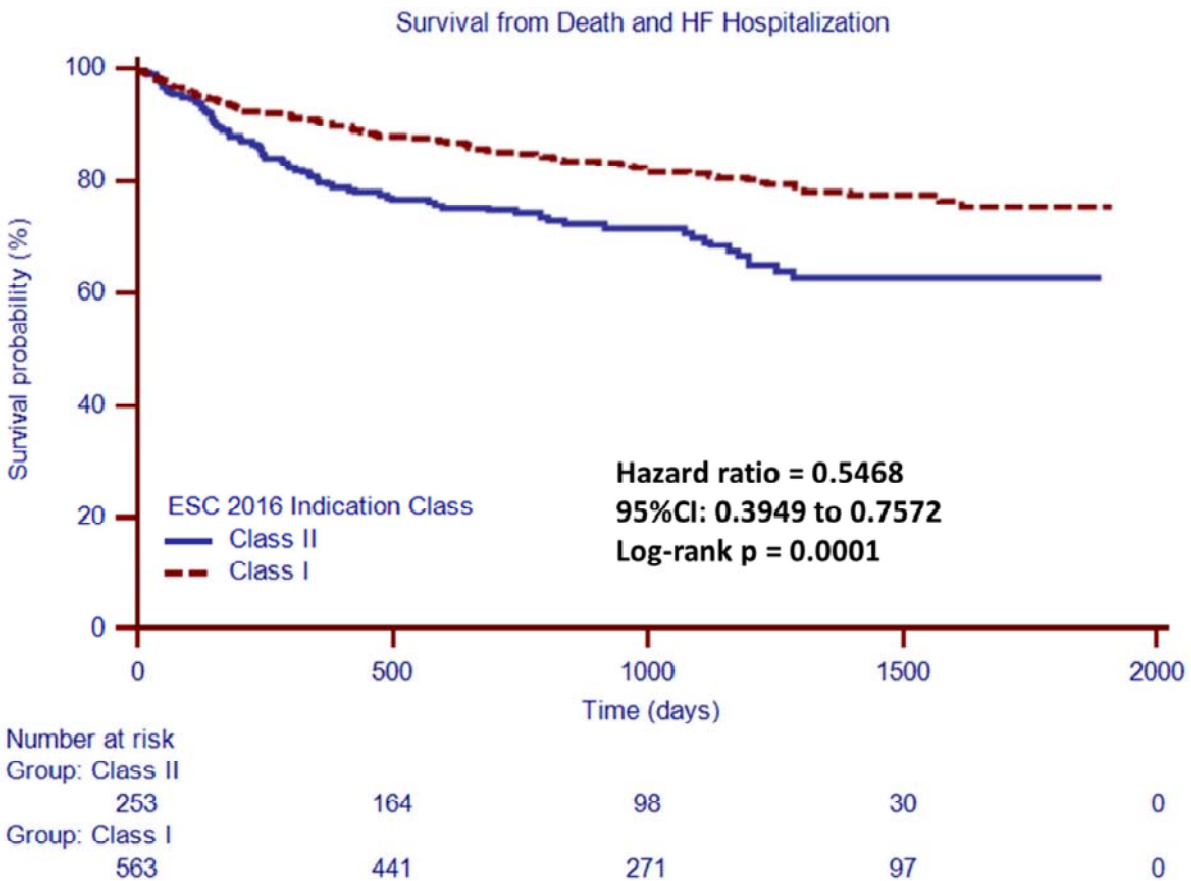
What's a boderline indication for CRT ?

- Proof of superiority of CRT over an alternative therapy is weak or is lacking
- ~ Questionable CRT indication
- ~ Class II indication of institutional guidelines

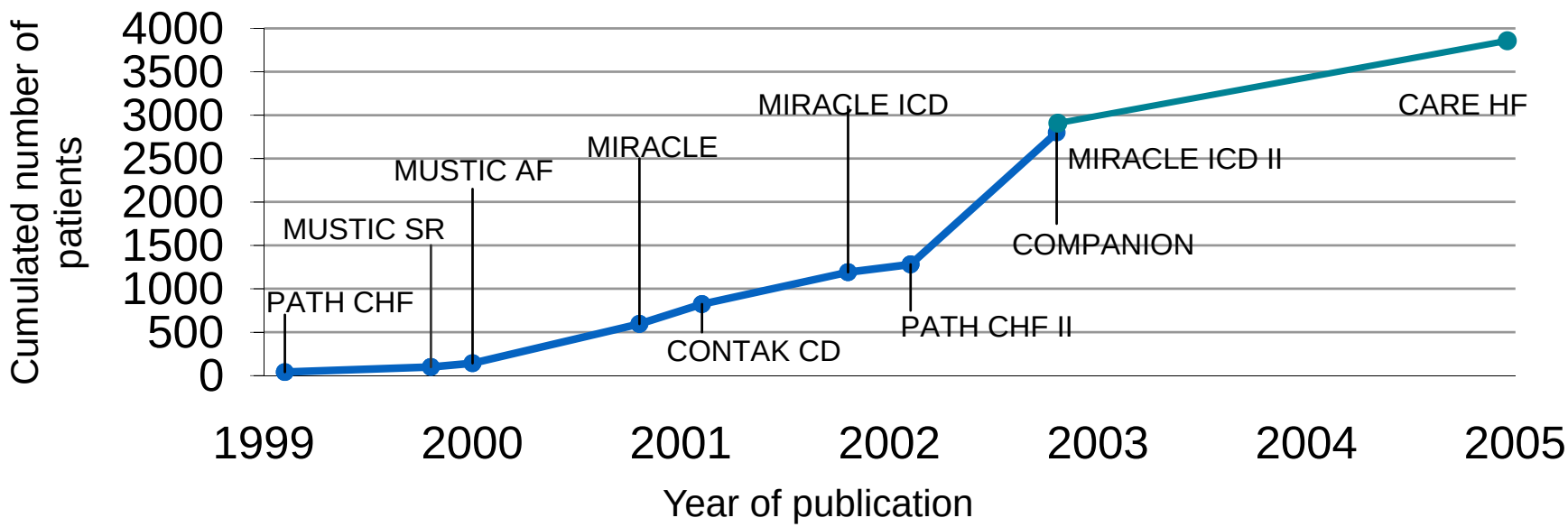
Prognosis of pts with Class I vs Class II CRT indication



Stabile G et al. Heart Rhythm 2018 in press

Scientific validation in NYHA class III/IV

- QRS≥120-130ms
- LVEF≤35%



What have we learned from studies on CRT in NYHA class III/IV patients ?

