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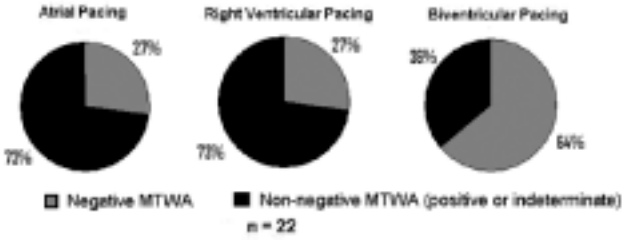
HIGHLIGHTS

Sesiones 2006 del American College of Cardiology

Rafael Rabinovich*

Clinical Electrophysiology: Supraventricular Arrhythmias (Poster Session)
Tuesday, March 14, 2006, 12:30 p.m.-4:00 p.m., Georgia World Congress Center, Hall B1
Abstract: 1015-126
Citation: Journal of the American College of Cardiology, February 21, 2006, Volume 47, Issue 4, Supplement A

Biventricular Pacing Reduces Incidence of Microvolt T Wave Alternans in Patients With Congestive Heart Failure
***Safwat A. Gassis**, Fernando Mera, Jonathan J. Langberg, David B. DeLurgio, Angel R. Leon, Paul F. Walter*
Carlyle Fraser Heart Center, Emory University, Atlanta, Georgia, United States
Background: *Microvolt T-Wave alternans (MTWA) is a useful non-invasive tool to asses risk for malignant ventricular arrhythmias. Cardiac resynchronization (CRT) with biventricular pacing (BiV) has been shown to improve hemodynamics and may reduce the risk of sudden cardiac death. The purpose of the current study was to determine the effect of CRT on MTWA.*
Methods: *Twenty two patients underwent implantation of a CRT device (9 ischemic, mean ejection fraction 18 +/- 7%). MTWA was measured during atrial pacing, DDD pacing with only right ventricular (RV) activation, and during DDD pacing with biventricular pacing in an integrated bipolar configuration.*
Results: *MTWA during atrial pacing was positive in 55%, negative in 27% and indeterminate in 18% of patients. MTWA results were dichotomized into negative and non-negative categories. BiV pacing increased the incidence of negative MTWA from 27% with atrial pacing to 64%. Overall MTWA concordance between atrial and BiV pacing was 55% whereas concordance between atrial and RV pacing was 73%. Concordance of atrial or RV pacing with BiV pacing was 44% for positive or indeterminate tests compared to 83% for negative MTWA tests.*



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Conclusion: *MTWA measurement during BiV pacing is feasible and reduces the proportion of positive or indeterminate results whereas atrial and RV pacing is more likely to lead to non-negative results. Whether the shift to a negative MTWA test during BiV pacing truly represents a decrease in risk for ventricular arrhythmia remains to be determined.*

Defibrillation and Implantable Antiarrhythmia Devices (Poster Session)
Monday, March 13, 2006, 9:00 a.m.-12:30 p.m., Georgia World Congress Center, Hall B1
Abstract: 947-135
Citation: Journal of the American College of Cardiology, February 21, 2006, Volume 47, Issue 4, Supplement A

