Heart, Lung and Circulation (2016) **25,** 471–475
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2015.10.014

ORIGINAL ARTICLE

Effect of Cardiac Resynchronisation Therapy on Electrical Remodelling

Amir Aslani, MD [a], Mehrdad Khajei, MD [a], Shahab Shahrzad, MD [b], Mohammad Hossein Nikoo, MD [a], Mohammad Vahid Jorat, MD [a], Mohammad Ali Babaee Bigi, MD [a*]

[a]Shiraz University of Medical Sciences, Shiraz, Iran
[b]Kowsar Hospital, Shiraz, Iran

Received 15 June 2015; received in revised form 15 September 2015; accepted 21 October 2015; online published-ahead-of-print 18 November 2015

Background Cardiac resynchronisation therapy (CRT) is an accepted device therapy in patients with low ejection fraction. Beneficial effects of CRT result from mechanical remodelling. Some controversial reports suggest that CRT may also induce electrical remodelling with intrinsic QRS narrowing but still the effect of CRT on electrical remodelling is an issue for debate. The aim of our study was to evaluate the effects of CRT on intrinsic QRS duration. For clarity, our analysis was performed by the signal averaged electrocardiogram (SAECG) which is a high resolution electrocardiographic signal suitable for accurate measurement of QRS duration. Signal averaged electrocardiogram provides a better value of QRS duration compared to 12-lead ECG by the ability to detect ventricular late potentials.

Methods A total of 48 consecutive patients with severe systolic dysfunction and typical left bundle branch block (LBBB) were enrolled in the study prospectively. Patients were scheduled for CRT-D implantation according to the current guidelines. Intrinsic QRS duration was accurately measured by SAECG before and at least 14 months after CRT implantation.

Results The mean intrinsic QRS duration remained unchanged during follow-up (from 149.9 ± 13.8 ms to 149.6 ± 18.4 ms; P= 0.3). Among 32 CRT responder patients, the mean intrinsic QRS duration remained unchanged during follow-up. Also, the mean intrinsic QRS duration showed no significant changes in 16 CRT non-responders.

Conclusion Structural remodelling induced by CRT does not necessarily translate into decrease of intrinsic ventricular activation. Despite significant left ventricular recovery, electrical characteristics of the left ventricular conduction system cannot generally be expected to recuperate.

Keywords Cardiac resynchronisation therapy • Intrinsic QRS duration • Signal averaged electrocardiogram

Introduction

Cardiac resynchronisation therapy (CRT) is an accepted device therapy in patients with systolic left ventricular dysfunction and left bundle branch block (LBBB) [1–10]. Left bundle branch block causes intra and inter-ventricular mechanical dyssynchrony in such patients [1,2,5]. It is known that CRT can increase exercise tolerance and functional class in addition to improved survival in such patients [4,5]. Survival benefits of CRT result from mechanical ventricular remodelling, a decrease in left ventricular systolic dimension and an increase in ejection fraction [6,8,10]. Some controversial reports suggest that CRT may also induce electrical remodelling. These recent researches revealed that CRT

*Corresponding author at: Cardiovascular Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. Tel.: +98 711 6125609,
Email: draslani@yahoo.com

may induce significant intrinsic QRS narrowing [3,11,12], but still the exact effect of CRT on electrical remodelling is an issue for debate.

The aim of our study was to evaluate the effects of CRT on intrinsic QRS duration before and after long-term CRT implantation. For clarity, our analysis (intrinsic QRS measurement) was performed by the signal averaged electrocardiogram (SAECG) which is a high resolution electrocardiographic signal suitable for accurate measurement of QRS duration. Signal averaged electrocardiogram provides a better value of QRS duration compared to 12-lead ECG because of its ability to detect ventricular late potentials.

Materials and Methods

Study Population

A total of 48 consecutive patients with severe systolic dysfunction and typical LBBB were enrolled in the study prospectively. Patients were scheduled for CRT-D implantation according to the current guidelines (left ventricular ejection fraction $\leq$ 30%, NYHA class III or IV on optimal medical therapy and QRS $\geq$ 120 msec). All patients were in sinus rhythm. The study was approved by the local ethics committee. Transthoracic echocardiography, 12-lead ECG and SAECG were done before and at least 14 months after CRT implantation.

Exclusion Criteria

Patients with the following criteria were excluded from the study:

1) Right bundle branch block; 2) Intra-ventricular conduction disturbance; 3) Patients who were pacemaker dependent; 4) Amiodarone administration (due to the potential to slow conduction).

Cardiac Resynchronisation Therapy Implantation

Standard implantation technique with commercially available trans-venous leads and devices (Medtronic and St-Jude) was used. Placing the left ventricular lead to the lateral or postero-lateral wall of the left ventricle was performed.

Echocardiography

M-mode and two-dimensional (2D) echocardiography (Simpson's method) were used to calculate left ventricular dimensions, volumes and ejection fraction.

Twelve-lead Surface Electrocardiogram Analysis

Unpaced 12-lead ECG (with a paper speed of 50 mm/s) was performed just prior to implantation and at least 14 months after CRT implantation. Intrinsic QRS was recorded at two stages: 1) Just before implantation; 2) At least 14 months after implantation with setting the CRT to CRT-Off mode. The operator ensured the ECG showed a stable QRS morphology. QRS duration was assessed using a digital caliper and magnifying lens on the lead displaying the widest complex by two independent investigators blinded to patient data. Intra- and inter-observer mean per cent error (absolute difference between two observations divided by the mean and expressed in per cent) for QRS duration changes was determined in 12 randomly selected study patients and was less than 5%. Twelve-lead surface ECG and SAECG were simultaneously performed.

Signal Averaged Electrocardiogram Analysis

Signal averaged electrocardiogram was recorded at two stages: 1) Just before implantation; 2) At least 14 months after implantation with setting the CRT to CRT-Off mode. Signal averaged electrocardiogram was recorded with standard bipolar X, Y, and Z leads. Signals were amplified, averaged, and filtered. The number of averaged beats during the recording was approximately 400 beats. Late potentials (LP) were measured as the duration of terminal signal below 40 mV.

Cardiac Resynchronisation Therapy Responders

Reduction of LVESV $\geq$ 15% or increase in LVEF $\geq$ 10% was used to identify CRT responders.

Statistical Analysis

Categorical variables were expressed as numbers or percentages. Continuous variables were expressed as mean $\pm$ SD. Categorical variables were analysed with the chi-square test or Fisher's exact test. Paired and Student's *t*-tests were used for comparisons between baseline and follow-up. Statistical significance was assumed for $P < 0.05$.

Results

Baseline Characteristics

A total of 48 consecutive patients were prospectively enrolled in the study. Of 48 patients studied, 16 (34%) had coronary artery disease, whereas in 32 patients (66%) the coronary arteriogram was normal. Patients were on optimal medical therapy (91.2% on beta-blocker and 88.3% on angiotensin converting enzyme inhibitor). Regarding device interrogation, the mean percentage of biventricular pacing at 14 months follow-up was 94 $\pm$ 2.1%. Mean heart-rate (without biventricular pacing) was similar on baseline and follow up ECG (64.4 $\pm$ 8.2 and 64.1 $\pm$ 9.3 /min; P = 0.12).

Results of Echocardiography

Thirty-two of 48 patients (66%) were considered CRT responders. Among CRT responders, the left ventricular ejection fraction (LVEF) increased from 22.1 $\pm$ 4.8% to 34.3 $\pm$ 6.3% (P < 0.001) during follow-up. Left ventricular end systolic volume (LVESV) and LVEF remained unchanged