- Improvement in symptoms (NYHA) and exercise capacity (6 min walking test, VO2)
- QoL improvement

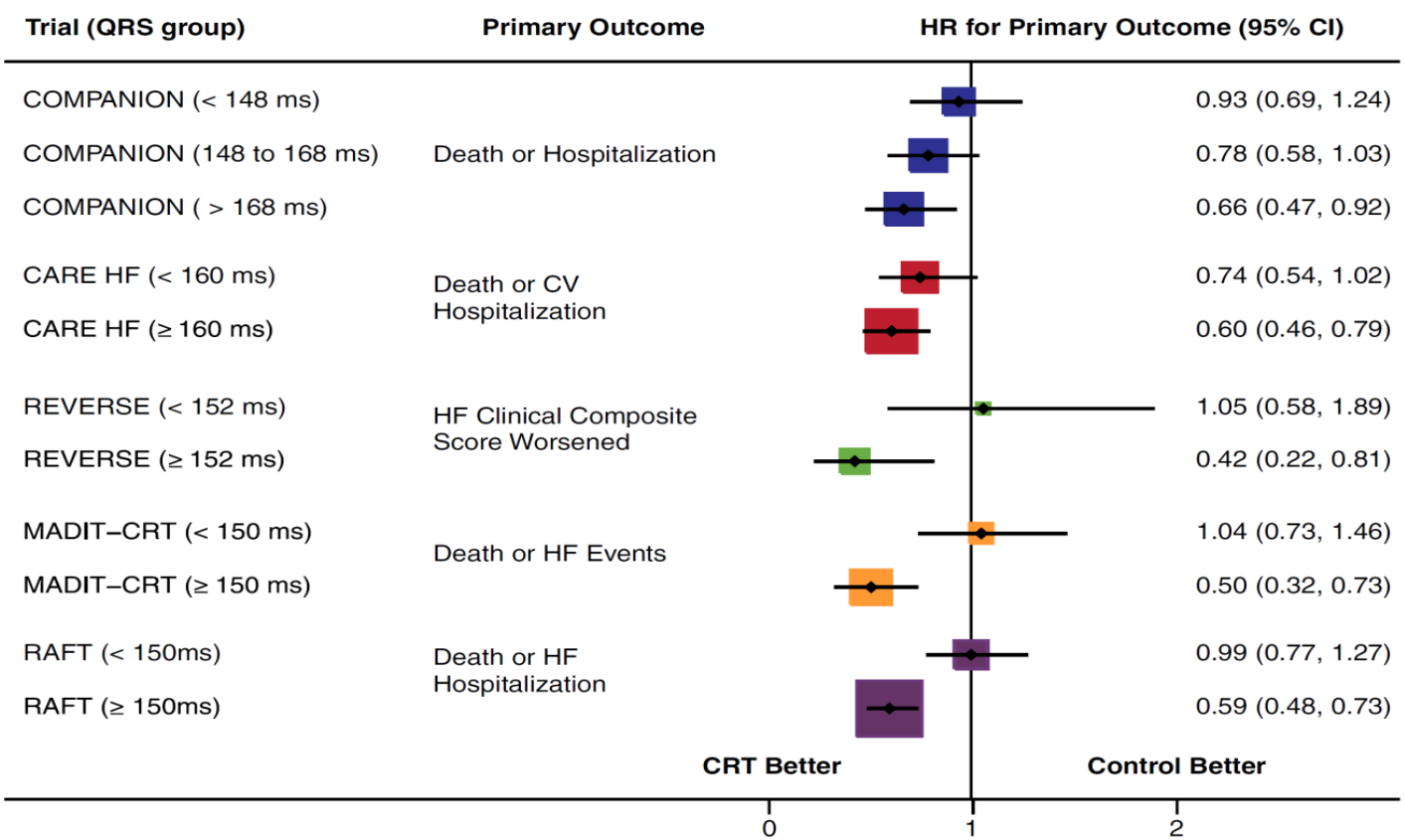
- LV reverse remodeling (LV volumes, LVEF, MR)

- Reduction in morbidity (hospitalization for HF)
- Reduction in mortality (CARE HF)

Scientific validation of CRT in NYHA class II

- **3 randomized studies: REVERSE, MADIT-CRT and RAFT, mainly evaluating CRT-D in NYHA II**
  - Few patients in NYHA I : 18% in REVERSE, 15% in MADIT-CRT and none in RAFT
  - Few patients with CRT-P: 17% in REVERSE and none in MADIT-CRT and RAFT
- **Results similar to those of studies evaluating patients in NYHA III/ambulatory IV**
  - Improvement in LV reverse remodeling and HF clinical criteria (REVERSE)
  - Decrease in morbidity (MADIT-CRT) and mortality (RAFT)

Impact of QRS width on CRT clinical benefit

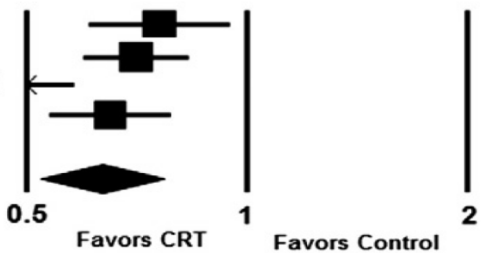


Bryant AR, J Electrocardiol 2013

Impact of QRS Morphology: LBBB

LBBB

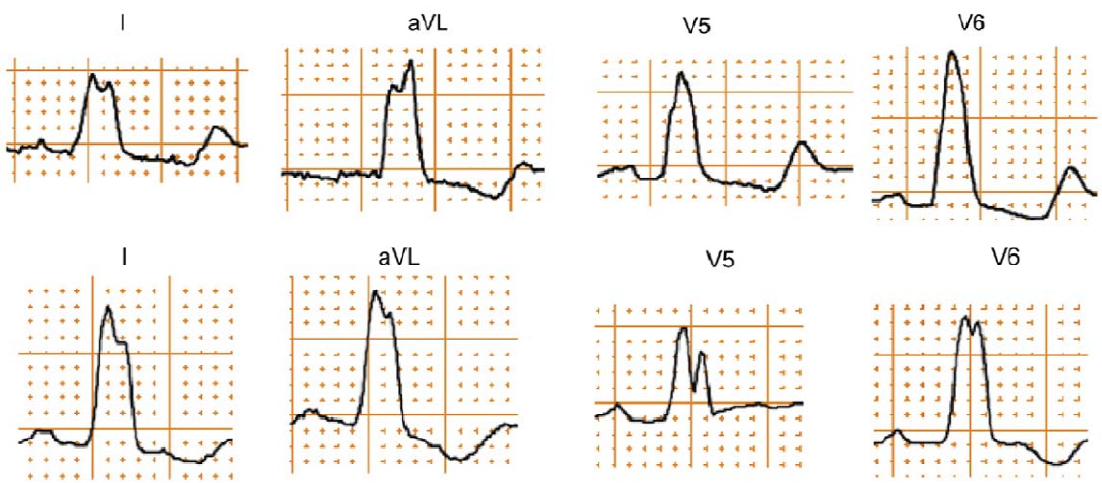
Study name	Risk Ratio	Lower Limit	Upper limit	Z-Value	p-Value
COMPANION[10] - LBBB	0.76	0.61	0.95	-2.43	0.016
CARE-HF[11,32] - LBBB	0.70	0.60	0.83	-4.21	<0.0001
MADIT-CRT[12,13,15] - LBBB	0.45	0.35	0.58	-6.20	<0.00001
RAFT[14] - LBBB	0.65	0.54	0.79	-4.44	0.00001
Meta Analysis	**0.64**	**0.52**	**0.77**	**-4.55**	**0.00001**



Sipahi I, Am Heart J 2012

We propose that criteria for complete LBBB should include QRS duration ≥140 ms (men) or 130 ms (women), QS or rS in leads V_1 and V_2, and mid-QRS notching or slurring in ≥2 of leads V_1, V_2, V_5, V_6, I, and aVL.

