Rev Esp Cardiol. 2014;67(10):813–821

Original article

Integration of Mechanical, Structural and Electrical Imaging to Understand Response to Cardiac Resynchronization Therapy

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Article history:
Received 13 August 2013
Accepted 4 December 2013
Available online 6 April 2014

Keywords:
Cardiac resynchronization therapy
Mechanical dyssynchrony
Electrical dyssynchrony
Electroanatomic mapping
Electromechanical coupling

ABSTRACT

Introduction and objectives: There is extensive controversy exists on whether cardiac resynchronization therapy corrects electrical or mechanical asynchrony. The aim of this study was to determine if there is a correlation between electrical and mechanical sequences and if myocardial scar has any relevant impact.
Methods: Six patients with normal left ventricular function and 12 patients with left ventricular dysfunction and left bundle branch block, treated with cardiac resynchronization therapy, were studied. Real-time three-dimensional echocardiography and electroanatomical mapping were performed in all patients and, where applicable, before and after therapy. Magnetic resonance was performed for evaluation of myocardial scar. Images were postprocessed and mechanical and electrical activation sequences were defined and time differences between the first and last ventricular segment to be activated were determined. Response to therapy was defined as a reduction in left ventricular end-systolic volume $\geq$ 15% after 12 months of follow-up.
Results: Good correlation between electrical and mechanical timings was found in patients with normal left ventricular function (r^2 = 0.88; P = .005) but not in those with left ventricular dysfunction (r^2 = 0.02; P = not significant). After therapy, both timings and sequences were modified and improved, except in those with myocardial scar.
Conclusions: Despite a close electromechanical relationship in normal left ventricular function, there is no significant correlation in patients with dysfunction. Although resynchronization therapy improves this correlation, the changes in electrical activation may not yield similar changes in left ventricular mechanics particularly depending on the underlying myocardial substrate.

Integración de la imagen mecánica, estructural y eléctrica para entender la respuesta a la terapia de resincronización cardiaca

Palabras clave:
Terapia de resincronización cardiaca
Disincronía mecánica
Disincronía eléctrica
Cartografía electroanatómica
Acoplamiento electroanatómico

RESUMEN

Introducción y objetivos: Debido a la controversia existente al determinar si la terapia de resincronización cardiaca corrige asincronía eléctrica o mecánica, el objetivo del estudio es determinar si hay correlación entre las secuencias eléctricas y mecánicas y si la cicatriz miocárdica tiene un impacto relevante.
Métodos: Se estudió a 6 pacientes con función ventricular izquierda normal y 12 pacientes con disfunción del ventrículo izquierdo y bloqueo de rama izquierda tratados con terapia de resincronización cardiaca. Se realizaron ecografías tridimensionales en tiempo real y cartografías electroanatómicas de todos los pacientes, antes y después de dicha terapia, así como una resonancia magnética para evaluar la cicatriz miocárdica. Se posprocesaron las imágenes, se definieron secuencias de activación mecánica y eléctrica y se determinaron diferencias temporales entre el primer y el último segmento del ventrículo izquierdo. Se consideró respuesta a la terapia una reducción del volumen telesistólico del ventrículo izquierdo $\geq$ 15% a los 12 meses.
Resultados: Se encontró buena correlación entre tiempos eléctricos y mecánicos en pacientes con función ventricular normal (r^2 = 0,88; p = 0,005), pero no en aquellos con disfunción (r^2 = 0,02; p = no significativa). Después de optimizar el dispositivo, se modificaron y mejoraron los tiempos y las secuencias, excepto los de aquellos con cicatriz miocárdica.
Conclusiones: A pesar de la estrecha relación electromecánica en ventrículos normales, no hay una correlación significativa en los pacientes con disfunción ventricular. Aunque la terapia mejora esta correlación, los cambios en la activación eléctrica no pueden producir cambios similares en la mecánica del ventrículo izquierdo, sobre todo en función del sustrato miocárdico subyacente.

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1885-5857/$ – see front matter
http://dx.doi.org/10.1016/j.rec.2013.12.010

Abbreviations

CRT: cardiac resynchronization therapy
ECG: electrocardiogram
LBBB: left bundle branch block
LV: left ventricular
RT3DE: real-time three-dimensional echocardiography
VV: interventricular interval

INTRODUCTION

Cardiac resynchronization therapy (CRT) aims to normalize electromechanical abnormities in order to improve left ventricular (LV) performance. However, up to one third of these patients do not respond to CRT, which underscores the lack of understanding of the complex relationship between LV electrical and mechanical activation, especially in dilated, dysfunctional hearts. Some studies have shown that QRS duration is a poor marker of mechanical asynchrony[1,2] and analysis of mechanical dyssynchrony, based on imaging, also has not delivered consistent and widely applicable results.[3] On the other hand, mechanical dyssynchrony does not necessarily correlate with electrical dyssynchrony as defined by QRS width.[4,5] Similar patterns in the surface electrocardiogram (ECG) show different electrical or mechanical sequences of activation.[6,7] Hence, a complex interplay might exist between electrical activation and mechanical events in patients with heart failure and LV dysfunction. The present study aimed to determine whether there is a correlation between electrical and mechanical sequences and whether myocardial scar has any relevant impact. We hypothesized that integrating mechanical, structural and electrical imaging could lead to a better understanding of the response to CRT and potentially to an improved selection of candidates for CRT.