Cardiac Resynchronization Therapy Reduces the Need for Shocks in Patients with Automated Implantable Cardioverter Defibrillators
***Nathan M. Segerson**, Feras M. Bader, Scott Walker, Roger A. Freedman*
University of Utah, Salt Lake City, Utah, United States
Introduction*: Cardiac resynchronization therapy (CRT) improves cardiac performance in heart failure. However, there are conflicting data on the effects of CRT on the frequency of ventricular arrhythmias. We tested the hypothesis that in patients with previously implanted cardioverter defibillators (ICDs) who meet established criteria for CRT, upgrading to CRT-defibrillators (CRT-Ds) reduces the frequency of ventricular tachyarrhythmias requiring shocks.*
Methods*: We conducted a retrospective analysis of all patients who had undergone upgrades from ICDs to CRT-Ds at our institution (N=39). We recorded the frequency (before and after upgrade) of ventricular arrhythmias requiring shock from ICD stored diagnostics, and assessed the change in frequency using a nonparametric Wilcox signed rank test. Additionally, QRS duration, ejection fraction, and functional class were assessed at the time of upgrade. The use of beta-blockers and antiarrhythmics was ascertained at the time of ICD implantation and at upgrade. All of these variables were analyzed for association with changes in shock frequency using a linear regression model.*
Results*: Upgrading from ICDs to CRT-Ds reduced the frequency of ventricular tachyarrhythmias requiring shocks by 76%. ICD diagnostic data were assessed for an average of 37 months prior to upgrade and 15 months after upgrade. The mean number of episodes per year decreased from 0.71 before upgrade to 0.17 after ($p<0.01$). In the linear regression model, QRS duration prolongation (beta=-0.01, $p<0.001$) and ejection fraction at the time of upgrade (beta=-0.06, $p=<0.001$) demonstrated independent effects on the reduction in shock frequency. Beta-blocker use increased from 24% before ICD implantation to 84% at the time of upgrade, but was not independently associated with the change in shock frequency ($p=0.67$). The prevalence of antiarrhythmic use did not change (52 vs. 50%).*
Conclusions*: In patients who meet criteria for CRT, upgrading their ICD to a CRT-D results in a reduction in ventricular tach-*

yarrhythmias requiring shock. Patients with greater QRS prolongation and higher ejection fraction at the time of CRT-D upgrade experienced the greatest reduction.

Arrhythmias and Dyssynchrony (Oral Contributions)
Tuesday, March 14, 2006, 2:00 p.m.-3:30 p.m., Georgia World Congress Center, Room B206
Abstract: 851-8
Citation: Journal of the American College of Cardiology, February 21, 2006, Volume 47, Issue 4, Supplement A

Is Cardiac Resynchronization Therapy Effective in Patients With Less Severe Symptoms?
*Daniel Gras, **John G. Cleland**, Melanie J. Calvert, Nick Freemantle, Luigi Tavazzi, Lukas Kappenberger, Jean-Claude Daubert, Erland Erdmann*
University of Hull, Kingston upon Hull, United Kingdom
***Background:** It is uncertain whether cardiac resynchronization therapy (CRT) is effective in patients with mild symptoms of heart failure.*
***Methods:** Patients with New York Heart Association (NYHA) class III/IV heart failure (physician-reported), LVEF <35% and evidence of cardiac dyssynchrony were enrolled in CARE-HF. Patients rated themselves by NYHA class, Euro Heart Failure Survey questionnaire (EHFSQ) and Euroqol EQ-5D. The effects of CRT on the primary end point of the main study (death or unplanned hospitalization for a major cardiovascular event), of the extension study (mortality) and NYHA class at 18 months (death/transplant ranked as V) were assessed according to baseline patient-reported symptom severity. Analyses were conducted by intention to treat.*
***Results:** Of 813 patients, 175 (22%) rated themselves NYHA I/II and 608 (75%) III/IV. NYHA I/II patients had similar LVEF (26%) but lower NT pro-BNP (mean difference -1156pg/ml, 95% CI -2129 to -184) compared to NYHAIII/IV patients. 399 (50%) patients felt that breathlessness greatly limited normal activity (score 4 or 5) and 229 (29%) rated their health as poor/very poor (score 5 or 6) on the EHFSQ. The effect of CRT on all three endpoints was similar regardless of baseline symptom severity. Patients with EQ-5D score >median (better quality of life) had a smaller benefit from CRT in terms of mortality and NYHA class at 18 months.*