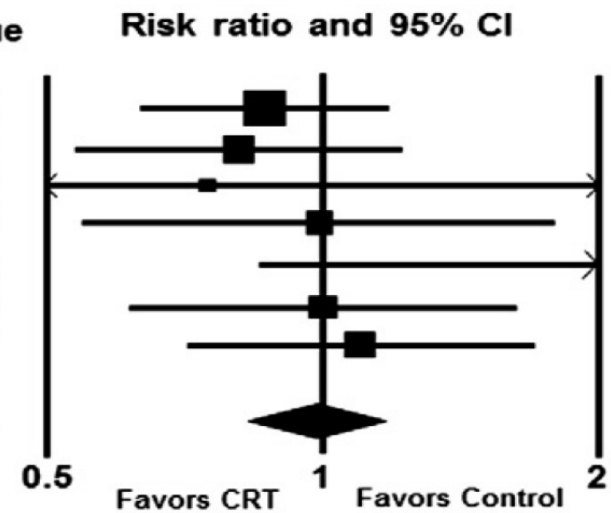
Strauss DG, Am J Cardiol 2011



Impact of QRS Morphology: no LBBB

No LBBB

Study name	Risk Ratio	Lower Limit	Upper Limit	Z-Value	p-Value
COMPANION[10] - Non-LBBB	0.86	0.63	1.17	-0.96	0.34
CARE-HF[11,32] - RBBB	0.81	0.54	1.22	-0.99	0.32
CARE-HF[11,32] - IVCD	0.75	0.24	2.33	-0.50	0.62
MADIT-CRT[12,13,15] - RBBB	0.99	0.55	1.79	-0.03	0.97
MADIT-CRT[12,13,15] - IVCD	1.44	0.88	2.36	1.45	0.15
RAFT[14] - RBBB	1.00	0.62	1.62	0.00	1.00
RAFT[14] – IVCD	1.10	0.71	1.69	0.43	0.67
Meta Analysis	**0.97**	**0.82**	**1.15**	**-0.32**	**0.75**

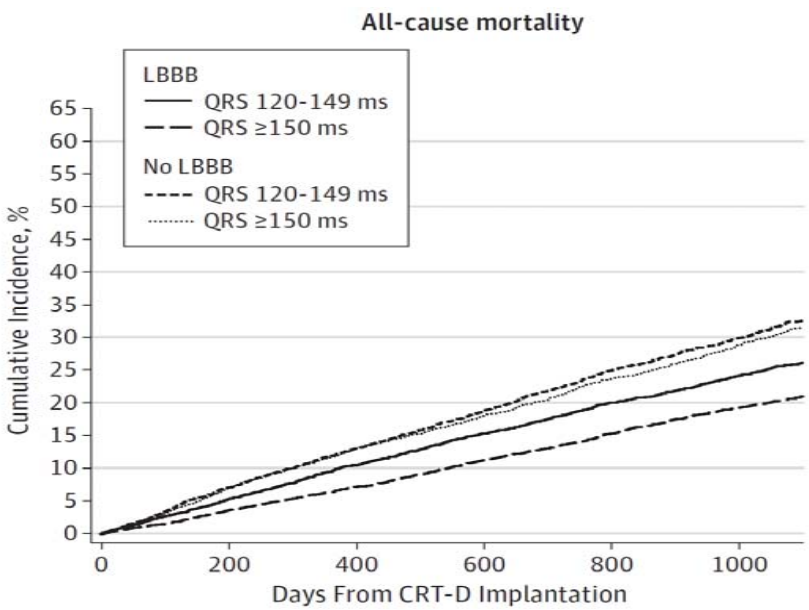


Sipahi I, Am Heart J 2012

Benefit of CRT according to QRS width and morphology : Registries

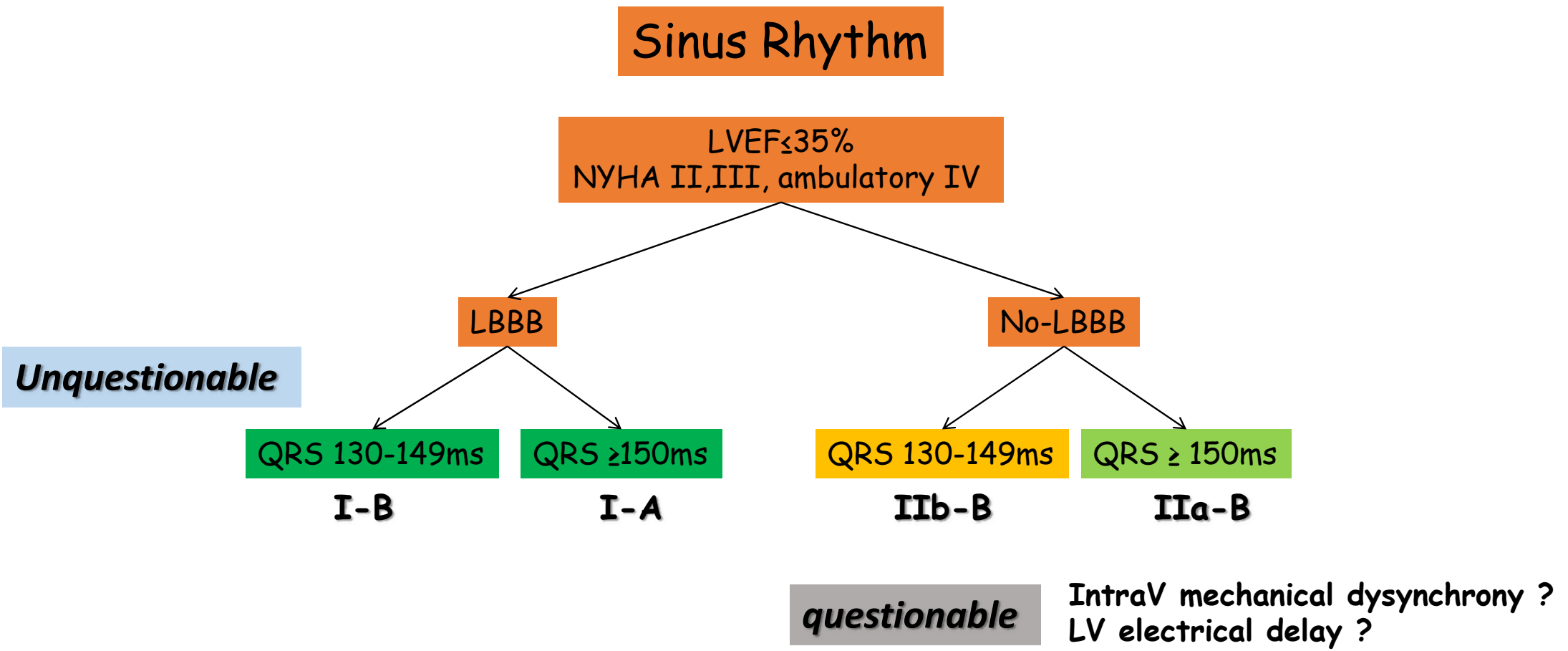
- Results similar to that of randomized studies
- **Wide LBBB QRS provides best response**

