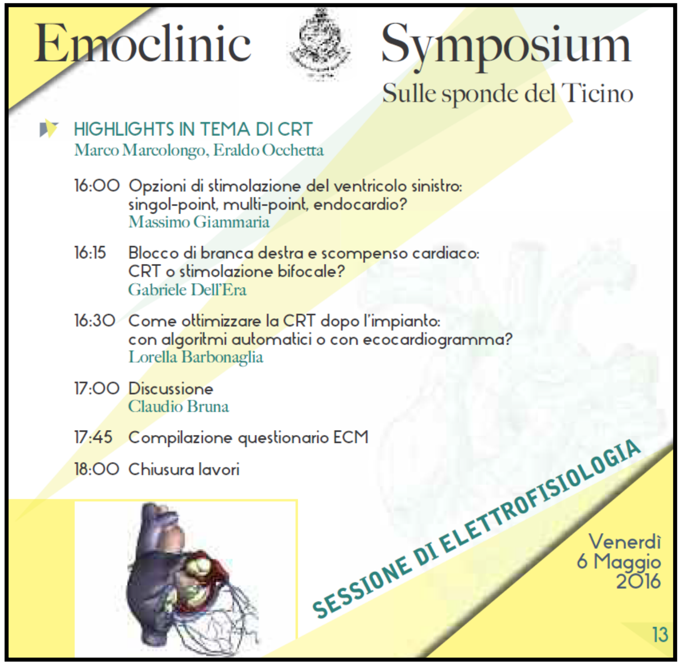
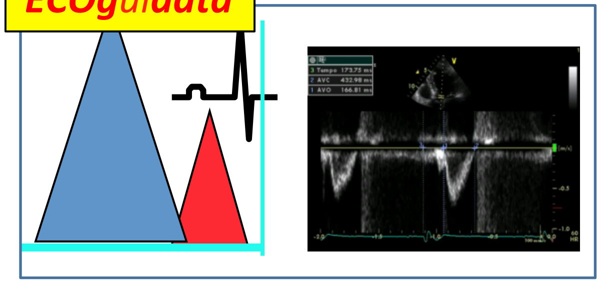
HIGHLIGHTS IN TEMA DI CRT

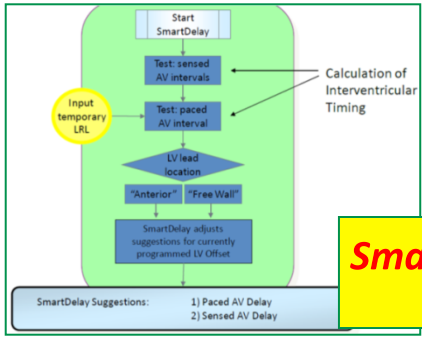
Come ottimizzare la CRT dopo l'impianto: con algoritmi automatici o con ecocardiogramma?

Lorella Barbonaglia
SC Cardiologia - Osp. S. Andrea - VC

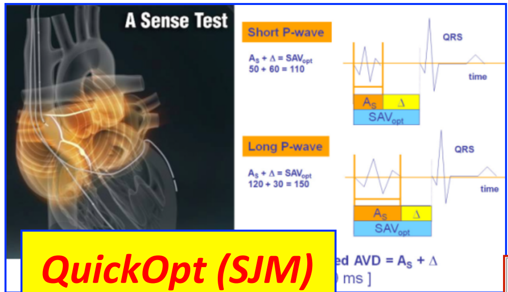


ECOguidata

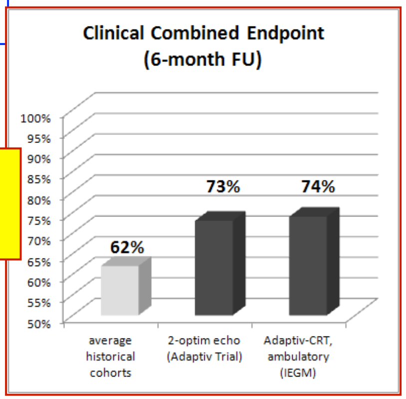




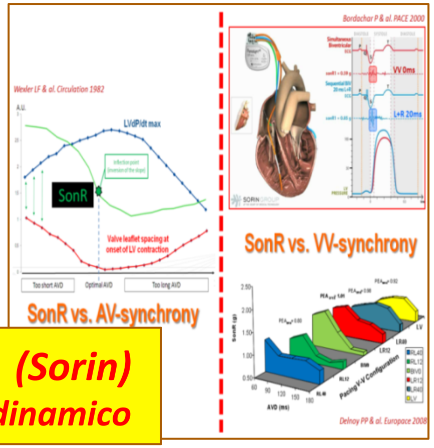
SmartDelay (BSc)
IEGM-based



QuickOpt (SJM)
IEGM-based



Adaptive CRT (Mdt)
IEGM-based



SonR (Sorin)
metodo emodinamico

CRT:

Pietra miliare terapia scompenso cardiaco

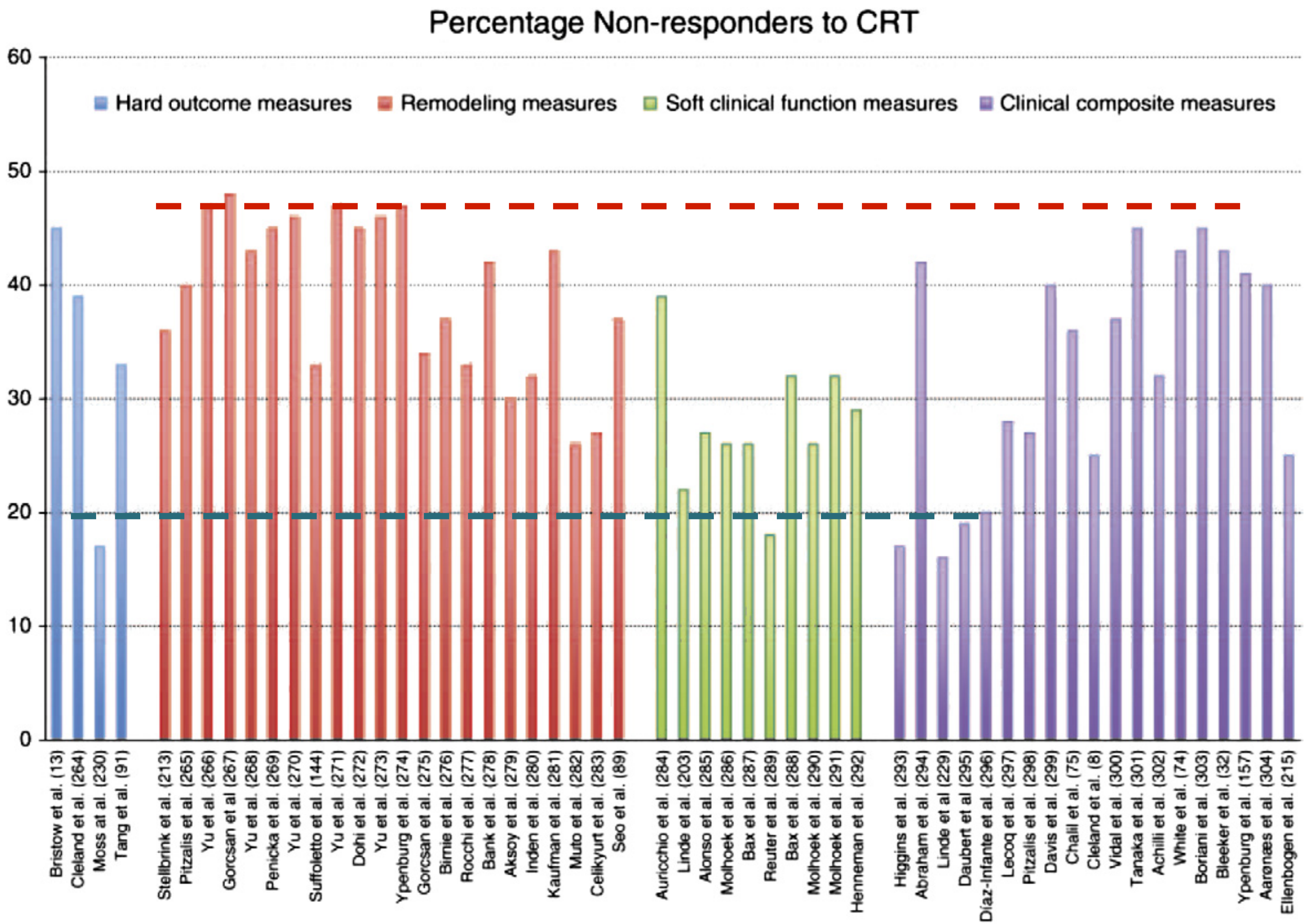
Table 10 Inclusion criteria, design, endpoints, and main findings of the randomized clinical trials evaluating cardiac resynchronization therapy in heart failure patients and sinus rhythm

Trial (ref)	No.	Design	NYHA	LVEF	QRS	Primary endpoints	Secondary endpoints	Main Findings
MUSTIC-SR[52]	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[51]	41	Single-blinded, crossover, randomized RV 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[49]	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[54]	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[53]	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[60]	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[55]	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[56]	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[61]	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[50]	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[62]	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

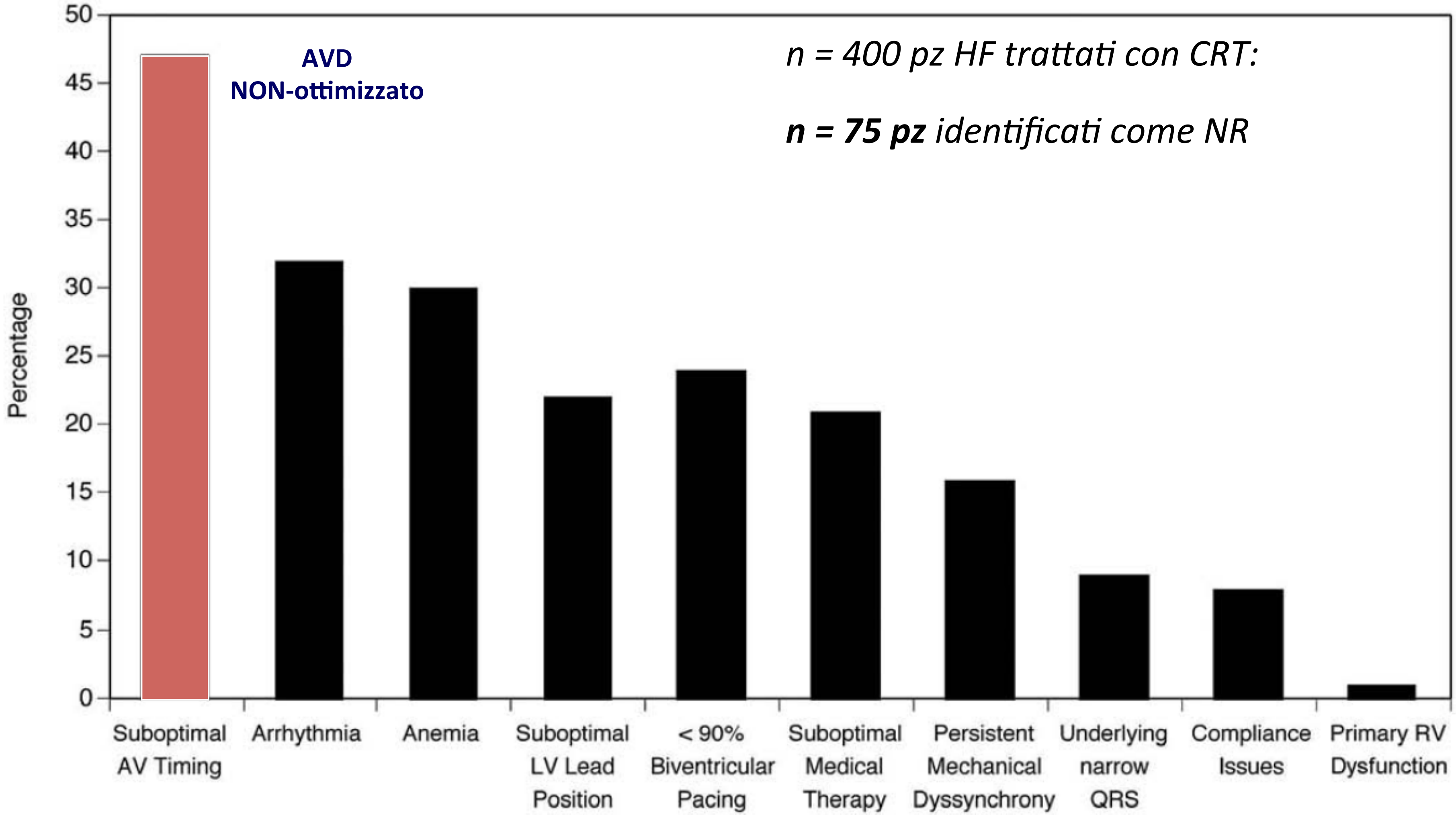
CARE-HF = Cardiac Resynchronization-Heart Failure; CONTAK-CD = CONTAK-Cardiac Defibrillator; COMPANION = Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure; CRT-D = cardiac resynchronization therapy with defibrillator; CRT-*P* = cardiac resynchronization therapy pacemaker; LV = left ventricular; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; MADIT-CRT = Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy; MIRACLE = Multicenter InSync Randomized Clinical Evaluation; MIRACLE-ICD = Multicenter InSync Implantable Cardioverter Defibrillator trial; MR = mitral regurgitation; MUSTIC = Multisite Stimulation in Cardiomyopathies; No. = number of patients; NYHA = New York Heart Association; PATH-CHF = Pacing Therapies in Congestive Heart Failure trial; QoL = quality-of-life score; RAFT= Resynchronization-Defibrillation for Ambulatory Heart Failure Trial; VE/VCO_2= minute ventilation/minute volume carbon dioxide production; VF = ventricular fibrillation; VO_2 = volume of oxygen; VT = ventricular tachycardia; 6MWD = 6-min walk distance.