P for interaction *0.01 ~ 0.02	Primary endpoint - main study HR (95% CI)	Death HR (95% CI)	NYHA I/II at 18 m OR (95% CI)
NYHA I/II	0.69 (0.44 to 1.09)	0.89 (0.51 to 1.6)	2.2 (1.1 to 4.6)
NYHA III/IV	0.62 (0.49 to 0.78)	0.53 (0.39 to 0.70)	3.5 (2.4 to 5.1)
EHFS SOB ≤4	0.64 (0.47 to 0.89)	0.66 (0.44 to 0.98)	3.0 (1.9 to 4.9)
EHFS SOB >4	0.64 (0.49 to 0.84)	0.54 (0.39 to 0.76)	3.1 (2.0 to 4.7)
EHFS Health ≤5	0.65 (0.50 to 0.84)	0.66 (0.48 to 0.92)	2.7 (1.8 to 3.9)
EHFS Health >5	0.60 (0.43 to 0.86)	0.49 (0.32 to 0.75)	4.5 (2.2 to 8.9)
EQ5D > median	0.78 (0.57 to 1.06)	0.87 (0.59 to 1.29)*	2.2 (1.4 to 3.6)~
EQ5D ≤ median	0.51 (0.38 to 0.69)	0.43 (0.30 to 0.63)	4.8 (2.9 to 8.0)

***Conclusions:** The effect of CRT on long-term morbidity and mortality is similar regardless of symptom severity in CARE-HF.*

Diabetes, Sleep Apnea and Lipids (Poster Session)
Monday, March 13, 2006, 9:00 a.m.-12:30 p.m., Georgia World Congress Center, Hall B1
Abstract: 964-90
Citation: Journal of the American College of Cardiology, February 21, 2006, Volume 47, Issue 4, Supplement A

Improvement of Obstructive Sleep Apnea in Heart Failure Patients after Cardiac Resynchronization
***Kristin Ellison**, Michael Stanchina, Maria Anderson, Alfred Buxton, Malcolm Kirk*
Rhode Island Hospital, Providence, Rhode Island, United States
***Background:** Cardiac resynchronization (CRT) has been shown to improve ejection fraction and cardiac output in heart failure (HF) pts with dysynchrony from LBBB. Up to 50% of HF pts have obstructive sleep apnea (OSA). OSA has not consistently improved with right ventricular pacing. CRT has been shown to improve central sleep apnea (CSA) but unclear in its benefit for OSA. We assessed the effect of CRT therapy in HF patients with OSA and CSA, and the effect of increased pacing rate on sleep function.*
***Methods:** Full in-home overnight polysommograms were performed on HF pts indicated for CRT. Pts were identified with disordered breathing (Apnea/Hypopnea Index [AHI] > 10/hr). All pts were implanted with CRT defibrillators. Pts had a baseline and 6 mo post CRT echo, sleep study and Minnesota QOL questionnaire. An additional study sleep study was performed after 6 mo of CRT with an increase of 15 BPM above the mean sleeping rate.*
***Results:** 24 HF pts were screened (mean age 68.6yrs, BMI 28.7 kg/m2. Thirteen pts (54%) were identified with sleep disordered breathing: 12/13 OSA, 1 with CSA. The mean base line ejection fraction was 22.5 % the mean 6 month post CRT ejection fraction was 33.6% p<0.001. The Minnesota QOL score decreased from 47 to 33.5 (p=0.3). The AHI was reduced from 40.9 to 32.1 events/hr (p=0.045). The Obstructive Apnea Index was reduced from 24 to 12 events/hr (p=0.008) The 1 pt with CSA had resolution of central AI with CRT. There was no further benefit in sleep function with increased base rate pacing.*
***Conclusions:** CRT improved ejection fraction and OSA. There was resolution of CSA in the one patient with CSA. Increased rate pacing made no additional improvements in AHI above CRT with base rate pacing. Improvement in cardiac output with CRT may stabilize the respiratory control system and thus improve sleep disordered breathing.*

Device and Surgical Therapy (Poster Session)
Tuesday, March 14, 2006, 8:30 a.m.-Noon, Georgia World Congress Center, Hall B1
Abstract: 1008-92
Citation: Journal of the American College of Cardiology, February 21, 2006, Volume 47, Issue 4, Supplement A