Outcome	LBBB		No LBBB	
	QRS ≥150 ms	QRS 120-149 ms	QRS ≥150 ms	QRS 120-149 ms
No.	9889	6259	3306	4715
3-y Mortality, No. (%)	1859 (20.9)	1511 (26.5)	929 (30.7)	1380 (32.3)
Adjusted HR (99% CI)	1 [Reference]	1.30 (1.18-1.42)	1.34 (1.20-1.49)	1.52 (1.38-1.67)
1-y All-cause re-admission, No. (%)	3752 (38.6)	2760 (44.8)	1489 (45.7)	2301 (49.6)
Adjusted HR (99% CI)	1 [Reference]	1.18 (1.10-1.26)	1.16 (1.08-1.26)	1.31 (1.23-1.40
1-y Cardiovascular readmission, No. (%)	1927 (19.8)	1552 (25.1)	873 (26.8)	1372 (29.5)
Adjusted HR (99% CI)	1 [Reference]	1.27 (1.17-1.38)	1.29 (1.17-1.44)	1.47 (1.34-1.62)
1-y Heart failure re-admission, No. (%)	845 (8.7)	794 (12.9)	491 (15.1)	793 (17.1)
Adjusted HR (99% CI)	1 [Reference]	1.47 (1.30-1.67)	1.62 (1.40-1.87)	1.92 (1.68-2.20)



Peterson PN, JAMA 2013

2016 CRT Guidelines



2016 CRT Guidelines

Need for Ventricular Pacing

HF with reduced LVEF
SR/AF
Whatever NYHA class

I-A

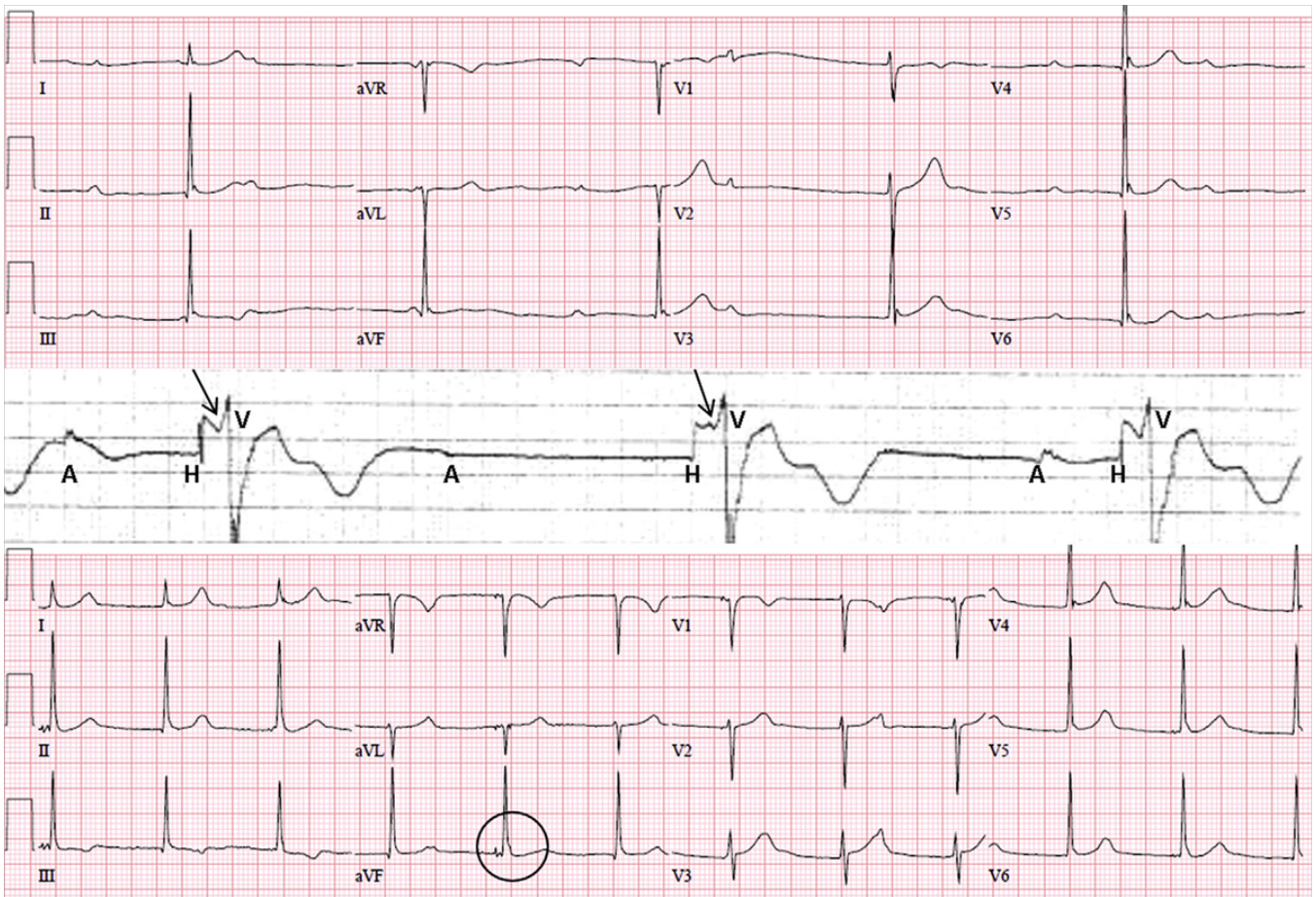
His bundle Pacing
if narrow native QRS ?

questionable

274. Curtis AB, Worley SJ, Adamson PB, Chung ES, Niazi I, Sherfesee L, Shinn T, St John Sutton M. Biventricular pacing for atrioventricular block and systolic dysfunction. *N Engl J Med* 2013;**368**:1585–1593.
275. Brignole M, Botto G, Mont L, Iacopino S, De Marchi G, Oddone D, Luzi M, Tolosana JM, Navazio A, Menozzi C. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. *Eur Heart J* 2011;**32**:2420–2429.
276. Leclercq C, Walker S, Linde C, Clementy J, Marshall AJ, Ritter P, Djiane P, Mabo P, Levy T, Gadler F, Bailleul C, Daubert J-C. Comparative effects of permanent biventricular and right-univentricular pacing in heart failure patients with chronic atrial fibrillation. *Eur Heart J* 2002;**23**:1780–1787.
277. Stavrakis S, Garabelli P, Reynolds DW. Cardiac resynchronization therapy after atrioventricular junction ablation for symptomatic atrial fibrillation: a meta-analysis. *Europace* 2012;**14**:1490–1497.

Electrophysiologic Insights Into Site of Atrioventricular Block

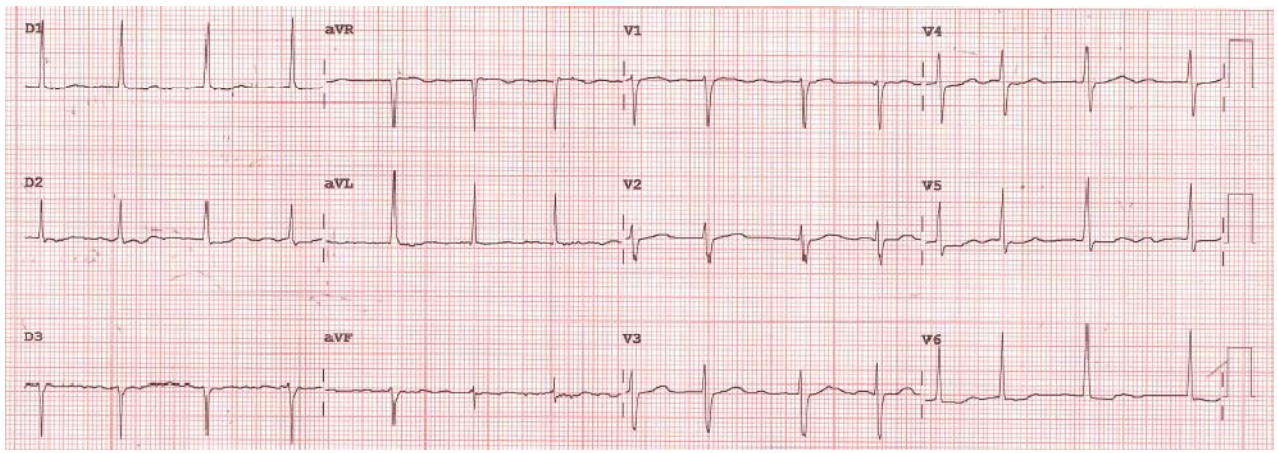
Lessons From Permanent His Bundle Pacing