To this aim, we used invasive endocardial electroanatomical maps and real-time three-dimensional echocardiography (RT3DE) to characterize the relationship and correlation of electrical and mechanical activation of the LV in different subsets of patients and attempted to determine the impact of CRT. Accordingly, this analysis could be considered as a pilot study to validate the use of RT3DE methods to evaluate mechanical motion time and correlate it to electrical time, and its potential role in predicting and improving understanding of the response to CRT.

METHODS

Patient Population

The present study included 6 patients recruited from a population undergoing catheter ablation of lone paroxysmal atrial fibrillation (group I), with no structural heart disease and with normal LV systolic function and a QRS duration < 120 ms on the surface ECG, and 12 patients with LV systolic dysfunction undergoing CRT implantation (group II), selected according to the currently accepted guidelines: heart failure, LV ejection fraction $< 35\%$, and a wide QRS (> 120 ms) on the surface ECG.[8] All patients in both groups underwent RT3DE to assess the LV mechanical motion sequence, as well as endocardial electroanatomical mapping to evaluate the LV electrical activation sequence. The study protocol was approved by the hospital's ethics committee and was conducted according to the Helsinki Declaration of Ethical Principles for Medical Research Involving Human Subjects. Written informed consent was obtained from all participants.

Cardiac Resynchronization Therapy

Patients with LV dysfunction (group II) were implanted with a CRT device. Leads were positioned at the right ventricular apex and, if the patient was in sinus rhythm, right atrial appendage. The LV lead was positioned in the lateral or posterolateral LV wall through the coronary sinus. All leads were implanted transvenously.

All devices were optimized based on an ECG-based method as previously described.[9]

Endocardial Electroanatomical Left Ventricular Mapping

Studies were performed during atrial fibrillation ablation (group I) or before and after CRT implantation (group II). A 4-mm-tipped mapping catheter (Navistar, Biosense-Webster Inc.) was advanced into the LV through the retrograde aortic approach. During sinus rhythm, the LV was mapped to achieve a mean (standard deviation [SD]) of 37 points (SD, 15 points) in each map. In CRT patients (group II), maps were obtained with the device inactivated (*Off*) and once the interventricular (VV) interval was optimized *(Optimized)*. Activation time at each point was determined as the time interval between the peak of the R wave from limb leads (or augmented limb leads) and the peak in the bipolar electrogram, which was associated with the steepest negative intrinsic deflection catheter tip. Figure 1 shows the electroanatomical maps of a patient in group I and from another in group II.

Once the full LV volume was reconstructed, the LV was divided into 16 segments (according to the American Heart Association LV segmentation) based on 3 anatomic reference landmarks (mitral valve, aortic valve, and LV apex). The LV endocardial breakthrough site was defined as the earliest activated LV site in the electroanatomical map. To obtain the sequence of electrical activation, activation times from all the points within each of the 16 LV segments were averaged. From this, we extracted: *a)* the sequence of electrical activation of 16 LV segments, and *b)* total activation time (ΔTe), defined as the time difference between the first and last activated LV points. The electrical propagation patterns were represented in classical LV "bull's-eye" plots by mapping every acquired point within the LV to a flattened ellipsoid (oriented based on the 3 reference points). For the visualization of the electrical activation sequence, "bull's-eye" plots were generated starting from the first point of activation until the last activated point, with a time step of 5 ms.

Real Time Transthoracic Three-dimensional Echocardiography

RT3DE was performed using a commercially available ultrasound scanner equipped with an X3-1 matrix array transducer (IE33, Philips Medical Systems; Andover, Massachusetts, United States). Scans were performed before the ablation procedure in group I. In group II, RT3DE was performed before *(Off)* and 48 h after CRT, once the VV interval was optimized optimized *(Optimized)*.

Full volumes of the LV were obtained in all patients from the apical window. Depth was minimized to include only the whole LV. The mean frame rate used was 15 fps (SD, 3 fps). The off-line analysis was done using commercially available software (Qlab, version 7.1, Philips). A shell of the LV cavity was then created, providing time-volume data for the entire cardiac cycle. Finally,