Significant Relation of Corrected QT Dispersion to Improvement of Symptoms in Patients Who Received Cardiac Resynchronization Therapy
Kazuyoshi Hina
Cardiovascular Center Sakakibara Hospital, Okayama, Japan Okayama University, Okayama, Japan
***Background:** Cardiac resynchronization therapy (CRT) has been introduced for treatment of patients with heart failure associated with prolonged QRS complexes. CRT is theoretically reasonable to affect repolarization as well as depolarization. Few studies, however, have examined the effects of CRT on repolarization. We studied the effects of CRT on corrected QT (QTc) dispersion in relation to symptomatic improvement.*
***Methods:** QTc dispersion was analyzed in 26 consecutive patients (64+/- 6 years, 18 men and 8 women) who underwent CRT. CRT responder and non-responder were defined as patients showing and not showing > 1 class NYHA symptomatic improvement 3 months after CRT, respectively. QTc interval, QRS width and QTc dispersion were measured automatically from digital data using an analyzing system (FDX-6521, Fukuda Denshi Co., Ltd., Tokyo, Japan). Tissue Doppler imaging (TDI) was also examined.*
***Results:** CRT responders and non-responders were observed in 18 and 8 patients, respectively. CRT responder showed significantly larger QTc dispersion than CRT non-responder before CRT (111+/-27 vs 43+/-15 msec, p<0.01) and overlap values of QTc between CRT responders and CRT non-responders were*

small. Significant decrease in QTc dispersion by CRT was observed in responders (to 49+/-11 p<0.01). In contrast, QTc dispersion was not decreased by CRT in non-responder (43+/-15 to 33+/-10 msec, NS). The difference in QTc dispersion observed before CRT was thus abolished after CRT (49+/-11 vs 33+/-10 msec, NS). QRS width and QTc were shortened after CRT. There were, however, no significant differences in QRS width or QTc between CRT responders and CRT non-responders before CRT. There were no differences in changes of QRS width or QTc after CRT between CRT responders and CRT non-responders. TDI did not show any significant differences in asynchrony of wall motion between CRT responders and CRT non-responders before or after CRT.
Conclusion: *The present study clarified that CRT responders showed significantly larger QTc dispersion than CRT non-responders before CRT. These findings indicate that QTc dispersion may be clinically useful to distinguish CRT responders from CRT non-responders before CRT.*

Comentario

No hay dudas que la CRT (Cardiac Resynchronization Therapy = terapia de resincronización cardíaca) tiene impacto en mejorar las funciones hemodinámicas del ventrículo izquierdo (VI), incluyendo la fracción de eyección (FE), disminución de los volúmenes de fin de diástole, mejora de la clase funcional (CF) y la calidad de vida. Pero poco se sabe acerca de los mecanismos fisiopatológicos que la CRT modifica para lograr su efecto final. Parece ser que el beneficio electromecánica *per se*, no explica todos los efectos observados luego del implante de estos dispositivos. Es poco razonable aplicar un criterio simplista, pues la mejora en el desacople electromecánico o reversión de la desincronía, es responsable de todo el efecto beneficioso de este modo de estimulación. Se ha puesto atención en que puedan existir otros cambios en el organismo que se suman al cambio del estado mecánico. Dado que en la población de pacientes con insuficiencia cardíaca (IC), se observa una hiperactividad simpática, la cual es una de las mayores responsables del efecto deletéreo del estado hemodinámico de estos pacientes, una modulación del tono simpático-parasimpático le ha sido atribuida a la resincronización cardíaca. Para sostener esta hipótesis, hemos seleccionado esta serie de trabajos presentados en ACC 2006, que están avalando dicha hipótesis. Tanto los cambios en la alternancia de la onda T, en la dispersión del QT y la reducción de terapias liberadas por el cardiodesfibrilador implantable (CDI), luego de someter a los pacientes a un implante con estimulación biventricular con o sin capacidad de liberar terapias de choque, parecen señalar que efectivamente se está modificando el tono autonómico con un "efecto protector". Evidentemente, esto constituye una interesante línea de investigación a desarrollar en trabajos futuros y que brinde una explicación más completa sobre los mecanismos fisiológicos involucrados en la mejora de los pacientes que son sometidos a este tipo de tratamiento. Otro hecho interesante de destacar, es la alta incidencia de episodios de apnea-hipoapnea del sueño registrados en la población con IC, lo cual como todos sabemos incrementa el riesgo de eventos cardiovasculares como *stroke*, hipertensión arterial, eventos coronarios, bradiarritmias severas e inclusive muerte súbita (MS). La terapia de resincronización mostró una interesante reducción de los registros de apnea de sueño. Esta observación, remarcada por el grupo del *Rhode Island Hospital*, abriría una línea interesante de investigación para solucionar esta grave afección detectada en esta población. Otros modos de estimulación cardíaca llamada "fisiológica" (estimulación AAI y DDD) parece no haber tenido un el impacto esperado en reducir los eventos de apnea. Los resultados de este grupo parecen estar en concordancia con los otros trabajos presentados y comentados previamente, pues los primeros cambios que la apnea del sueño genera en el organismo, estarían vinculados con alteraciones a nivel del sistema neurovegetativo, con cambios en el tono simpático-parasimpático y alteración en los parámetros que lo pueden evaluar como la HRV.