ESC guidelines 2013

NON-Responders in CRT: ancora un problema



Daubert JC & al. Heart Rhythm 2012 (CRT consensus document)



Adapted from:
"Insights from a CRT Optimization Clinic as Part of a HF Disease Management Program".
Mullens W & al, JACC 2009:53;765-73

Ottimizzazione programmazione device

- **Ridurre percentuale non-responder**

- **Cosa?**
  - **2 momenti:**
    - **Diastole (A-V)**
    - **Sistole (V-V)**
- **Come?**
  - **2 metodi:**
    - **Ecoguidata**
    - **Algoritmi device-based**

Ottimizzazione diastolica (AVD) nei pz BAV/CRT: Approcci e Metodi

Antonini L & al., Europace 2012 (background & critical review)

Table 1 Methods for atrioventricular setting

References and methods	Methodology	Type	Used in	Compared	Trials
Ismer[5]	Echo and oesophageal EGM	Formula Opt AV = AEA – LVEC	DDD, CRT	No	
Ritter[6]	Echo-Doppler	Formula Opt AV = AV long – (QA short – QA long)	DDD, CRT	MI VTI, DFT, EEHF, ICG, Ao VTI, PEA, Standard	MUSTIC SR,[7] MIRACLE,[3] MIRACLE ICD,[8] MIRACLE ICD II[9]
Meluzin[10]	Echo-Doppler	Formula Opt AV = AV long – t1	CRT	No	
Ishikawa[11]	Echo-Doppler	Formula Opt AV = AV long – DMR	DDD	No	
Auricchio[12]	Intracardiac electrogram	Formula Opt AV = (IAVD × 0.7) – 55 ms	CRT	No	
DFT[13]	Echo-Doppler	Iterative	DDD, CRT	Ritter, SMARTDelay, Standard	CARE-HF[1]
MI-VTI[14]	Echo-Doppler	Iterative	DDD, CRT	Ritter, DFT, Ao VTI	
LVOT-VTI-CO[15]	Echo-Doppler	Iterative	CRT	No	
Ao VTI[16]	Echo-Doppler	Iterative	CRT	Ritter, Standard, Quick Opt, EEHF	
IdP/dt[12]	Haemodynamic	Iterative	CRT	No	
Doppler dP/dt[17]	Echo-Doppler	Iterative	CRT	Standard	
MPI[18]	Echo-Doppler	Iterative	CRT	No	
FPPG[19]	Photoelectric Pletismography	Iterative	CRT	Aortic invasive pulse pressure	
ICG[20]	Impedance	Iterative	DDD, CRT	Ritter	
PEA[21]	Mechanical acceleration	Automatic	DDD, CRT	Ritter	CLEAR[22]
Quick Opt[23]	Intracardiac electrogram	Automatic	CRT	Ao VTI, Standard	FREEDOM[24]
EEHF[25]	Intrinsic measures	Automatic	CRT	Standard, Ritter, Ao VTI	
SMARTDelay[26]	Intracardiac electrogram	Automatic	CRT	DFT, Standard	SMARTAV[27]
Standard	Fixed predefined	Fixed	DDD, CRT	Ao VTI, Doppler dP/dt, EEHF, DFT, Ritter	

FORMULE (predefinite)

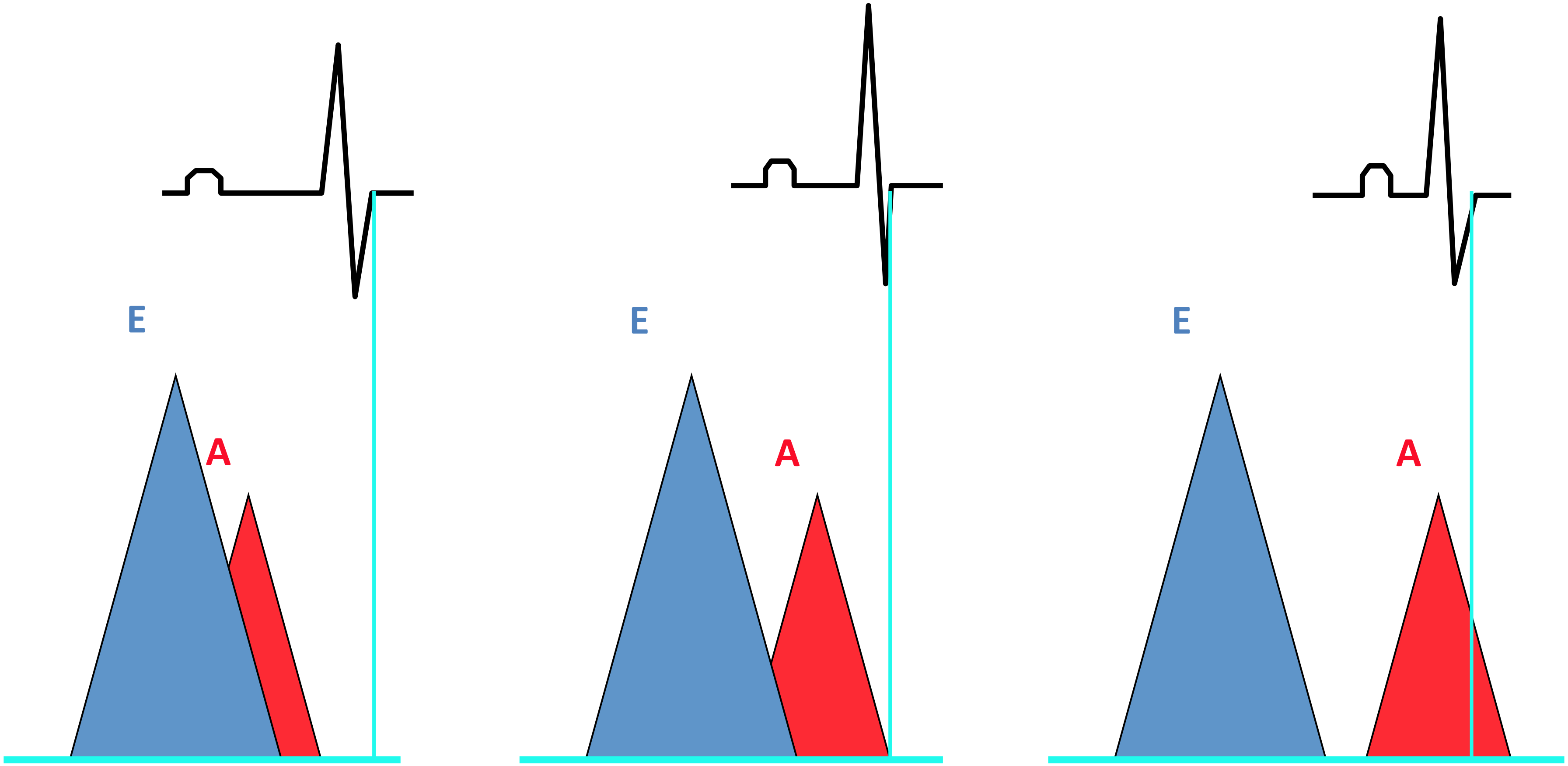
Metodi ITERATIVI

Echo Optimization

- Echocardiography is considered the "gold standard" of timing optimization
- Mitral velocity Doppler echo is used for AV timing optimization
  - CRT systems and conventional systems (ICDs, pacemakers)
  - Sensed and paced AV delays
- Aortic velocity time integral (VTI) echo is used for VV timing
  - RV and LV synchronization

ASINCRONIA ATRIO-VENTRICOLARE

Metodo iterativo basato sul DFT



Long AVD | Appropriate AVD | Short AVD

CAZEAU S. Heart 2000;84:579

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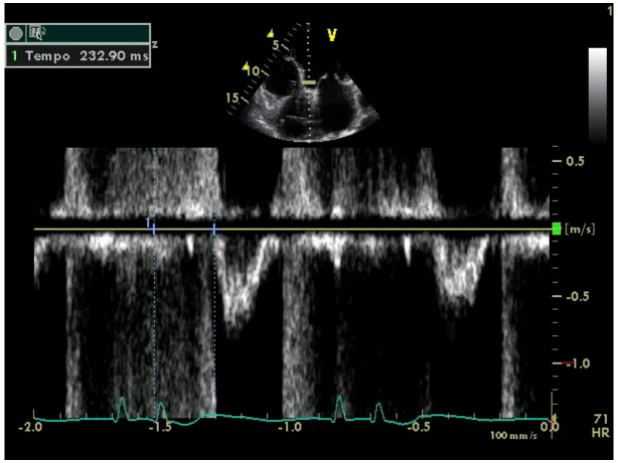
Calcolo stroke volume con VTI aortico

- Obtain Pulsed Wave **Doppler of LVOT** with several different sequential ventricular intervals
- **Select the largest VTI**
- CSA is assumed constant, therefore variations in SV is based on VTI alone



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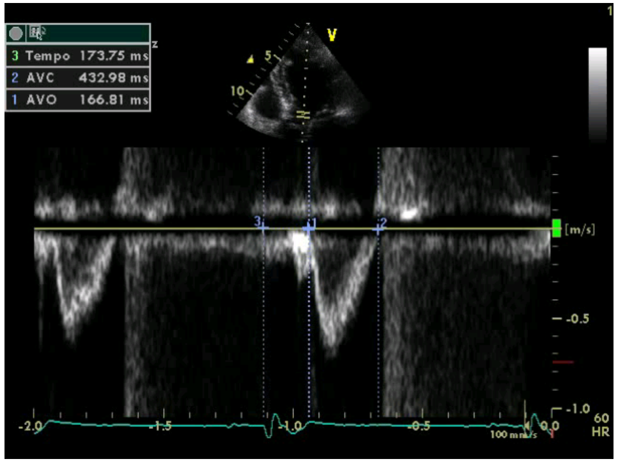


Post-CRT

Ottimizz. VVD nei pz CRT

Reference	n	Optimization method	Effect of optimization	Timing of optimization after implant	Mean VV delay (ms)	Optimal pre-excitation LV/Sim/RV (%)	AV delay optimized	Randomized	Blinded	Mean follow-up (months)	Further optimization
Rao et al.[9]	306	EEHF+	None significant	2 weeks	48 ± 14 ms	Not stated	EEHF+	Yes	Double	6 months	–
Boriani et al.[11]	121	Echocardiographic LVOT VTI	None significant	Pre-discharge	Not stated	35/28/34	Ritter method	Yes	Single	6 months	No
Leon et al.[10]	359	Echocardiographic LVOT VTI	+8.6% stroke volume +15.1 m 6MWT	Pre-discharge	Not stated	58/19/23	Ritter method	No	No	6 months	Not stated
Bordachar et al.[12]	41	Echocardiographic LVOT VTI	+0.8 L/min CO by LVOT VTI	Time of implant	Not stated	61/15/24	Ritter method	No	No	3 months	Not stated
Mortensen et al.[13]	34	Echocardiographic LVOT VTI	+0.1 NYHA +7.3 m 6MWT	Pre-discharge	Discharge: +27.4 ms 3 months: +22.7 ms	38/21/41	Ritter method	No	No	6 months	3 months
Vanderheyden et al.[14]	20	Echocardiographic LVOT VTI	+26% LVOT VTI	2–5 days	Not stated	60/25/15	Ritter method	No	No	6 months	Not stated
Sogaard et al.[15]	20	Tissue Doppler imaging	+3.9% LVEF +7% DFT	24 h	Not stated	45/0/55	Ritter method	No	No	3 months	Not stated
Vidal et al.[16]	100	Tissue Doppler synchrony	+0.7 L/min CO AV VTI +52 m 6MWT	24–72 h	Not stated	72/21/6	Iterative	No	No	6 months	–
Novak et al.[17]	16	Strain rate synchrony	+0.3 L/min CO by Fick	3 months	15.4 ± 10.7 ms	14/2/0	Meluzin method	No	No	None	–
Perego et al.[18]	12	Invasive dP/dt_{max}	+6% invasive dP/dt	Time of implant	−25 ms	75/25/0	Invasive dP/dt	No	No	None	–
Hay et al.[19]	9	Invasive dP/dt_{max}	Simultaneous optimal	Time of implant	Not stated	33/67/0	No	No	No	None	–
van Gelder et al.[20]	53	Invasive dP/dt_{max}	+8% invasive dP/dt	<24 h	Ischaemic: −52 ms Idiopathic −28 ms	83/11/6	Invasive dP/dt	No	No	None	–
Kurzidim et al.[21]	22	Invasive dP/dt_{max}	+3% invasive dP/dt	Time of implant	−37 ms	64/32/4	Invasive dP/dt	No	No	None	–
Burri et al.[99]	27	Radionuclide ventriculography	+0.4% LVEF	<3 days	Not stated	44/33/22	Ritter method	No	No	None	–
Whinnett et al.[22]	15	Finger photo-plethysmography	+4 mmHg systolic BP	3–30 months	−8 ms	Not stated	FPPG	No	No	None	–

6MWT, Six-minute walk test; CO, cardiac output; DFT, diastolic filling time; EEHF, Expert Ease for Heart Failure algorithm; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; VTI, velocity time integral; LV, left ventricle; RV, right ventricle; FPPG, finger photoplethysmography.