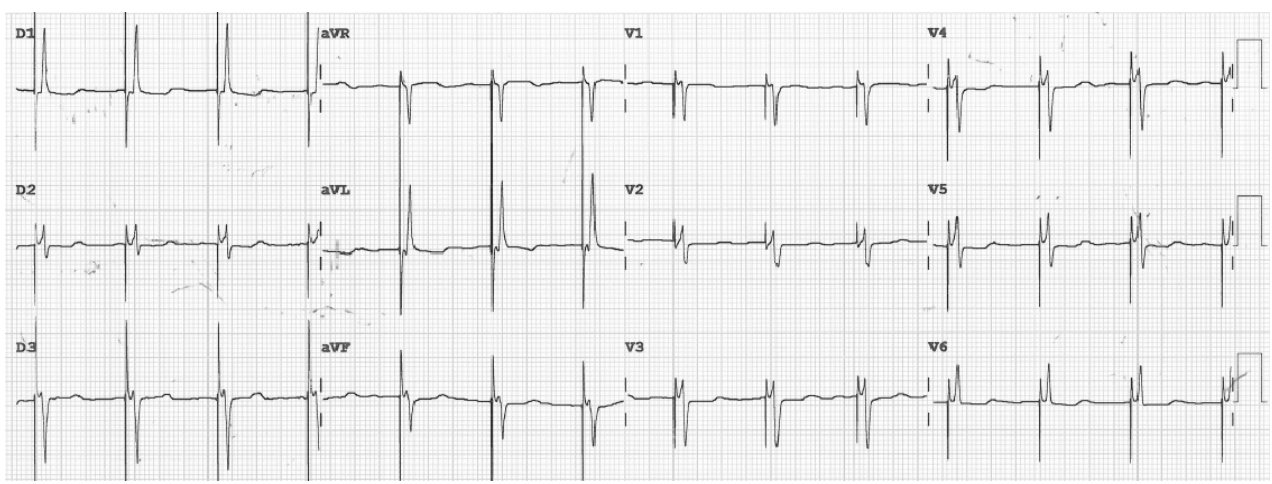


2 months	1.5 ± 0.9	7.2 ± 5.5	442 ± 109	1.7 ± 1.3	9.9 ± 8.3*	469 ± 81
Last follow-up (19 ± 12 months)	1.6 ± 0.9	6.4 ± 4.4	437 ± 75	1.7 ± 1.1	9.6 ± 9.1*	463 ± 78

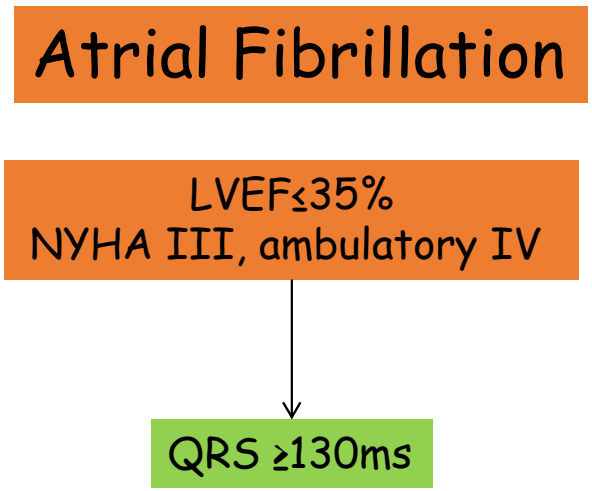
JACC EP, 2015

His Bundle Pacing & AVN Ablation for HF patients in uncontrolled AF





2016 CRT Guidelines



Provided strategy to ensure biV capture : AV node ablation

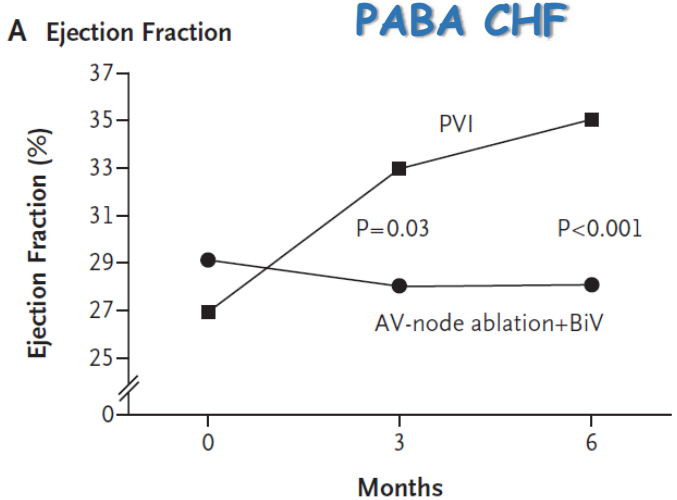
questionable

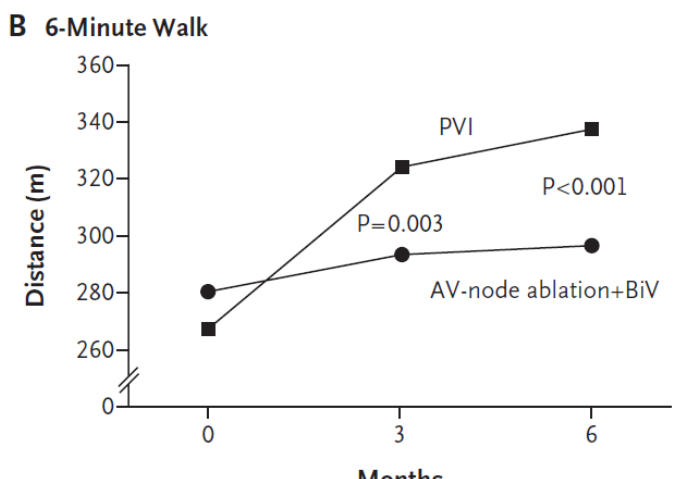
IIa-B

- **AF ablation ? (PABA CHF; CASTLE-AF)**
- **His bundle Pacing and AV node ablation**
  If no LBBB /QRS < 149 ms ?