Device and Surgical Therapy (Poster Session)
Tuesday, March 14, 2006, 8:30 a.m.-Noon, Georgia World Congress Center, Hall B1
Abstract: 1008-52
Citation: Journal of the American College of Cardiology, February 21, 2006, Volume 47, Issue 4, Supplement A

Do Simple Clinical and Echocardiographic Parameters Predict Long Term Responsiveness to Cardiac Resynchronization Therapy? Results from the CARE-HF Trial
*L. Scelsi CARE-HF Investigators, **Stefano Ghio**, Nick Freemantle, A. Serio, G. Magrini, JGF Cleland, M. Pasotti, L. Tavazzi*
IRCCS Policlinico S. Matteo, Pavia, Italy
Background: *Refinement of selection criteria for the implantation of biventricular devices is crucial to improve cost-effectiveness of cardiac resynchronization therapy (CRT). The CARE-HF trial gives the opportunity to verify whether clinical criteria and the interventricular mechanical delay (IVMD), a dyssynchrony parameter easily measurable using conventional Doppler echocardiography, may predict long term responsiveness to CRT.*
Methods: *Echocardiographic examinations were performed at baseline and at 18 months in 735 patients enrolled in the CARE-HF trial and randomized 1:1 to CRT and control. Echocardiographic recordings were quantitatively analysed in a core laboratory. A long term responder to CRT was defined as a patient who survived and whose end-systolic volume was reduced at the 18 month evaluation by more than twice the standard deviation of inter-observer variability in the core laboratory (40 mL).*
Results: *According to the above definition, the percentage of long term responders was 49.2% in the CRT group as compared to 18.6% in the control group. In a multivariate model which included age, sex, aetiology of heart failure (ischemic vs non ischemic), systolic blood pressure, end-diastolic and end-systolic volumes, ejection fraction, mitral regurgitation, left ventricular filling pattern, tricuspid annular plane excursion and IVMD, IVMD and etiology were significantly predictive of response (p<0.001). The probability of being a responder increased linearly with the increase in IVMD in both ischemic and non ischemic patients with a fairly smooth slope but it was substantially lower in ischemic patients. For an IVMD of 20, 40 or 60 ms the cal-*

culated probability was respectively 52%, 58% and 64% in non ischemic patients and 28%, 33% and 39% in ischemic patients.
Conclusions: *In patients with non ischemic aetiology the probability of a positive response to CRT is never zero: low values of IVMD should therefore not be used to negate the benefits of CRT in such patients. In ischemic patients, the probability of being a long term responder is lower and the risk of non response is therefore higher for low values of IVMD.*

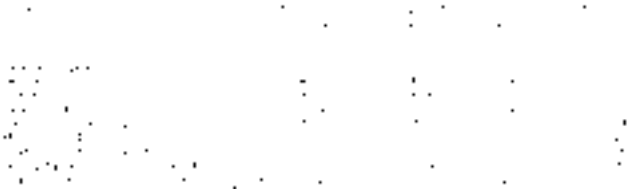
Comentario

Sin dudas, este estudio es uno de los más importantes en mostrar el beneficio del tratamiento con CRT; basado, fundamentalmente, en criterios que demuestren presencia de desincronía cardíaca independientemente de las condiciones clínicas. La demostración de demoras mecánicas, en este caso demostradas por criterios ecocardiográficos, aunque mínimas, pueden aparejar mejoras en los pacientes independientemente de su cuadro clínico. Por lo tanto, pone un punto de atención en el médico tratante que tiene una tendencia en excluir a los pacientes con mejor condición clínica, del implante de un sistema de estimulación biventricular.