EUROPEAN SOCIETY OF CARDIOLOGY®
European Heart Journal (2008) 29, 2458
doi:10.1093/eurheartj/ehn380

How should we optimize cardiac resynchronization therapy?

Tony Stanton[1]*, Nathaniel M. Hawkins[2], Kerry J. Hogg[3], Nicholas E.R. Goodfield[3], Mark C. Petrie[4], and John J.V. McMurray[5]

[1]Department of Medicine, University of Queensland Princess Alexandra Hospital, Ipswich Road, Brisbane Q4102, Australia; [2]University Hospital Aintree, Liverpool, UK; [3]Stobhill Hospital, Glasgow, UK; [4]Golden Jubilee National Hospital, Glasgow, UK; and [5]Western Infirmary, Glasgow, UK

Risultati molto diversi anche con metodiche sovrapponibili …

Stanton T & al. Eur Heart J 2008;29:2458-72

Beneficio clinico non chiaro

Metodiche ecocardiografiche

- **Miglioramento emodinamico in ACUTO, ma risultati controversi a lungo termine**

- **Limitazioni:**
  - **variabilità inter/ intra-operatore**
  - **bassa riproducibilità**
  - **ottimizzazione in specifiche condizioni in-Lab** ***(a riposo)***
  - **non possibili valutazioni ripetute nel tempo** ***(time and resource-consuming)***

⇒ ***limite alla loro applicabilità nella pratica clinica***

OTTIMIZZAZIONE dei parametri CRT:
LG ESC 2013 *(Pacing & CRT)*

Table 13 **Summary of current evidence for CRT optimization**

Parameter	Standard (current practice)	CRT optimization	Additional clinical benefit (compared to standard)	References
LV lead position	Posterolateral	• Avoid apical • Target latest activated area	Benefit likely (less hospitalization for HF) Benefit likely (one RCT more responders, less hospitalization for HF)	70–72 73
AV delay	Fixed empirical AV interval 120 ms (range 100–120 ms)	• Echo-Doppler: shortest AV delay without truncation of the A-wave (Ritter's method) or change in LV systolic function	• Uncertain or mild (one small RCT and several observational positive)	74
		• Device-based algorithms (SmartDelay, QuickOpt)	• Uncertain (two RCTs negative)	76, 79
VV delay	Simultaneous BiV	• Echo: residual LV dyssynchrony	• Uncertain or mild (one RCT showed mild benefit)	77
		• Echo-Doppler: largest stroke volume	• Uncertain (one RCT negative, one controlled positive)	78, 80
		• ECG: narrowest LV-paced QRS; difference between BiV and preimplantation QRS	• Unknown (no comparative study)	75
		• Device-based algorithms (Expert-Ease, Quick-Opt, Peak endocardial acceleration)	• Uncertain (three RCTs negative)	76, 82, 83

Raccomandazioni tiepide: beneficio clinico "incerto" o "lieve"

*Brignole M et al.- **ESC Pacing/CRT Guidelines.** EHJ 2013;34:2281-329*

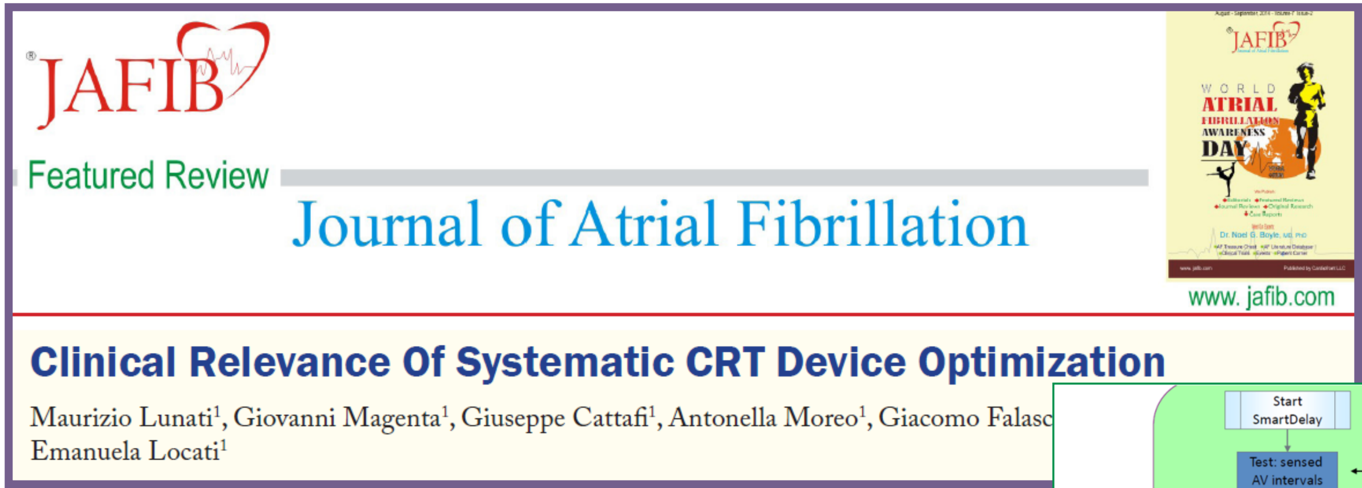
Choice of pacing mode (and CRT optimization)

Recommendations	Class	Level
1) The goal of should be to achieve biventricular pacing as close to 100% as possible since the survival benefit and reduction in hospitalization are strongly associated with an increasing percentage of biventricular pacing.	IIa	B
2) Apical position of the LV lead should be avoided when possible.	IIa	B
3) LV lead placement may be targeted at the latest activated LV segment.	IIb	B

Clinical perspectives

- The usual (standard) modality of CRT pacing consists of simultaneous biventricular pacing (RV and LV) with a fixed 100-120 ms AV delay with LV lead located in a posterolateral vein, if possible. ...Current evidence does not strongly support the performance of AV and VV optimization routinely in all patients receiving CRT.
- LV pacing alone... seems to be non-inferior to biventricular pacing for improving soft end-points (quality of life, exercise capacity and LV reverse remodelling) and might be considered to lower the costs and complexity of the procedure and to increase the longevity of the device. LV pacing alone seems particularly appealing in children and young adults.

Strumenti device-based per ottimizzare AVD / VVD


JAFIB
Featured Review
Journal of Atrial Fibrillation
www. jafib.com

Clinical Relevance Of Systematic CRT Device Optimization

Maurizio Lunati[1], Giovanni Magenta[1], Giuseppe Cattafi[1], Antonella Moreo[1], Giacomo Falasc
Emanuela Locati[1]

Lunati M & al.
JAFIB 2014 Aug/Sep
Vol. 7(2)

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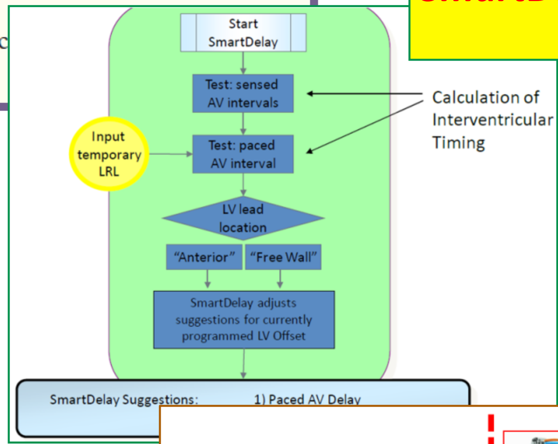

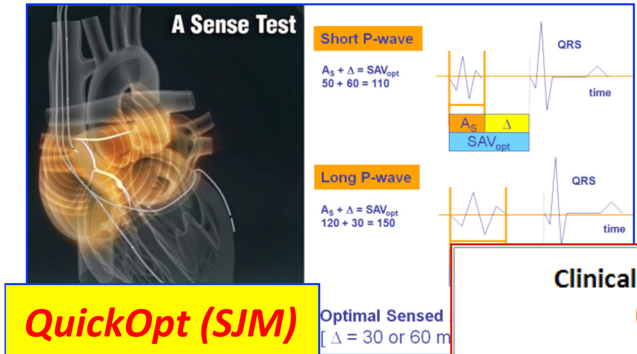

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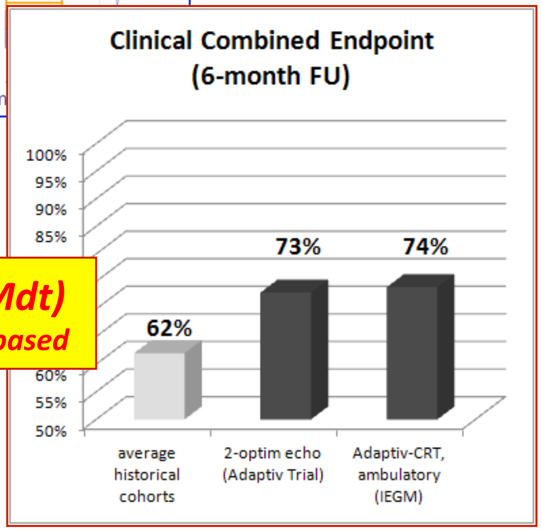

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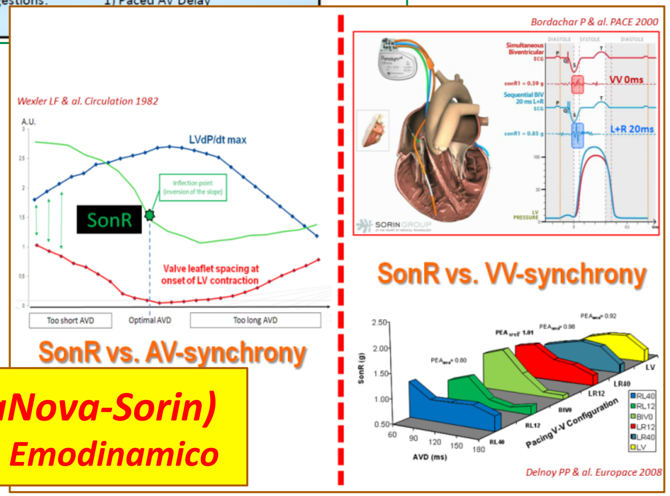
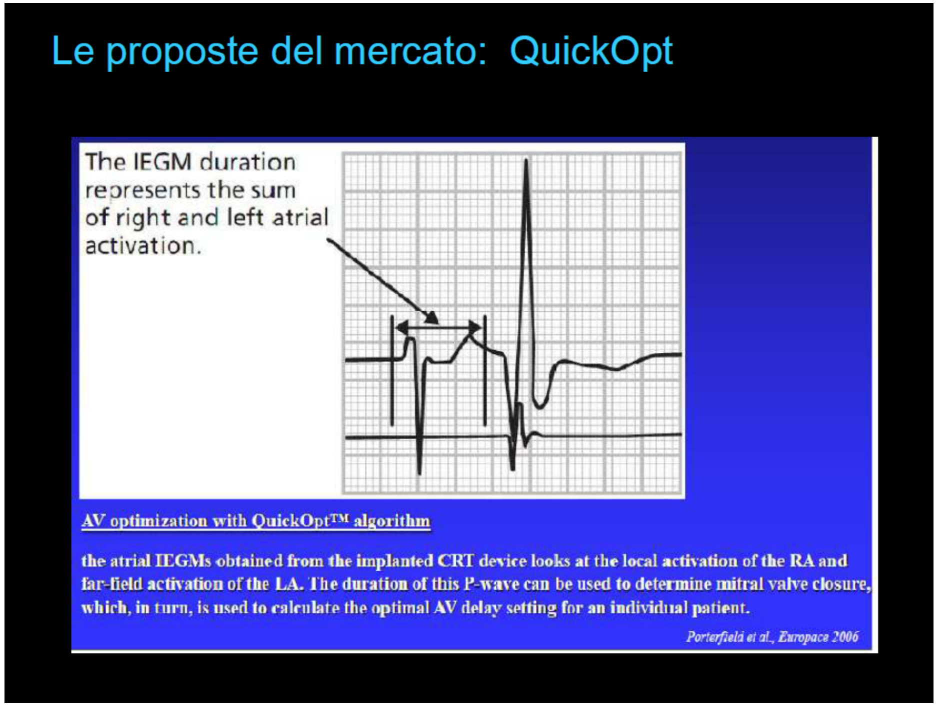