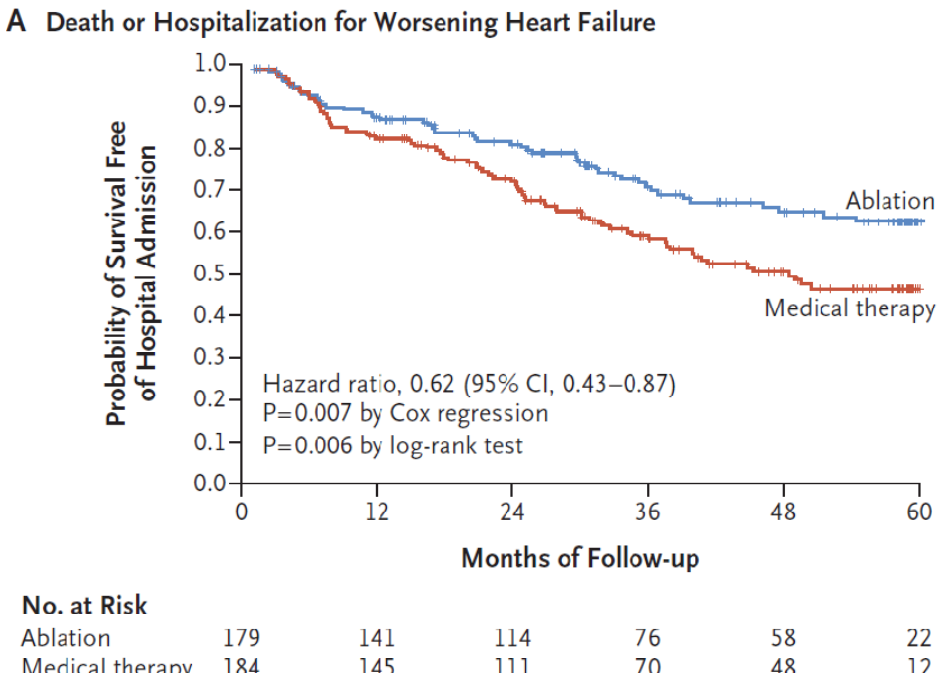
AF Ablation in CHF patients

PABA CHF





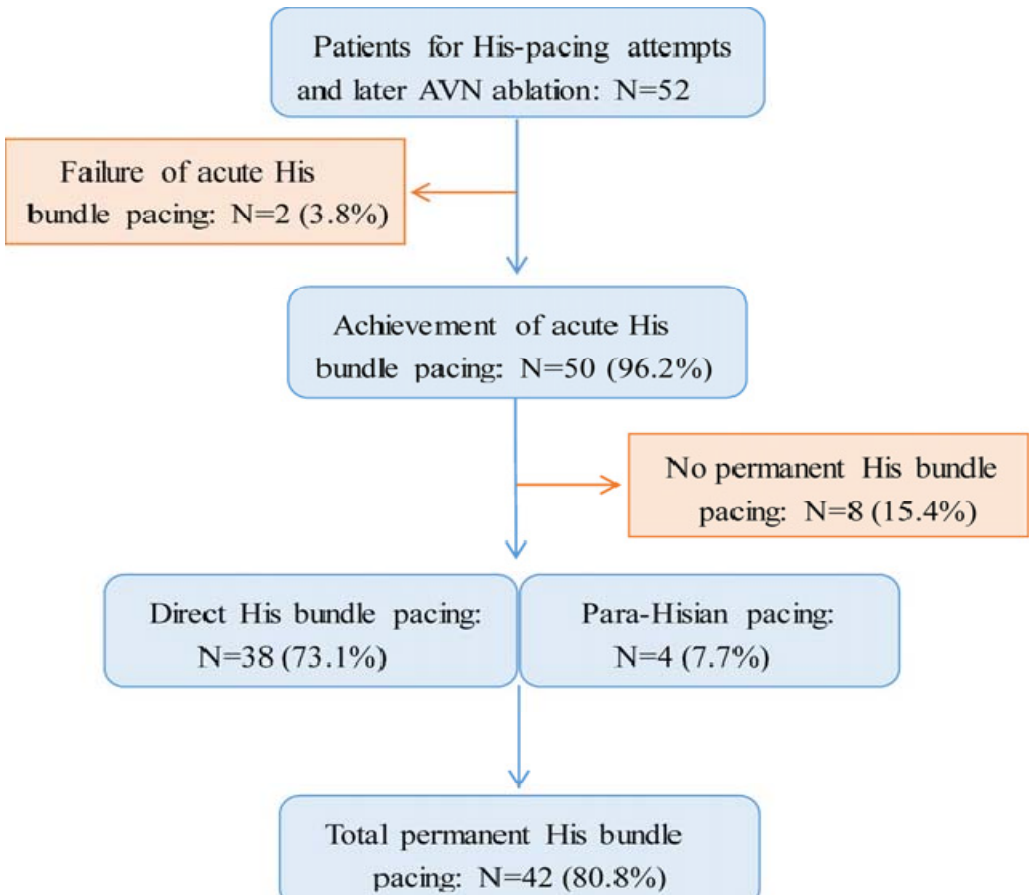
CASTLE AF



Khan M, et al. NEJM 2008;359/1778
Marrouche N, et al. NEJM 2018;378:417

Benefits of Permanent His Bundle Pacing Combined With Atrioventricular Node Ablation in Atrial Fibrillation Patients With Heart Failure With Both Preserved and Reduced Left Ventricular Ejection Fraction

Weijian Huang, MD; Lan Su, MD; Shengjie Wu, MD; Lei Xu, MD; Fangyi Xiao, MD; Xiaohong Zhou, MD; Kenneth A. Ellenbogen, MD



	BNP		
	Baseline	1 year	p
HFpEF	298 ± 212	308 ± 254	0,831
HFref	726± 730	148 ± 232	< 0,001

	NYHA		
	Baseline	1 year	p
HFpEF	2,7 ± 0,6	1,4 ± 0,5	< 0,001
HFref	2,9 ± 0,6	1,4 ± 0,4	< 0,001