Defibrillation and Resynchronization Devices (Oral Contributions)
Monday, March 13, 2006, 11:00 a.m.-12:30 p.m., Georgia World Congress Center, Room B312
Abstract: 818-6
Citation: Journal of the American College of Cardiology, February 21, 2006, Volume 47, Issue 4, Supplement A

Cardiac Resynchronization Device Placement During Hospitalization for Heart Failure is Associated With a Significant Improvement in Early Clinical Outcomes
William T. Abraham, Nancy M. Albert, Gregg C. Fonarow, Wendy G. Stough, Christopher O'Connor, Mihai Gheorghiade, Clyde Yancy, Barry Greenberg, Karen Chiswell, Jie-Lena Sun, James B. Young OPTIMIZE-HF Investigators and Hospitals
The Ohio State University Heart Center, Columbus, Ohio, United States
Introduction: CRT devices with or without ICD have demonstrated benefit in heart failure (HF) patients and are recommended by current guidelines. However, little is known about CRT placement during a HF hospitalization and its association with early clinical outcomes.
Methods: OPTIMIZE-HF is a registry/performance improvement program for pts hospitalized with HF. 60-90 day post discharge follow-up (f/u) data were prospectively collected in a pre-specified 10% sample. Multivariable analysis was performed for 60-90 day f/u death and death + rehospitalization.
Results: 5791 pts from 91 hospitals were included in this analysis. 132 pts (2.3%) underwent placement of CRT during hospitalization (1.5% CRT only and 0.8% w/ CRT-D). Pts receiving CRT were of similar age and more likely to be male and have an ischemic etiology. Length of stay (LOS) and inhospital mortality were 6.4 / 5.6 days and 1.3 / 3.8% in those receiving and not receiving CRT device therapy. During 60-90 day f/u there were significantly less rehospitalizations in CRT pts and a trend for lower mortality (Table 1). After multivariable risk adjustment, CRT placement remained associated with significantly lower rates of death and/or rehospitalization OR 0.38 95% CI 0.23-0.62, $P<0.0001$.
Conclusions: CRT device placement at the time of HF hospitalization, while associated with a modest increase in LOS, appears to be safe and was associated with a significantly lower risk of death or rehospitalization during the first 60-90 days post hospital discharge.

Table 1: Patient Characteristics and Clinical Outcomes



Comentario

La terapia con CRT ha sido reservada como último resorte terapéutico para aquellos pacientes en estado avanzado de IC, luego que el "*tratamiento farmacológico optimo*" no es suficiente para controlar a los pacientes. Esta disposición de las actuales “Guías”, inevitablemente nos hace recordar a la historia de las indicaciones de los cardiodesfibriladores implantables (CDI).
Inicialmente sólo se recomendaba su implante en pacientes terminales que habían tenido la suerte haber sobrevivido a dos episodios de MS exitosamente reanimados. Haciendo un paralelo con la evolución de los CDI, en cuanto a las indicaciones actuales comparadas con las de sus inicios, una interesante observación nos propone el grupo de *OPTIMIZE-HF Investigators and Hospitals*. Este es un registro que incluye a más de 5700 pacientes. En un pequeño subgrupo se implantó un sistema de CRT durante la admisión hospitalaria del paciente con IC, no como último recurso, sino como complemento inicial de la terapia farmacológica. Los resultados durante el seguimiento fueron comparados con un grupo de enfermos con similares características clínicas que sólo recibieron el mejor tratamiento farmacológico. El grupo *OPTIMIZE-HF Investigators and Hospitals* observó diferencias estadísticamente significativas comparando ambas estrategias en favor del implante de CRT en estadíos más tempranos de la evolución de pacientes con IC. Estimamos que los resultados preliminares de este registro pueden ser objeto de futuras investigaciones para confirmar o no los resultados mostrados.