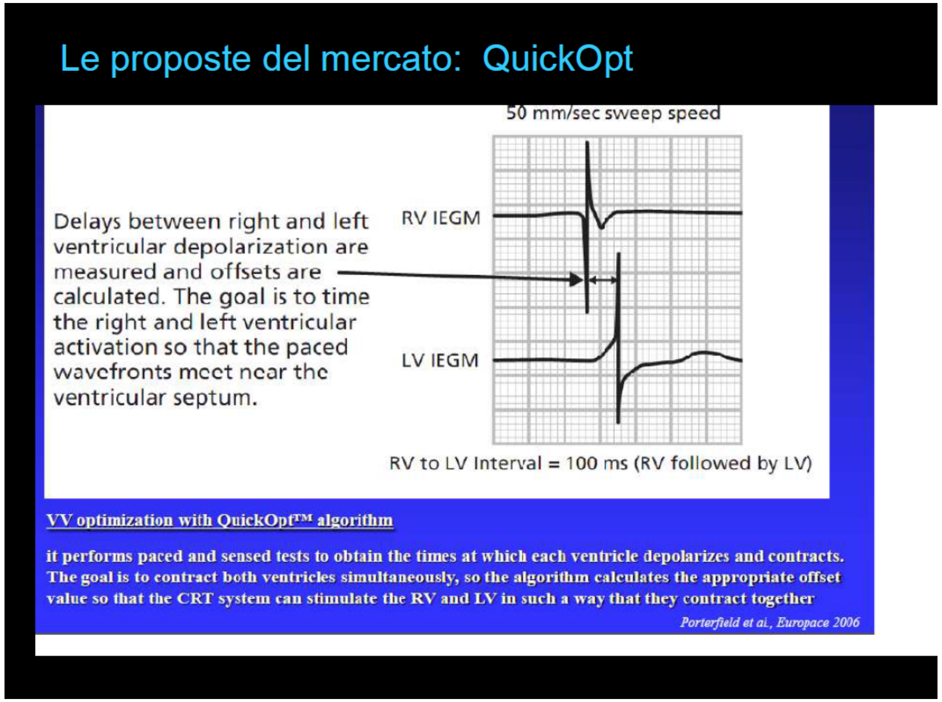
SonR (LivaNova-Sorin)
Metodo Emodinamico

Ottimizzazione con metodo ELETTRICO (IEGM) ⇒ NON-inferiorità vs. metodi ecoguidati

	QuickOpt (SJM)	SmartDelay (BSc)	Adaptive CRT (Mdt)
Ottimizzazione AVD	Solo **@ RIPOSO**; Paced & sensed	Solo **@ RIPOSO**; Paced & sensed	**RIPOSO e ESERCIZIO** Paced & sensed
Ottimizzazione VVD	OK	OK	OK (LV synchro opp. BiV)
@ visita FU (In-clinic) vs. AUTOMATICO ("ambulatory")	**In-clinic (@ visita FU)**	**In-clinic (@ visita FU)**	**Automatica**
Outcome dai trial: SICUREZZA	OK	OK	OK
Outcome dai trial: EFFICACIA	Ottim CRT @ visita FU **NON- INFERIORE alla pratica clinica** **CCS a 1Y (FREEDOM)**	Ottim CRT @ visita FU **EQUIVALENTE a programm. ECO-guidata o empirica**, strutturalmente & funzionalmente a **6M** **(SMART-AV)**	Approccio Adaptive-CRT **NON-INFERIORE ad approccio pacing BiV Eco-ottimizzato** **CCS a 6M** **(Adaptive-CRT)**

Quick Opt


Le proposte del mercato: QuickOpt
The IEGM duration represents the sum of right and left atrial activation.
AV optimization with QuickOpt™ algorithm
the atrial IEGMs obtained from the implanted CRT device looks at the local activation of the RA and far-field activation of the LA. The duration of this P-wave can be used to determine mitral valve closure, which, in turn, is used to calculate the optimal AV delay setting for an individual patient.
Porterfield et al., Europace 2006

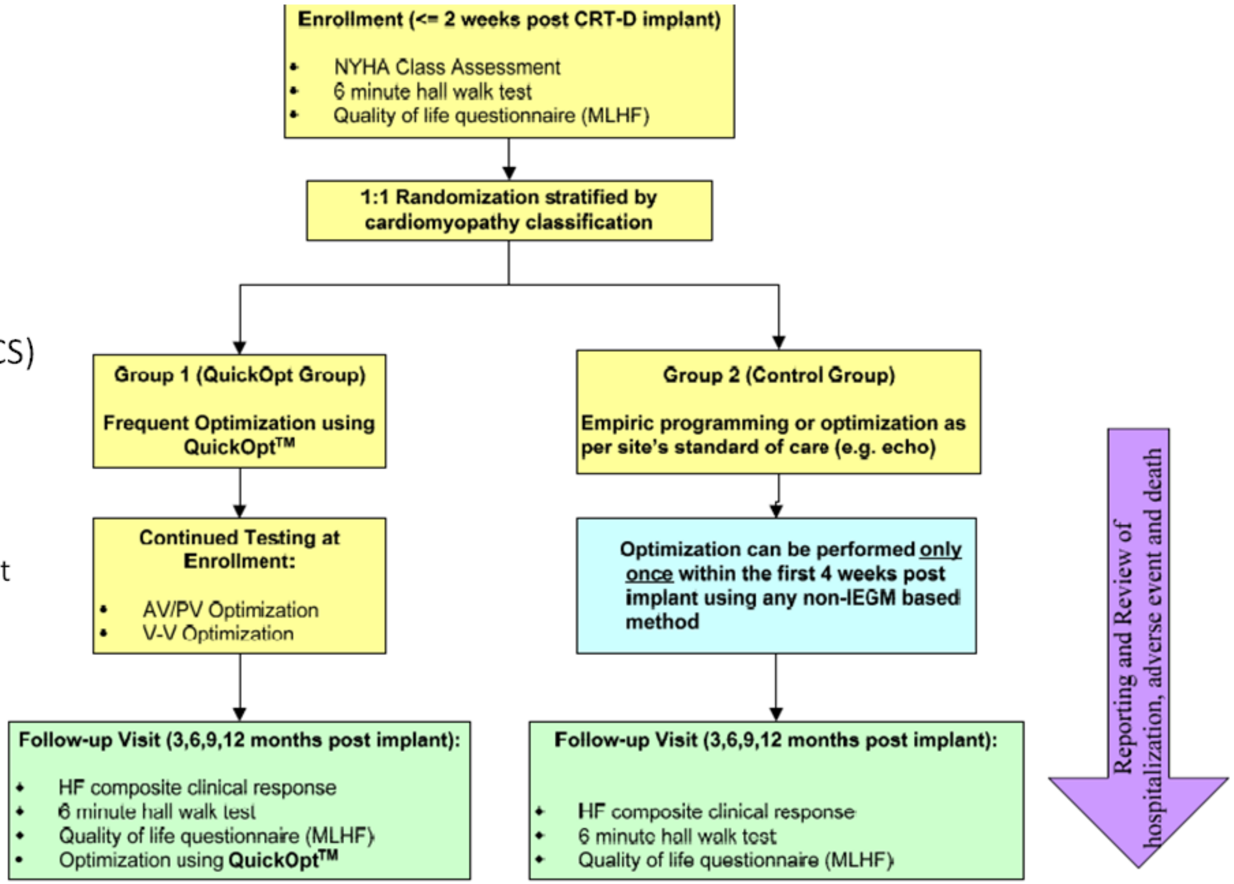

Le proposte del mercato: QuickOpt
50 mm/sec sweep speed
Delays between right and left ventricular depolarization are measured and offsets are calculated. The goal is to time the right and left ventricular activation so that the paced wavefronts meet near the ventricular septum.
RV IEGM
LV IEGM
RV to LV Interval = 100 ms (RV followed by LV)
VV optimization with QuickOpt™ algorithm
it performs paced and sensed tests to obtain the times at which each ventricle depolarizes and contracts. The goal is to contract both ventricles simultaneously, so the algorithm calculates the appropriate offset value so that the CRT system can stimulate the RV and LV in such a way that they contract together
Porterfield et al., Europace 2006

Metodi di ottimizzazione basati su EGM *(QuickOpt, SJM)*
FREEDOM trial: disegno/obiettivi

QuickOpt (SJM)

ST. JUDE MEDICAL
MORE CONTROL. LESS RISK.

- Prospective, randomized (1:1), double-blinded, multicenter study
- Treatment: **frequent optimization** using **QuickOpt**® timing **@ every FU visit**
- Controls: **Empiric** programming **or one-time optimization** using a non-IEGM method (usually echo) within first month
- FU duration: **12 months**



Primary Endpoint

HF clinical composite score (CCS) as defined by Packer*:

- hospitalization
- all-cause mortality
- NYHA class
- Pt Global Assessment

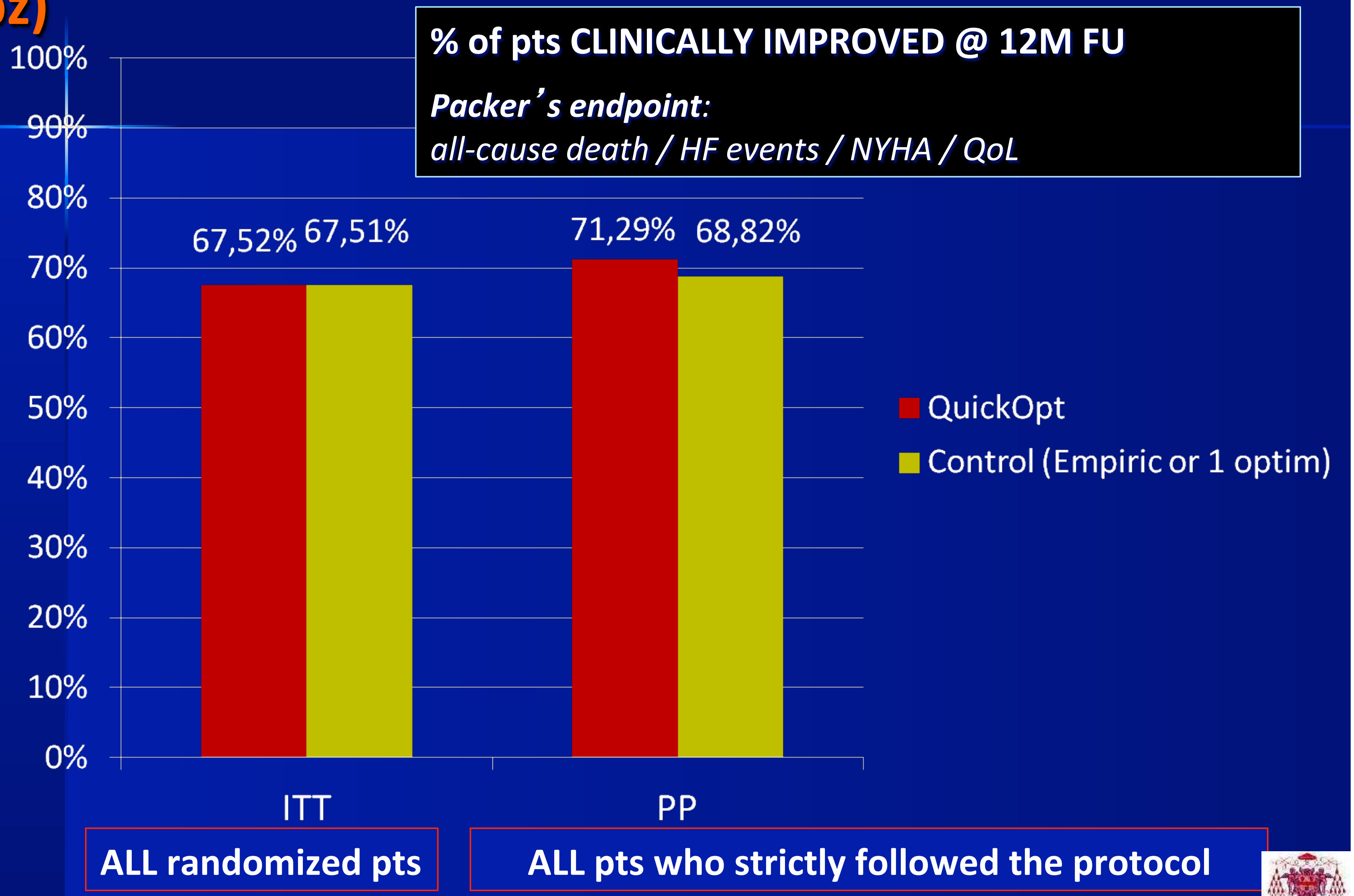
Secondary Endpoints

- All-cause, CV & HF mortality
- All-cause, CV & HFH

** Packer M. J Card Fail 2001*

Metodi di ottimizzazione basati su EGM *(QuickOpt, SJM)*

FREEDOM trial: RISULTATI ad 1 anno di FU (n = 1644 pz)