American Heart Association® 2017

2016 CRT Guidelines

PM or ICD upgrading

Worsening of HF with reduced LVEF
SR/AF
High proportion of RV pacing

questionable

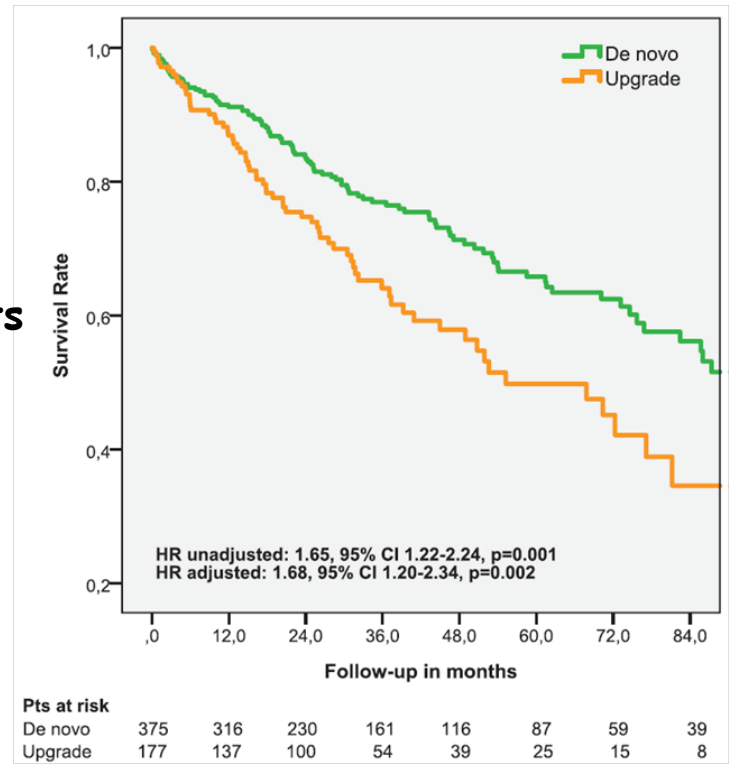
IIb-B

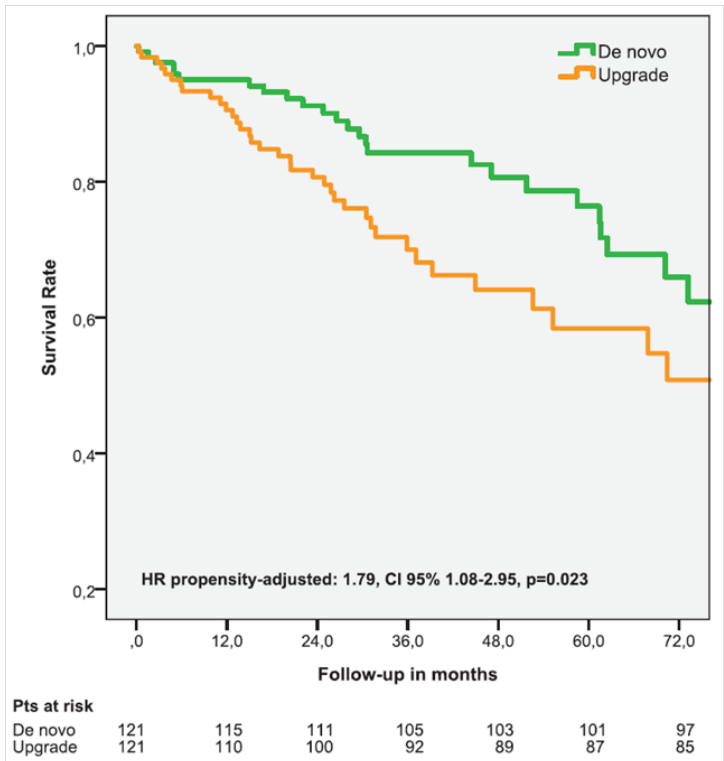
Effects of Upgrade Versus De Novo Cardiac Resynchronization Therapy on Clinical Response and Long-Term Survival

Results from a Multicenter Study

Mate Vamos, MD; Julia W. Erath, MD; Zsolt Bari, MD; Denes Vagany, MD; Sven P. Linzbach, MD; Tatsiana Burmistrava, MD; Carsten W. Israel, MD; Gabor Z. Duray, MD, PhD; Stefan H. Hohnloser, MD

All Patients





Propensity-matched Patients

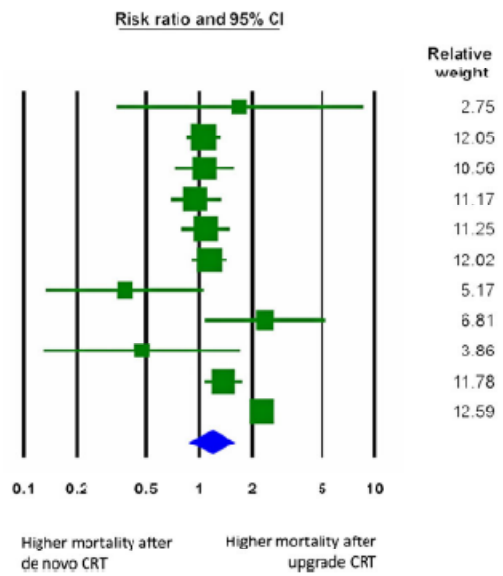
Circ Arrhythm Electrophysiol. 2017

De novo implantation vs. upgrade cardiac resynchronization therapy: a systematic review and meta-analysis

Annamaria Kosztin[1] · Mate Vamos[2,3] · Daniel Aradi[1,4] · Walter Richard Schwertner[1] · Attila Kovacs[1] · Klaudia Vivien Nagy[1] · Endre Zima[1] · Laszlo Geller[1] · Gabor Zoltan Duray[3] · Valentina Kutyifa[1,5] · Bela Merkely[1]

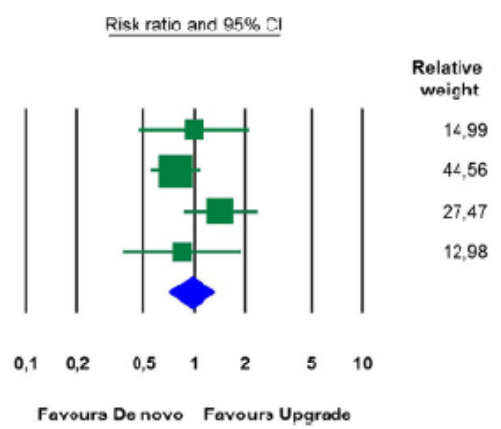
Risk of mortality after de novo vs. upgrade CRT

Study name	Events / Total		Statistics for each study				Relative weight
	Upgrade	De novo	Risk ratio	Lower limit	Upper limit	p-Value	
Duray	2 / 18	4 / 61	1.69	0.34	8.51	0.52	2.75
Nagee	60 / 107	117 / 221	1.06	0.86	1.31	0.59	12.05
Foley	20 / 58	108 / 336	1.07	0.73	1.56	0.72	10.56
Wokhlu	41 / 167	87 / 338	0.95	0.69	1.32	0.77	11.17
Bogale	52 / 601	118 / 1489	1.09	0.80	1.49	0.58	11.25
Gage	76 / 190	163 / 465	1.14	0.92	1.41	0.23	12.02
Tayal	4 / 50	18 / 85	0.38	0.14	1.05	0.06	5.17
Horst	19 / 134	8 / 134	2.38	1.08	5.24	0.03	6.81
Lipar	3 / 116	9 / 165	0.47	0.13	1.71	0.25	3.86
Vamos	68 / 177	105 / 375	1.37	1.07	1.76	0.01	11.78
Cheung	368 / 19564	3823 / 464246	2.28	2.05	2.54	0.00	12.59
			1.19	0.88	1.60	0.27	



Risk of HF events after de novo vs. upgrade CRT

Study name	HF events / Total		Statistics for each study				Relative weight
	De novo	Upgrade	Risk ratio	Lower limit	Upper limit	p-Value	
Parapella	11 / 43	10 / 39	1,00	0,48	2,09	1,00	14,99
Bogale	96 / 1489	50 / 601	0,77	0,56	1,08	0,13	44,56
Gage	63 / 465	18 / 190	1,43	0,87	2,35	0,16	27,47
Lipar	12 / 165	10 / 116	0,84	0,38	1,89	0,68	12,98
			0,96	0,70	1,32	0,81	



Heart Fail Rev Oct. 2017

Conclusion

- After 2 decades of CRT experience, it is recognized that patients with borderline indication don’t get as much benefit from CRT as class I indication patients
- We need to question ourselves about alternative therapy or better selection for those patients not fulfilling class I criteria for CRT
- In patients without LBBB, especially if intermediate QRS duration (need for additional criteria such as LV electrical / mechanical / imaging data)
- In PM / ICD patients candidate for upgrading to BiV pacing (too late ?)
- In patients requiring ventricular pacing (His bundle pacing ?)
- In patients with AF, catheter ablation should be discussed
- In case of borderline indication for CRT, a tailored approach is required

European Heart Journal
doi:10.1093/eurheartj/eht150

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

The Task Force on cardiac p
European Society of Cardio
with the European Heart Rh

Authors/Task Force Members: Mi
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(France), Giuseppe Boriani (Italy)
Jean-Claude Deharo (France), Vic
Bulent Gorenek (Turkey), Carsten
(France), Cecilia Linde (Sweden),
Richard Sutton (UK), Panos E. Va

