Cardiac Resynchronization Therapy: Past, Present, and Future

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KEYWORDS

• Cardiac resynchronization therapy • Heart failure • Electrical dyssynchrony • Biventricular pacing

KEY POINTS

- Cardiac resynchronization therapy (CRT) has revolutionized the care of patients with heart failure and electrical dyssynchrony.
- CRT fundamentally modifies the natural history of the pathologic ventricle, improves patient symptoms and functional capacity, and incrementally improves survival beyond optimized medical therapy.
- Ongoing studies will identify expanding populations who may benefit from CRT and further identify novel pacing approaches and technologies that augment the efficacy of resynchronization.
- Consensus efforts toward defining the response to CRT, earlier identification of those at risk for nonresponse, and enhancing implantation rates in those meeting contemporary guideline indications will only improve the delivery and effectiveness of CRT in our patients.

Videos of unipolar isochrones assessed via noncontact mapping, cardiac computed tomography kinematics to reflect mechanical activation pattern, and modalities of coronary vein assessment accompany this article at http://www.heartfailure.theclinics.com/

INTRODUCTION

Cardiac resynchronization therapy (CRT), or biventricular pacing, has become a standard therapeutic modality for patients with symptomatic heart failure (HF), depressed left ventricular (LV) function, and electrical dyssynchrony.[1,2] Resynchronization of the failing ventricle leads to improvement in mechanical pumping efficiency, reduction in mitral regurgitation, and optimization of ventricular filling. Over time, CRT facilitates favorable remodeling of the ventricle, characterized by reductions in LV volumes and improvement in ejection fraction, which in turn translates to significant improvement in quality of life, functional capacity, and survival.[3–7] In the nearly 20 years of clinical implementation,[8] the deployment of CRT has catalyzed cooperation and integration of multiple fields of cardiology, including HF, electrophysiology, and cardiovascular imaging.[9]

Despite the overall success of CRT in improving morbidity and mortality in selected patients with HF, a significant minority demonstrates nonresponse. This review describes the electrical and physiologic rationale for biventricular pacing therapy, summarizes landmark clinical trials assessing CRT efficacy, highlights strategies to optimize the response to CRT, and frames future

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Heart Failure Clin 11 (2015) 287–303
http://dx.doi.org/10.1016/j.hfc.2014.12.007
1551-7136/15/$ – see front matter

challenges in the use, delivery, and care of patients undergoing CRT.

ELECTRICAL DYSSYNCHRONY AND THE FAILING HEART: IMPACT OF CARDIAC RESYNCHRONIZATION THERAPY

The coordinated electrical activation of the heart is a critical determinant of coordinated mechanical contraction, myocardial relaxation, and mechanical efficiency.[10] Approximately half of all patients with LV systolic dysfunction (LVSD) demonstrate evidence of electrical conduction delay.[11–13] Although primary abnormalities of the electrical conduction system yield dyssynchronous ventricular activation that diminishes cardiac function,[14] pathobiologic changes underlying cardiomyopathy (eg, myocyte hypertrophy, inflammation, fibrosis, electrical remodeling[15]) as well as additional myocardial characteristics (eg, scar, ischemia) can also affect the ventricular conduction system.

Late-activated segments of myocardium (eg, the lateral wall in patients with left bundle branch block [LBBB]) demonstrate unique metabolic, transcriptional, and electrical signatures of dyssynchrony[16] characterized, for example, by pathologic changes in mitochondrial function,[17,18] abnormalities of calcium handling,[19,20] and alteration in action potential duration.[19] Asynchronous ventricular activation is associated with a localized increase in myocardial work, heterogeneity of myocardial blood flow, increased oxygen consumption, and reduced mechanical pumping efficiency as late-activated segments are passively stretched early in systole and early activated segments are relaxing and stretched at the time of late segment activation (**Fig. 1**).[20–23] To the extent that biventricular pacing reverses underlying electrical dyssynchrony, CRT restores coordinated mechanical contraction with related improvements in cardiac function. These mechanical improvements are mirrored by normalization of subcellular dysfunction ranging from improved calcium handling, upregulation of cell

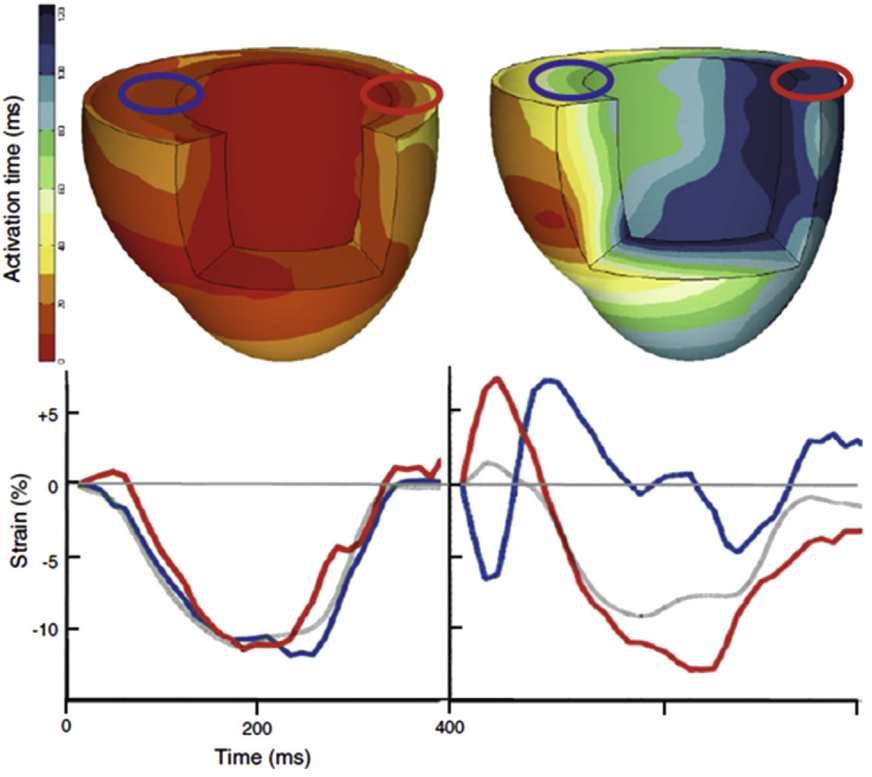

Fig. 1. Electrical and mechanical dyssynchrony in LBBB. Colorimetric representation of electrical activation (*upper panels*) and mechanical strain (*lower panels*) in a normal (*left panels*) versus LBBB (*right panels*) canine heart. Compared with the normal heart, in the LBBB heart there is early electrical activation of the septum (*right upper panel*, *blue circle*) correlating to early mechanical shortening of the septum (*right lower panel*). In addition, there is relatively delayed electrical activation of the lateral LV wall (*right upper panel*, *red circle*), which is mechanically stretched during early systole (*right lower panel*, *red tracing*) with subsequent shortening in late systole. (*Adapted from* Prinzen FW, Vernooy K, De Boeck BW, et al. Mechano-energetics of the asynchronous and resynchronized heart. Heart Fail Rev 2011;16:216; with permission.)