Le proposte del mercato: SmartDelay

- Theory:
  - Achieve fusion between instrinsic activation (through septum) and paced activation of the late region (LV free wall)
- Measures:
  - Intrinsic AV interval (to first V chamber, typically RV) – 15 beat average
  - Paced AV interval, at atrial rate 10-20 beats over intrinsic rate
- Requires:
  - QRS (widest of II, V1, V6) and Lead location (LV free wall, or anterior)
- Provides:
  - Sensed and paced AV delays, not VV
- General equation (for BiV, Free wall) – also has LV only version
  - $AVD_{p,s}$ = -0.728*QRS + 0.757*AVip,s + 71.3
  - Narrower the QRS (more intact Purkinje), the longer the AVD
  - All AVD are limited to between 50ms and 70% of AV interval

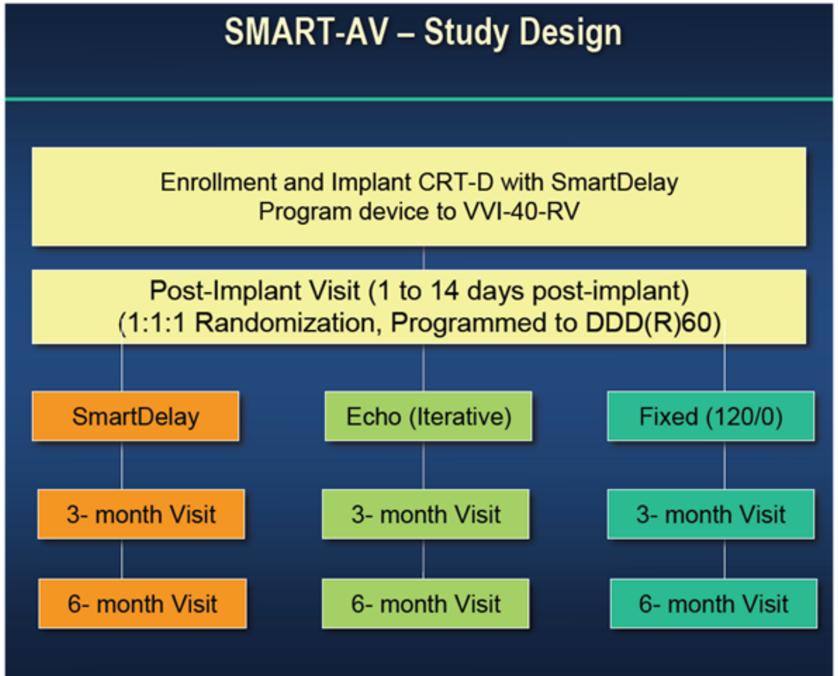
Metodi di ottimizzazione basati su EGM *(Smart-AV, BSc)*
SMART-AV trial: disegno / obiettivi

SmartDelay (SD); BSx

Compare **3 alternative AVD optimization** techniques, to assess the hypotheses that:

•AVD-optimization by **ECHOCG** &/or the **SmartDelay** algo is superior to a **Fixed nominal AVD** (as demonstrated by improved **LVESV after 6M**), &

•Programming according to SmartDelay is non-inferior to using ECHOCG AVD optimization.



Stein KM, et al. Pacing Clin Electrophysiol. 2010;33

SMART-AV Inclusion

- NYHA class III or IV
- EF < 0.35
- QRS >120ms
- Expected to be in sinus rhythm at the time of implant
- Willing and capable of undergoing a device implant and participating in all testing
- Receiving OPT

SMART-AV Exclusion

- Complete heart block or unable to tolerate pacing at VVI-40-RV for up to 14 days
- Previously received CRT

Primary Endpoint:

- LVESV at 6 months

Secondary Endpoints:

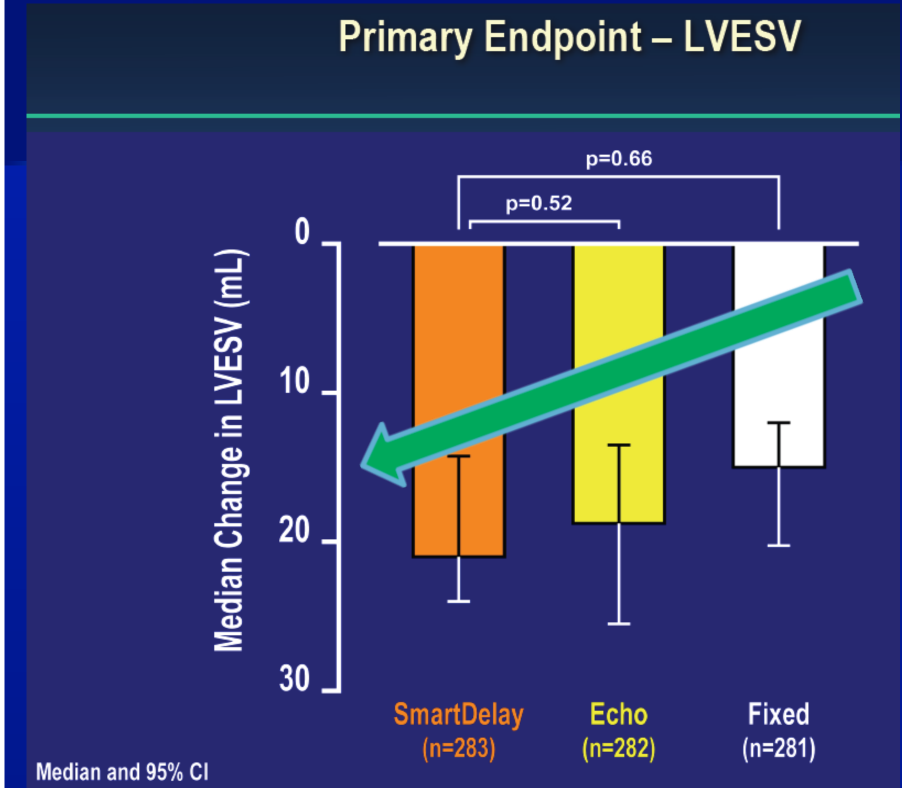
- 6 min walk, EF, NYHA Class, LVEDV, QOL (MLWHF)

Statistics:

- Continuous outcomes: general linear model - F test
- Categorical outcomes: risk difference of proportions – Chi-squared test
- Applicable to primary, secondary and subgroup analyses

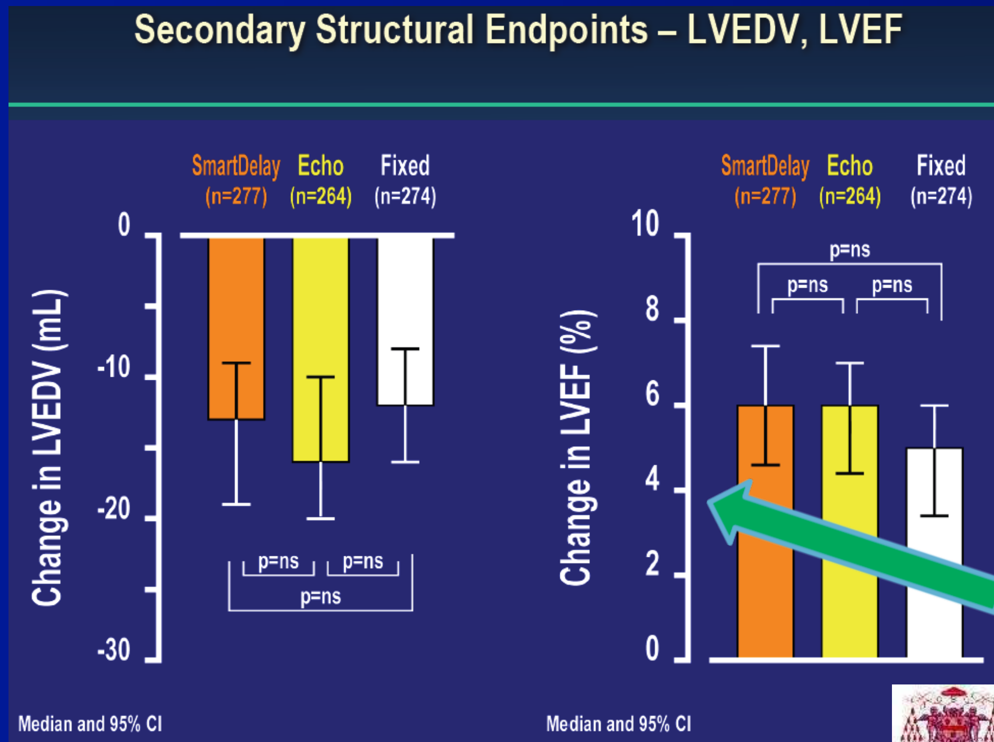
Metodi di ottimizzazione basati su EGM *(Smart-AV, BSc)*

SMART-AV trial (n = 980 pz): rimodellamento LV a 6M

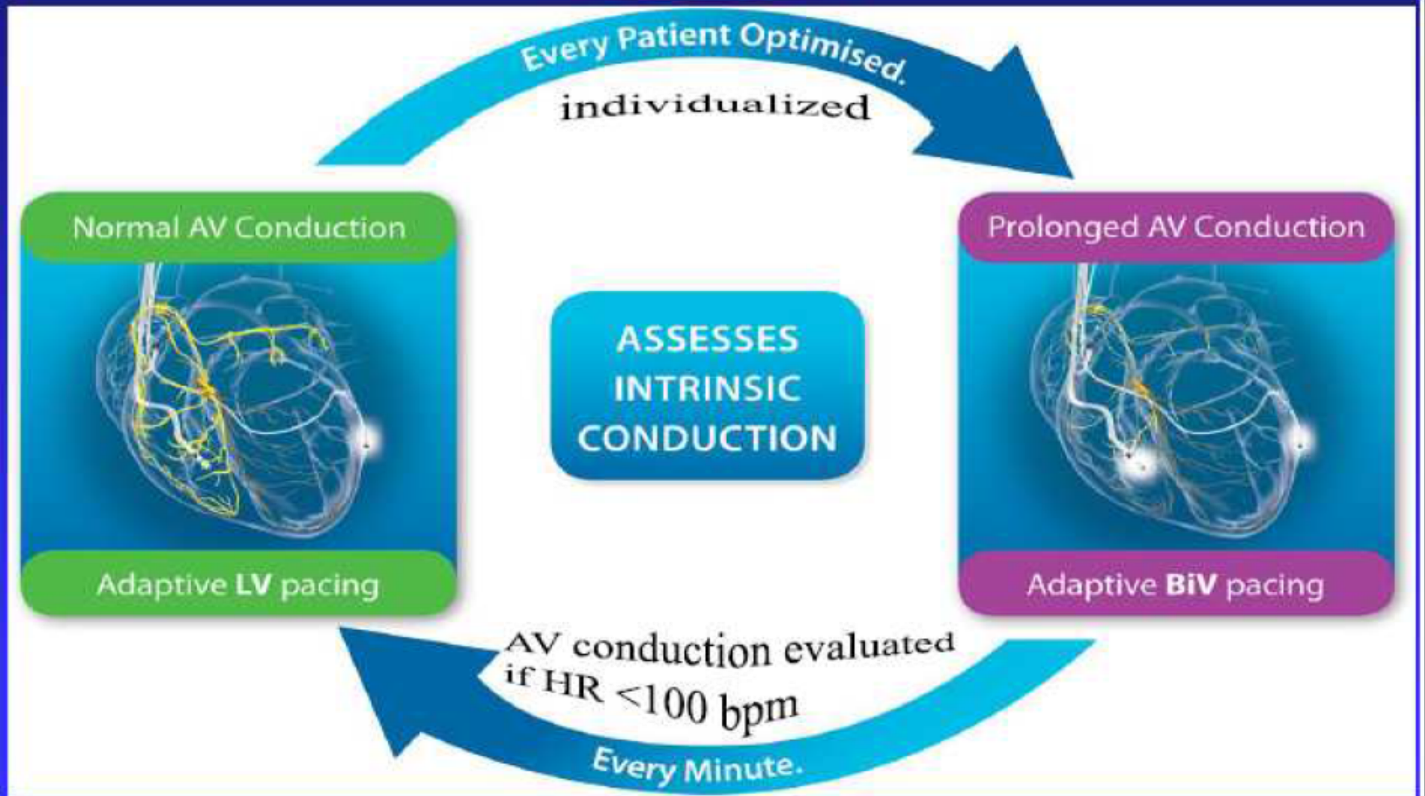


- **LVESV e LVEF**: **trend a favore** dell' AVD ottimizzato (eco o algoritmo) vs. AVD fisso, nonostante le p = ns

- Questo studio era suffic. POTENZIATO per dare risultati significativi ?
- Gli assunti statistici erano corretti ?