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Piotr Ponikowski* (Chairperson) (Poland), Adriaan A. Voors* (Co-Chairperson) (The Netherlands), Stefan D. Anker (Germany), Héctor Bueno (Spain), John G. F. Cleland (UK), Andrew J. S. Coats (UK), Volkmar Falk (Germany), José Ramón González-Juanatey (Spain), Veli-Pekka Harjola (Finland), Ewa A. Jankowska (Poland), Mariell Jessup (USA), Cecilia Linde (Sweden), Petros Nihoyannopoulos (UK), John T. Parissis (Greece), Burkert Pieske (Germany), Jillian P. Riley (UK), Giuseppe M. C. Rosano (UK/Italy), Luis M. Ruilope (Spain), Frank Ruschitzka (Switzerland), Frans H. Rutten (The Netherlands), Peter van der Meer (The Netherlands)

Recommendations	Class [a]	Level [b]	Ref [c]
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A	261–272
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B	261–272
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B	266, 273
CRT may be considered for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B	266, 273
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	274–277
CRT should be considered for patients with LVEF ≤35% in NYHA Class III–IV[d] despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

Table 1 Study definitions of indication for cardiac resynchronization therapy based on published clinical guidelines

Guideline	EF (%)		NYHA class		QRS (ms)	Chronic AF	LBBB	COR
	<30	30–39*	II	III–IV				
QRS ≥120† (reference)	X	X	X	X	≥120	#	#	N/A
ESC 2005/2007	X	X	•	X	≥120	•	#	I
	X	X	•	X	≥120	X	#	IIa
ESC 2010	X	X	•	X	≥120	•	#	I
	X	X	•	X	≥130	X	#	IIa
	X	X	X	•	≥150	•	#	I
ESC 2012	X	X	•	X	≥120	•	X	I
	X	X	•	X	≥150	•	•	IIa
	X	•	X	•	≥130	•	X	I
	X	•	X	•	≥150	•	•	IIa
	X	X	•	X	≥120	X	#	IIa
ESC 2013	X	X	X	X	≥120	•	X	I
	X	X	X	X	≥150	•	•	IIa
	X	*X*	*X*	*X*	*≥120, ≤149*	•	•	*IIb*
	X	X	•	X	≥120	X	#	IIa
ESC 2016	X	X	X	X	≥150	•	X	I
	X	X	X	X	≥150	•	•	IIa
	X	X	X	X	130–149	•	X	I
	X	*X*	*X*	*X*	*130–149*	•	•	*IIb*
	X	X	•	X	≥130	X	#	IIa

For CRT to be indicated by one guideline, all criteria in at least one of the rows for that guideline must be fulfilled.

AF, atrial fibrillation; COR, class of recommendation; EF, ejection fraction; ESC, European Society of Cardiology; LBBB, left bundle branch block; NYHA, New York Heart Association; N/A, not applicable.

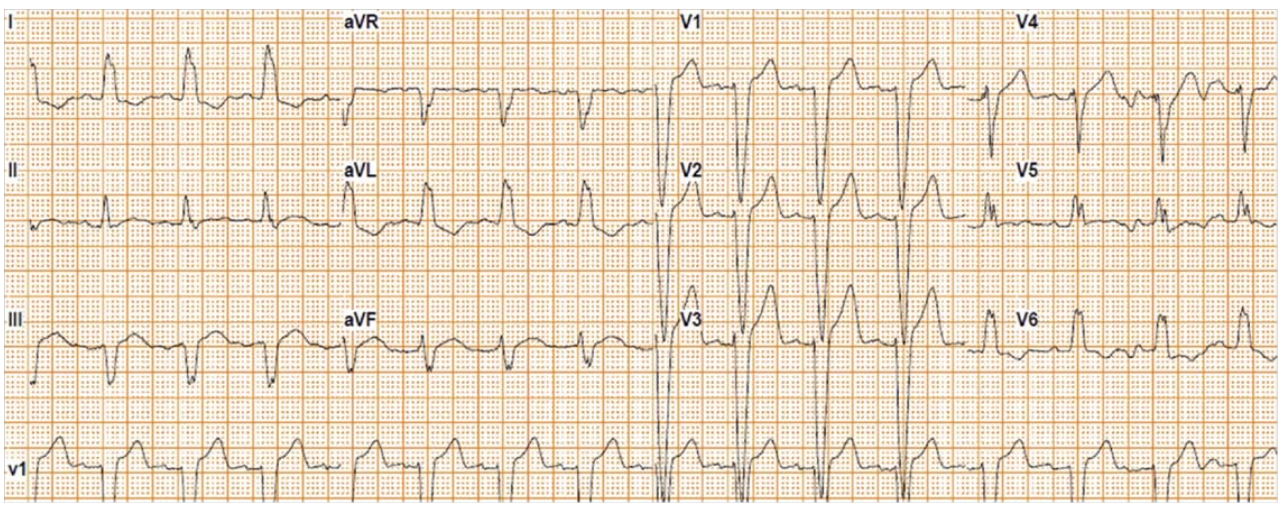
X, 'yes' criteria for CRT indication; •, 'no' criteria for CRT indication; #, both 'yes' or 'no' are valid for CRT indication. Rows with *letters in italics* are IIb recommendations, not valid for CRT indication in the main analysis but only in sensitivity analysis 1.

*EF 30–39% not a valid criteria in sensitivity analysis 2 (EF <30% required).

†The first row requires only QRS ≥120 ms, is least restrictive and functions as a reference.

Troubles de la conduction et insuffisance cardiaque

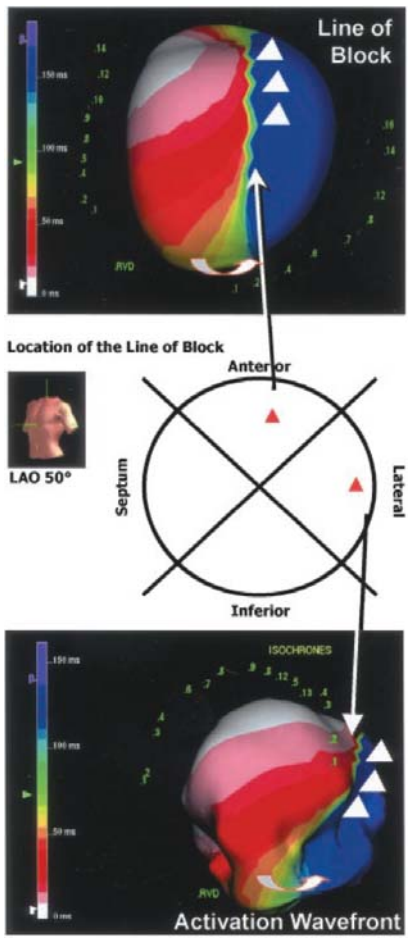
- Allongement PR, BBG, BBD, anomalies indéterminées
- 30-50% dans l'IC sévère
- S'aggravent avec le temps
- Facteurs indépendants de mortalité
- Induisent un asynchronisme mécanique



Activation électrique dans l'IC avec BBG

- La conduction électrique vers l'endocarde du VG se fait après l'activation du VD, **le plus souvent à travers le septum apical**

- Activation en « U » du VG avec des lignes fonctionnelles de bloc de conduction
  - QRS >150ms: région antérieure
  - QRS <150ms: plus latérale



Auricchio A, Circulation 2004