Le proposte del mercato: 3 Adaptive CRT



normal AV conduction : AS-VS < 200 ms; AP-VS < 250 ms

Metodi di Ottimizzazione basati su EGM

Algoritmo Adaptive CRT (Mdt)

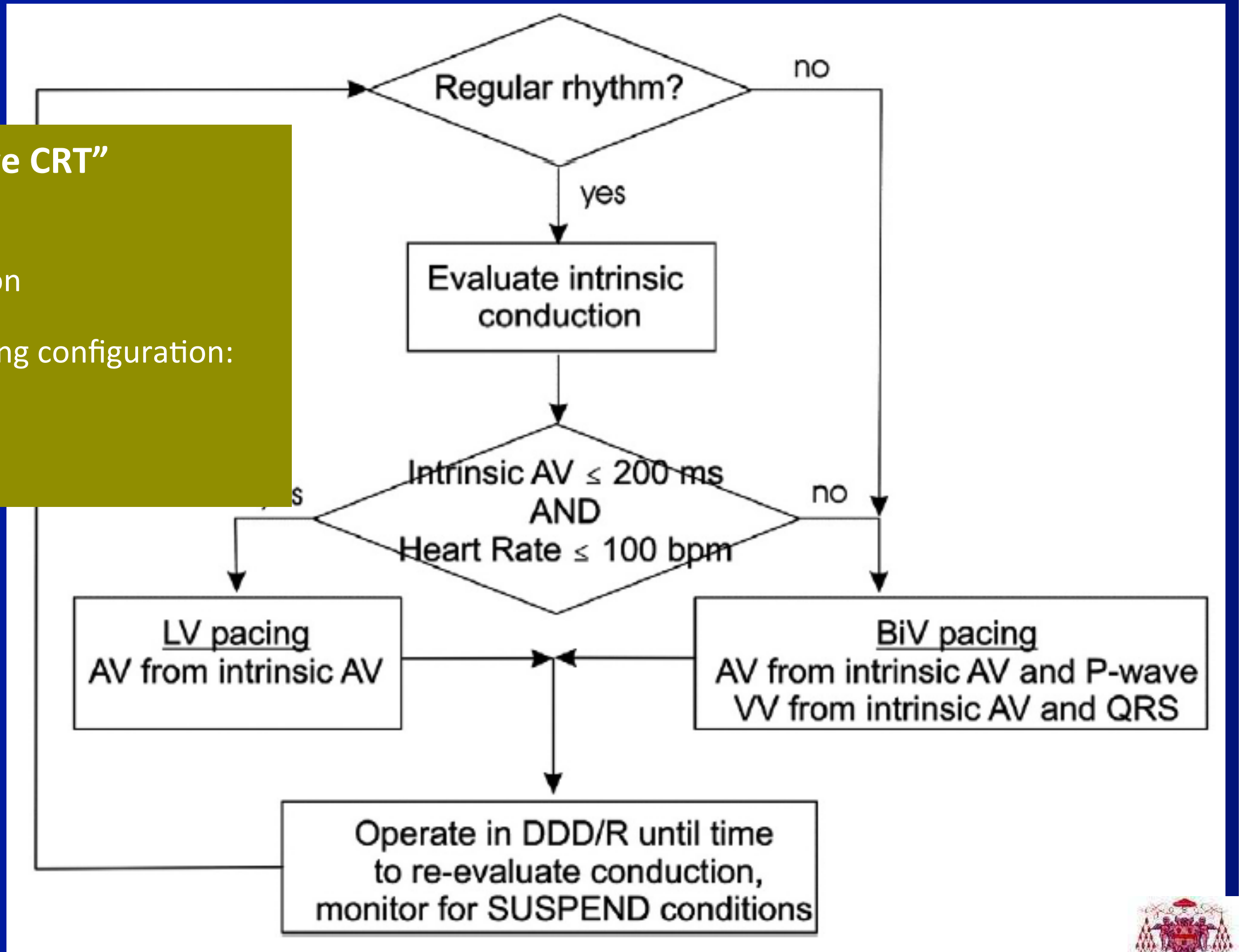
Assunto FISIOPATOLOGICO dell'algoritmo:

nei pz con true-LBBB (con fronte d'attivazione RV spontaneo), un pacing "LV-sincrono" è un'opzione raccomandabile alternativa al pacing standard BiV

KEY elements of the "Adaptive CRT" algorithm:

1. evaluation of intrinsic conduction

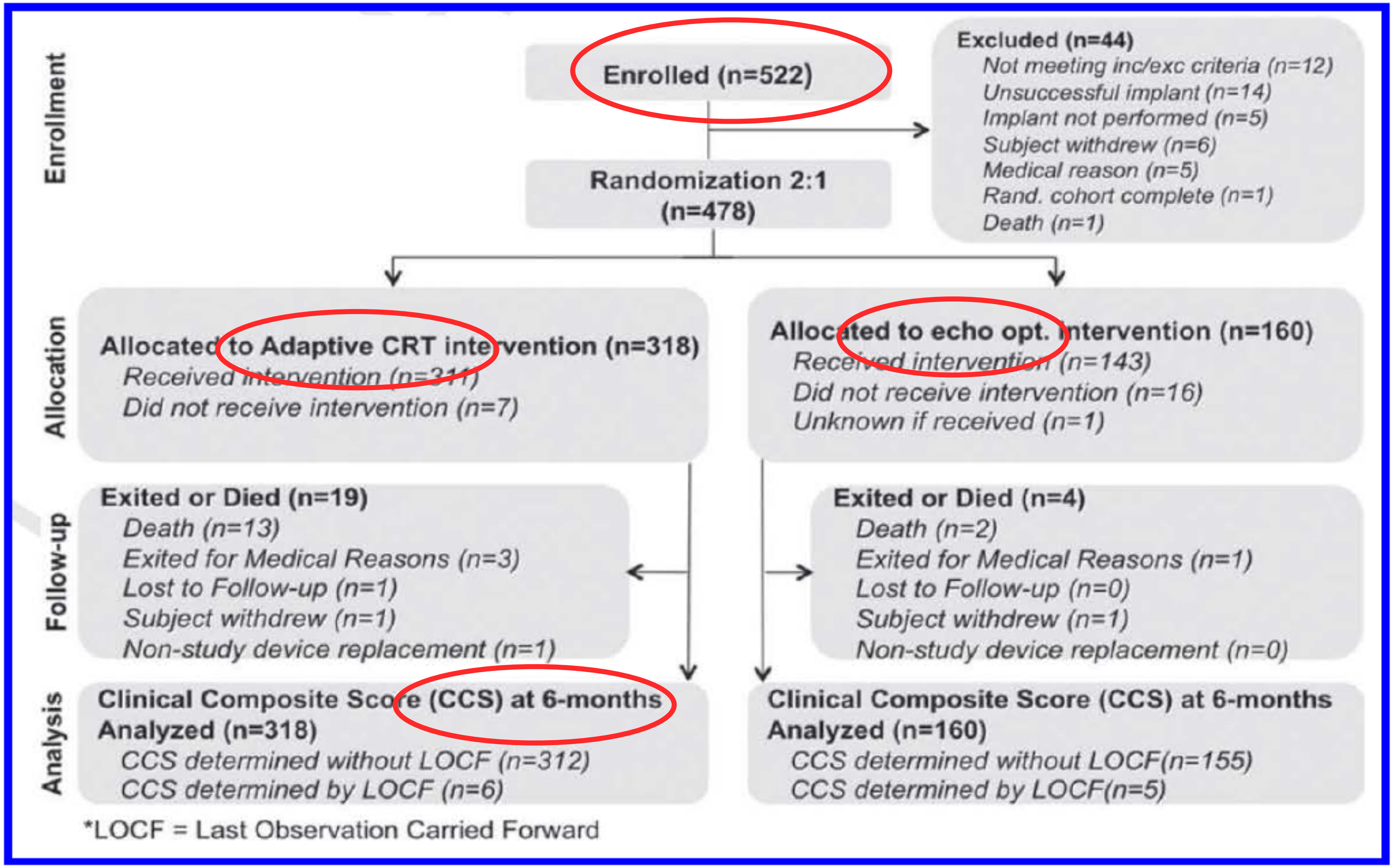
2. determination & update of pacing configuration:
   - LV or BiV
   - AV delays (p/s)
   - VV delay



Krum H & al. Am Heart J 2012

Adaptive CRT trial

Flow diagram of clinical composite score



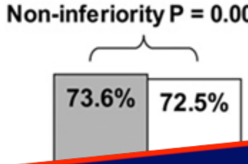
Metodi di Ottimizzazione basati su EGM

Algoritmo Adaptive CRT (Mdt): outcome @ 6 mesi

Martin DO &al. Heart Rhythm 2012 Jul [Epub ahead of print]

RESULTS: the study met all 3 non-inferiority 1-ary objectives:

a) **% CLINICAL RESPONSE** to CRT @ 6M (Packer's combined endpoint):



Outcome @ 6M FU:

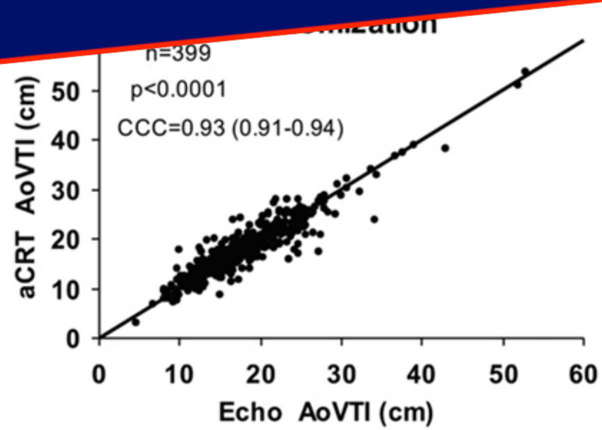
Sicurezza &

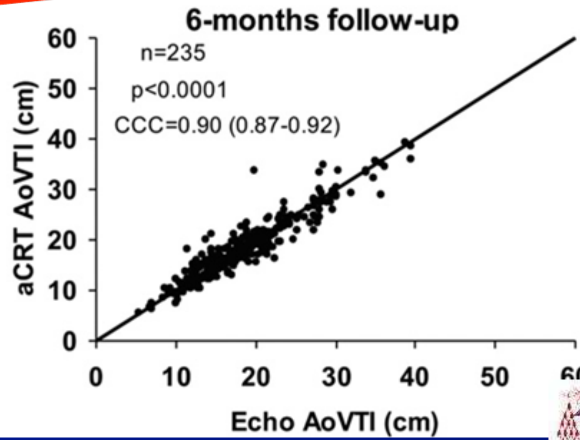
NON-INFERIORITA' clinica vs. ecocardio

b) a-CRT an

high Conc

after);





c) a-CRT did **NOT result in inappropriate device settings.**

Sub-analisi Adaptive-CRT: "synchronized LV pacing"

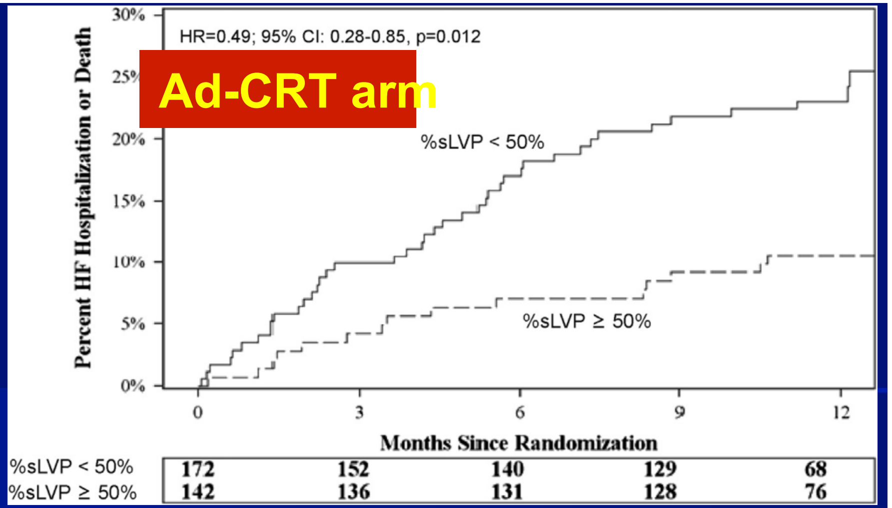
OBJECTIVE

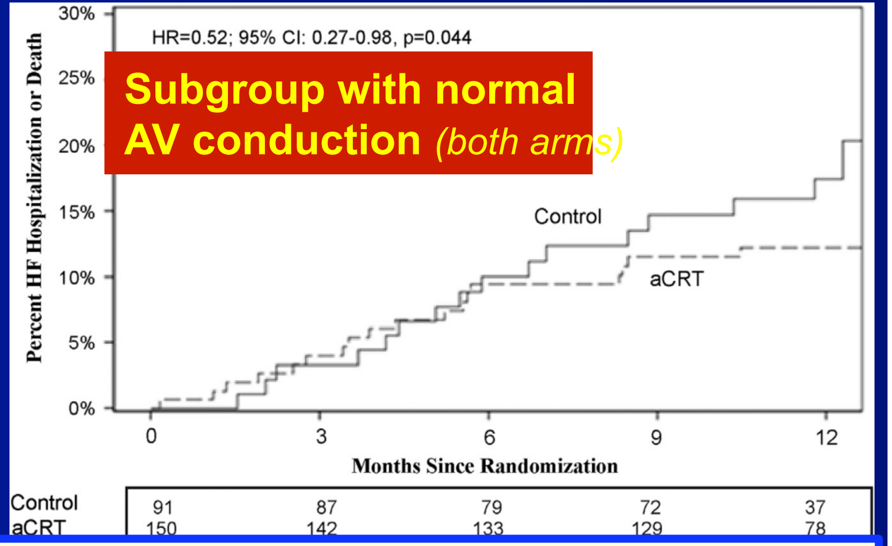
To examine whether synchro-LVP resulted in better clinical outcomes.

METHODS

Stratification by % synchro-LVP and multivariate Cox proportional hazards model used to assess the relationship between % synchro-LVP and clinical outcomes.

Outcomes were compared between pts in the Adaptive-CRT arm and control pts stratified by intrinsic AVD at randomization





Clinical outcomes with synch
Analysis of the adaptive CRT

David Birnie, MD, MB, ChB,* Bernd Lemke, M
Kathy Lai-Fun Lee, MD,‖ Maurizio Gasparini, M
John Gorcsan III, MD,†† Mahmoud Houmsse,
Alex Sambelashvili, PhD,§§ David O. Martin, M

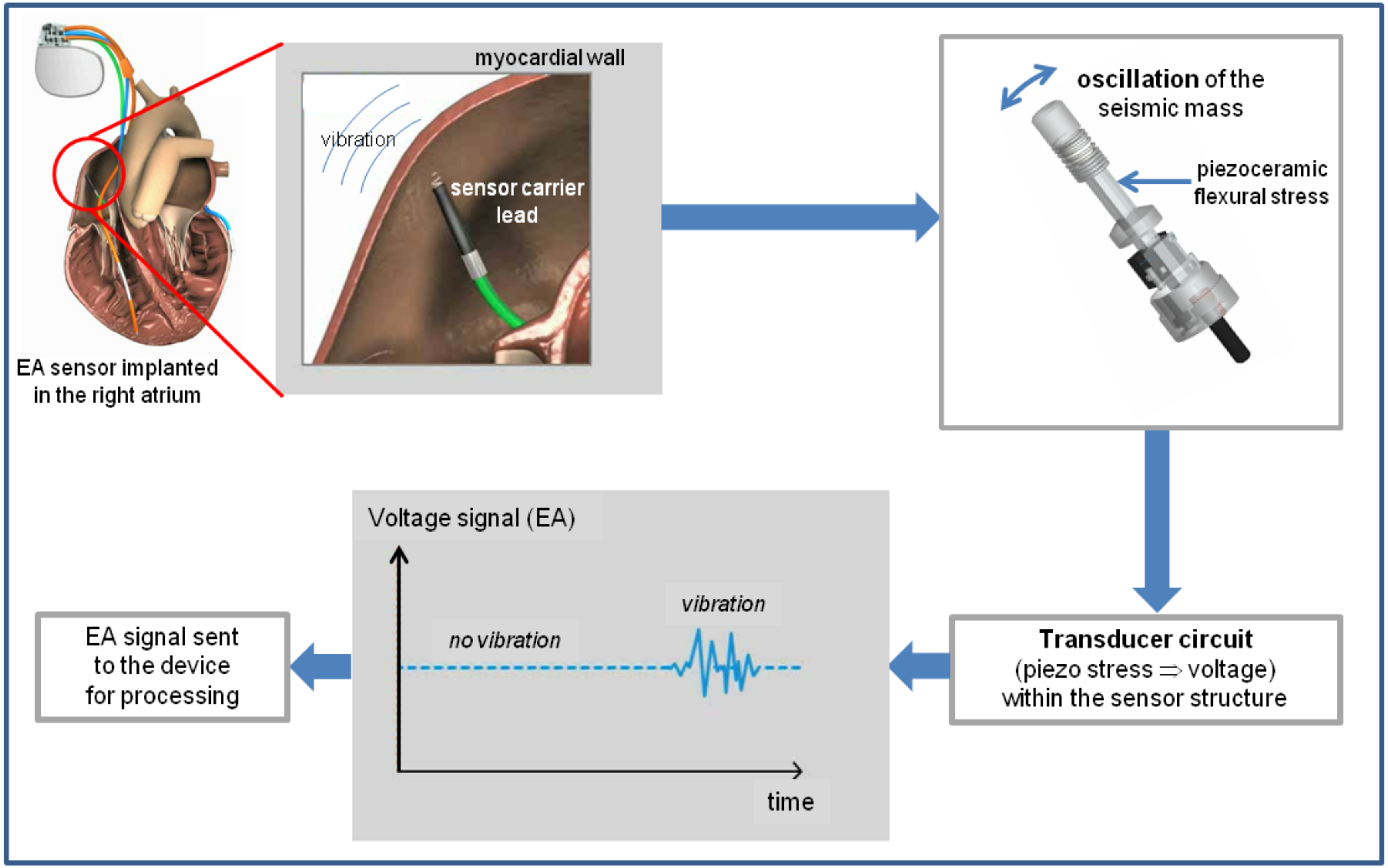
Birnie D & al. Heart Rhythm 2013

Conclusion

Higher % synchronized-LVP was independently associated with superior clinical outcomes.

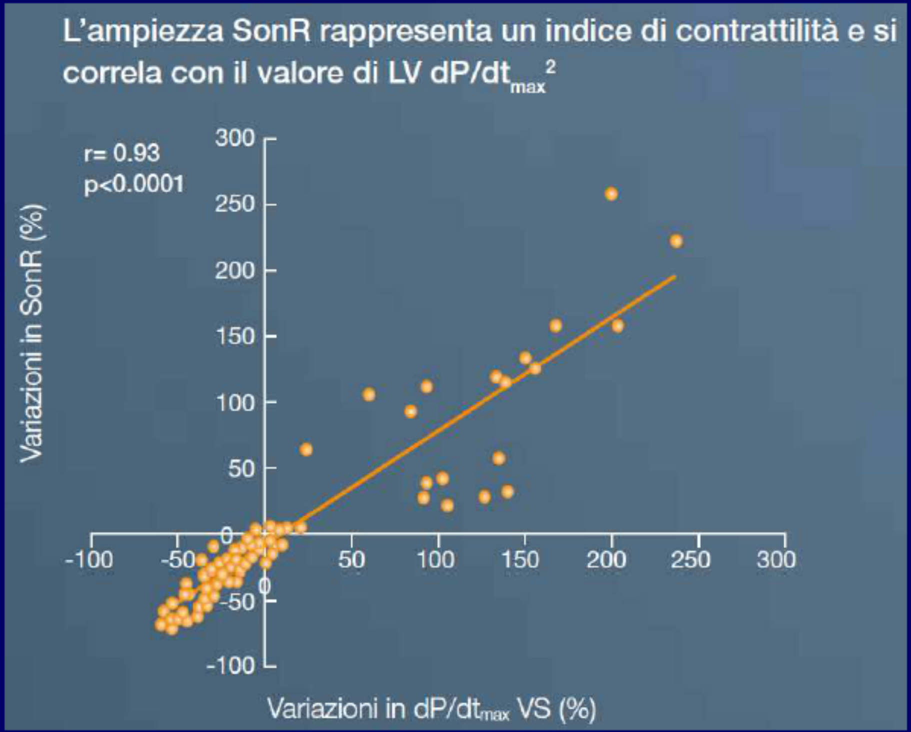
In pts with normal AV conduction, the Adaptive-CRT algorithm provided mostly synchronized-LVP and demonstrated better clinical outcomes compared to echo-optimized BiV-pacing

Ottimizzazione AUTOMATICA su base emodinamica: la tecnologia SonR



Sacchi S & al (Univ. Careggi, Florence, Italy). *Hemodynamic Sensors in Cardiac Implantable Electric Devices: The Endocardial Acceleration Technology*. J Healthcare Eng. 2013;4:453-64

Il segnale SonR correla con la misura di contrattilità cardiaca (LVdP/dt)



Bordachar P & al. JCE 2008

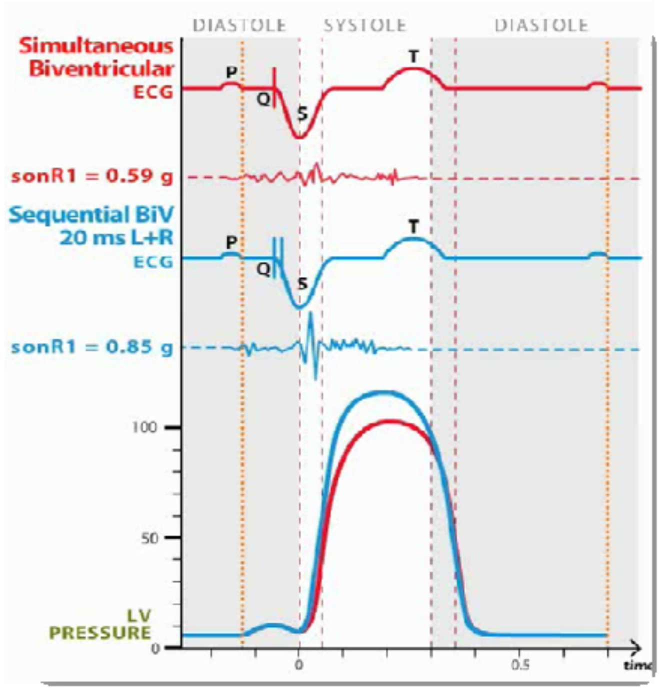
La **contrattilità cardiaca** è un ottimo indicatore di performance cardiaca.

Di norma, quantificare la contrattilità cardiaca obbliga all'utilizzo di metodiche costose, invasive, non utilizzate di fatto nella pratica clinica.

Con la tecnologia SonR, misurare la contrattilità direttamente con il dispositivo è fattibile e semplice, e non necessita di inserire cateteri addizionali durante le procedure.

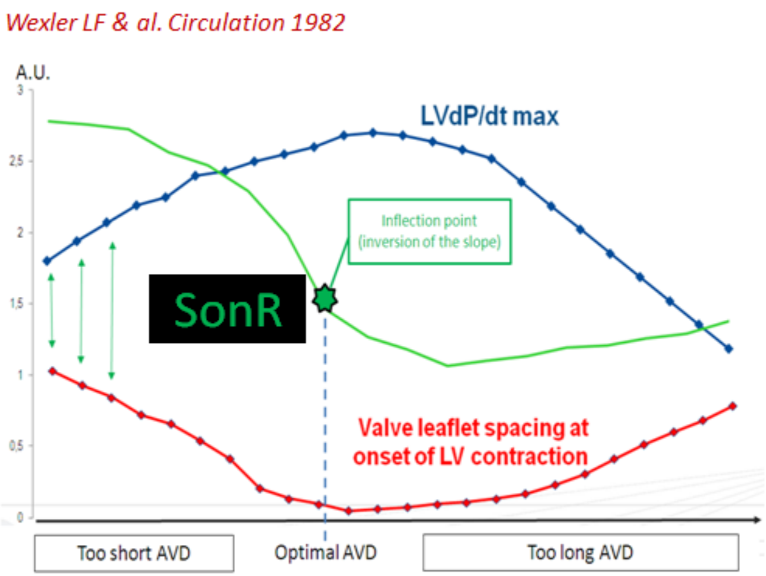
SonR & ottimizzazione emodinamica CRT

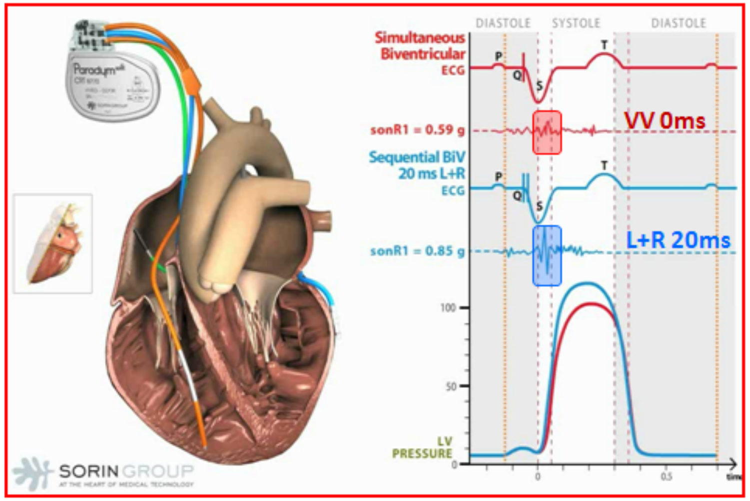
- SonR rileva vibrazioni che riflettono la contrattilità cardiaca, indip. dal sito di rilevazione [1,2]
- Progettato per rilasciare la terapia CRT secondo informazioni di natura emodinamica
- Permette di **ottimizzare la CRT in modo automatico**



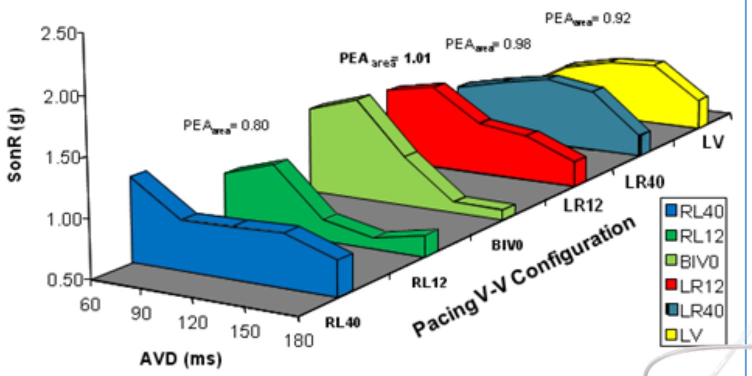
1. *Rickards et al. An implantable intracardiac accelerometer for monitoring myocardial contractility. PACE1996; 19:2066-71*
2. *Bongiorni et al Is local myocardial contractility related to endocardial acceleration signals detected by a transvenous pacing lead PACE 1996;19:1682-8*

Algoritmo SonR: riprogrammazione automatica settimanale dei ritardi AV/VV (su base emodinamica)





SonR vs. VV-synchrony

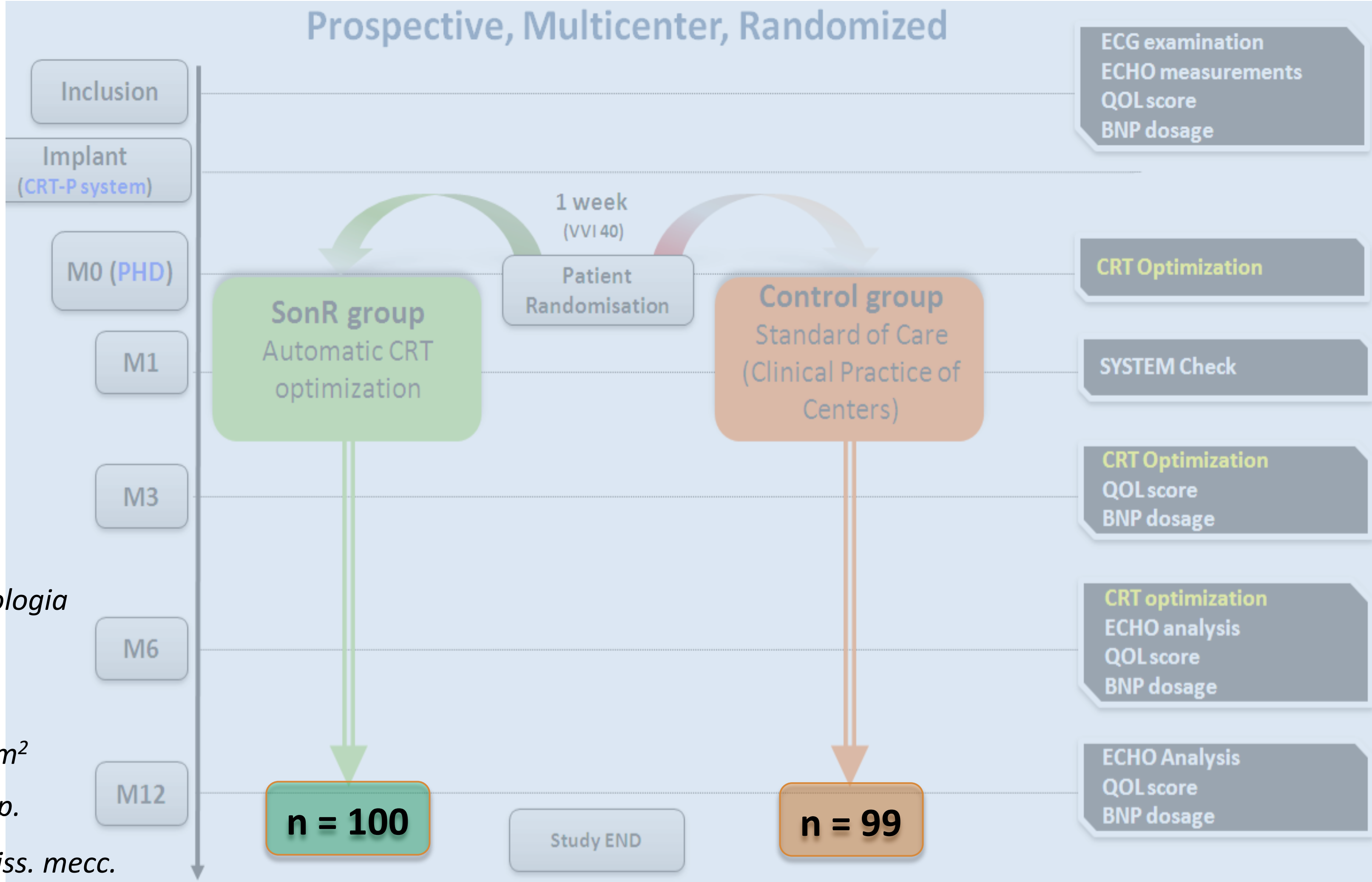


Sacchi S & al (Univ. Careggi, Florence, Italy). *Hemodynamic Sensors in Cardiac Implantable Electric Devices: The Endocardial Acceleration Technology*. J Healthcare Eng. 2013;4:453-64

Tecnologia SonR: studio pilota CLEAR

n = 268

n = 238



- *RS, qualsiasi eziologia*
- *NYHA III/IV*
- *LVEF<35%*
- *LVEDD≥30 mm/m²*
- *QRS>150 ms, opp.*

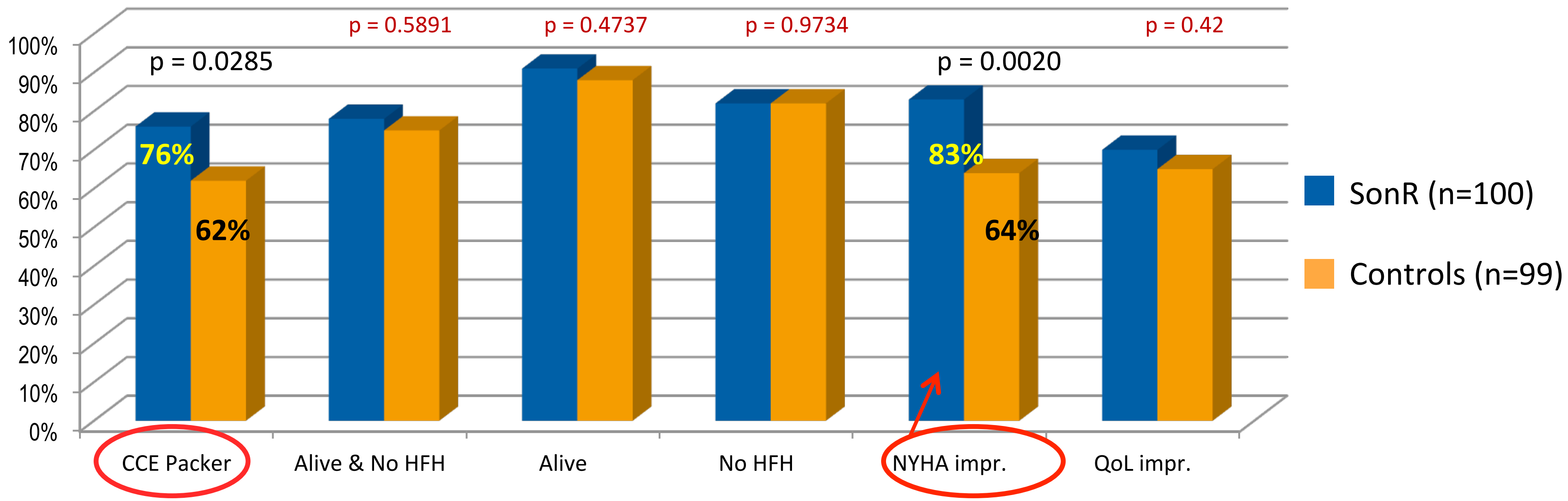
  QRS>120 ms + diss. mecc.
- *Terapia medica ottimale*

n = 268 pz (51 Centri, 8 Paesi) inclusi dal 2005 al 2009;

Endpoint Clinico Combinato (Packer's): *All-cause Death, HF events, NYHA class, QoL*

Ritter P & al. A randomized pilot study of CRT optimization in SR pts using a PEA sensor vs standard methods. Europace 2012.

Studio pilota CLEAR: endpoint 1-ari & 2-ari



Conclusions:

The optimization of CRT by an automated PEA-based method in sinus-rhythm patients significantly improved clinical outcomes from CRT-P after 1 year of follow-up, mainly driven by improvements in NYHA class. These encouraging observations warrant further studies of the PEA sensor on a larger scale, using CRT-D devices to comply with current international treatment guidelines.

Delta [12M vs BL]: PEA vs Controls

- BNP p = 0.5045
- QRS p = 0.5475
- LVEF p = 0.8482
- LVESD p = 0.5475

Adverse Events (Fatal & Non-Fatal):

NO significant differences (PEA vs Controls)

Ritter P & al.: A randomized pilot study of CRT optimization in SR pts using a PEA sensor vs standard methods; Europace 2012.

RESPOND CRT

Clinical TRial of thE SonRtiP Lead and Automatic AV-VV OptimizatioN Algorithm in the ParaDym RF SonR CRT-D

Study Design

(n = 1032 pz)

Endpoint 1-ario:

Combinato Clinico di Packer @ 12M

ENROLLMENT
Baseline : NYHA, QOL
n = 1032

IMPLANT
Paradym SonR CRT-D & SonRtip
(0-7 days post enrollment)
SonRtip Complications

VVI 40

PREDISCHARGE / RANDOMIZATION (2:1)
(0-14 days post implant)

2/3

SonR Group (treatment)
n=688

Echocardiographic assessment
sonR Optimization
CRT Optimization = AV+VV
Vital Signs, Standard Device Check,
SonRtip Complications

6W FOLLOW-UP
Vital Signs, Standard Device Check
SonRtip Complications

OTTIMIZZ. SETTIMANALE (automatica, SonR-based) dei ritardi AV / VV

3M / 6M / 12M / 18M FOLLOW UP
Standard Device Check
Mortality, HF-related Hospitalizations, NYHA, QOL
SonRtip Complications

24M FOLLOW UP
Standard Device Check
Mortality, HF-related
Hospitalizations, NYHA, QOL
SonRtip Complications

OUS

US

Each 6M until Study End
(US only)
Standard Device Check
SonRtip Complications

1/3

Echo Group (control)
n = 344

Echocardiographic assessment
Echocardiographic Optimization
Optimization = OFF
Vital Signs, Standard Device Check,
SonRtip Complications

SINGOLA OTTIMIZZAZ. AVD / VVD con ECHO @ PRE-DIMISSIONE

6W FOLLOW-UP
Vital Signs, Standard Device Check
SonRtip Complications

NO ri-ottimizzazioni dei ritardi AV / VV durante il FU

3M / 6M / 12M / 18M FOLLOW UP
Standard Device Check
Mortality, HF-related Hospitalizations, NYHA, QOL
SonRtip Complications

24M FOLLOW UP
Standard Device Check
Mortality, HF-related
Hospitalizations, NYHA, QOL
SonRtip Complications

OUS

US

Each 6M until Study End
(US only)
Standard Device Check
SonRtip Complications

Ad ogni visita di FU:

Valutazione in CIECO: classe NYHA, QoL (KCCQ), eventi clinici, terapia medica

Study End

clinicaltrials.gov ID: NCT01534234
(sponsor: SORIN Group)

SORIN AT THE HEART OF MED

Brugada J . (HRS, 2016)

Conclusioni:

- L’ottimizzazione automatica con SonR è risultata efficace quanto l’ottimizzazione ecoguidata (responders 75% vs 70.4%):
  L’end-point primario efficacia è stato centrato.

- Per la maggior parte dei sottogruppi è stata riscontrata risposta clinica a favore di SonR, specialmente nei pazienti con storia di fibrillazione atriale o disfunzione renale.

- L’ottimizzazione SonR guidata ha mostrato una riduzione di rischio relativo del 35% relativamente all’ospedalizzazione per scompenso cardiaco.

Follow-up pz CRT: effetti dell' **ottimizzazione** (… e della sua **frequenza**)

- **Ottimizzazione** CRT → beneficio emodinamico in acuto
- **Ottimizzazione con device al FU** (IEGM) → beneficio clinico sovrapponibile al metodo ecocardiografico
- **Ottimizzazione automatica** (IEGM/SonR) → beneficio clinico superiore in sottogruppi di pazienti selezionati

Frequenza di ottimizzazione crescente

Rif: Coorti storiche CRT, FREEDOM, Smart-AV, Adaptive CRT, CLEAR , RESPOND-CRT

Conclusioni

- L' ottimizzazione della programmazione dei dispositivi per CRT, comportando il miglioramento sia della diastole che della sistole, possiede i presupposti teorici per produrre beneficio clinico

- Seppure i benefici in acuto dell' ottimizzazione con **metodi ecocardiografici** non siano stati confermati nel lungo periodo e non sia sostenibile ricorrere ad essa sistematicamente nel FU (limiti di tempo/risorse) la scelta di non ottimizzare potrebbe non essere ragionevole

- Essendo attualmente disponibili **sistemi** di ottimizzazione **"device-based"** meno time-consuming , alcuni anche automatici e in grado di lavorare sistematicamente, per i quali è stata dimostrata la non inferiorità, se non addirittura la superiorità in termini di beneficio clinico vs l' ottimizzazione ECO-guidata, perchè non utilizzarli?

Ottimizzare la terapia di resincronizzazione per tutti i pazienti… un po’ meno sogno e un po’ più realtà