

QRS analysis using wavelet transformation for the prediction of response to cardiac resynchronization therapy: A prospective pilot study[☆]

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Abstract

Background: Wider QRS and left bundle branch block morphology are related to response to cardiac resynchronization therapy (CRT). A novel time-frequency analysis of the QRS complex may provide additional information in predicting response to CRT.

Methods: Signal-averaged electrocardiograms were prospectively recorded, before CRT, in orthogonal leads and QRS decomposition in three frequency bands was performed using the Morlet wavelet transformation.

Results: Thirty eight patients (age 65 ± 10 years, 31 males) were studied. CRT responders ($n = 28$) had wider baseline QRS compared to non-responders and lower QRS energies in all frequency bands. The combination of QRS duration and mean energy in the high frequency band had the best predicting ability (AUC 0.833, 95%CI 0.705-0.962, $p = 0.002$) followed by the maximum energy in the high frequency band (AUC 0.811, 95%CI 0.663-0.960, $p = 0.004$).

Conclusions: Wavelet transformation of the QRS complex is useful in predicting response to CRT.

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Keywords:

Heart failure; Biventricular pacing; Morlet wavelet transform; QRS complex; Signal processing

Introduction

Cardiac resynchronization therapy (CRT) was introduced as a revolutionary treatment for patients with advanced heart failure and left ventricular (LV) conduction delay, aiming to restore the electrical dyssynchrony, improve LV mechanics and thus reduce heart failure morbidity and mortality.^{1–3} Nevertheless, about one third of patients fulfilling the criteria for CRT implantation, as suggested by guidelines,^{4,5} show no benefit from this treatment. Patients with wider QRS are more likely to respond possibly because QRS duration correlates with the degree of LV posterolateral wall conduction delay in the presence of left

bundle branch block (LBBB).⁶ However, QRS duration does not consistently reflect the underlying severity of mechanical dyssynchrony.⁷

Since echocardiographic indices of mechanical dyssynchrony are unreliable and difficult to obtain consistently,⁸ the effort to define electrical measures of LV depolarization has become attractive again. Different patterns of LV electrical activation sequence both during intrinsic conduction in LBBB and in response to pacing have been recorded, allowing the conclusion that not all LBBBs are created equally.⁶ Surface ECG provides a time-domain analysis of the electrical activation of the heart. However the frequency content of the signal may provide additional information. The wavelet transform is a mathematical function that has been used for almost two decades as an alternative to the traditional time-domain methods providing a time-frequency domain analysis.^{9,10} Wavelet decomposition of the signal-averaged electrocardiogram has been

[☆] Disclosures: None.

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proposed as a method of detecting small and transient irregularities hidden within the QRS complex¹¹ with marked accuracy and reproducibility.¹²

In the current prospective study we tested the hypothesis that wavelet analysis of the QRS complex may predict the response to CRT in patients with heart failure and LBBB who fulfill the classic criteria for CRT implantation.

Methods

Study population

The study complied with the Declaration of Helsinki and was approved by the Medical Ethics Committee of our Institution. All study subjects gave written informed consent for the participation to the study. We enrolled 40 consecutive patients with heart failure referred for CRT to our hospital from September 2009 to March 2011. Inclusion criteria were LBBB (QRS duration > 120 ms, QS or rS in V1 and RsR' in V6) and standard indications for CRT (i.e. EF ≤ 35%, QRS > 120 ms, NYHA III–IV, or NYHA II with QRS > 150 ms on optimal medical therapy). Two patients were excluded from final analysis because of unsuccessful implantation of the LV lead and loss of biventricular pacing (<90%) during follow-up, respectively.

Baseline evaluation before CRT implantation consisted of medical history, clinical examination, surface 12-lead ECG, standard echocardiographic study and orthogonal electrocardiographic recordings for wavelet analysis. At six months follow up all patients were reviewed by two study investigators. Clinical assessment and echocardiographic study were performed using exactly the same methodology as at baseline. Regarding the definition of response to CRT a great heterogeneity exists among the published studies. We chose to define response to CRT as the combination of NYHA class improvement by ≥ 1 and reduction in the left ventricular end-systolic volume (LVESV) by ≥ 15% as it is more objective and provides a measure of reverse remodeling which is more likely to depend on the electrical activation properties of the myocardial tissue.

Echocardiographic study

All echocardiographic studies were performed at baseline and at 6 months follow-up with the same device (Vivid 7, General Electric, USA) by a single experienced echocardiographer. A study investigator blinded to the clinical data performed the measurements off-line including left ventricular ejection fraction and left ventricular end systolic volume using the Simpson's biplane method from the 4-chamber and 2-chamber apical views.

Orthogonal ECG

Orthogonal ECG recordings were obtained from each patient at baseline before CRT implantation using a 3-channel digital recorder (GBI-3SM, Galix Biomedical Instrumentation, USA) as previously described.¹³ The recordings were performed for 3 minutes using a sampling frequency of 1000 samples per second per channel at the very high resolution mode (VHR ECG 0.05–500Hz) with

the patient at the supine position in a quiet environment. Seven patches were attached to the anterior and the posterior thoracic wall as indicated by the Holter manufacturer in order to record signals in horizontal (*x* axis), frontal (*y* axis) and sagittal plane (*z* axis) forming an orthogonal lead system (Fig. 1). Five QRS complexes were manually selected (by a study investigator to avoid artifacts) from each subject's ECG and pre-processed with normalization (mean subtraction and division by standard deviation), baseline correction and application of a denoising wavelet filter (wavelet-wiener filtering with biorthogonal mother function).¹⁴

QRS complex transform

QRS complex transform was performed by a dedicated software built by the Department of Medical Informatics of our Institution using Morlet wavelet analysis (appendix) in three orthogonal leads (*x*, *y*, *z*).^{15,16} The beginning and the end of the selected QRS complexes were manually marked in each of the 3 leads (*x*, *y*, *z*). Then the mean and maximum (max) energies of the selected QRS complexes were automatically calculated in each of the 3 leads, in 3 frequency bands [band 1 (high frequency): 200–160 Hz, band 2 (medium frequency): 150–100 Hz, band 3 (low frequency): 90–50 Hz]. In total 18 variables were calculated for every patient (6 in each lead). “Mean” QRS complex amplitude in a given band corresponded to the time-scale (or equivalently spectrotemporal) components of QRS curve in that band, adjusted for the duration of the QRS, whereas the “Maximum (Max)” energy corresponded to the global maximum spectrotemporal energy of the curve of QRS complex in that band. The terminology used to describe the variables was mean{band}{lead} or max

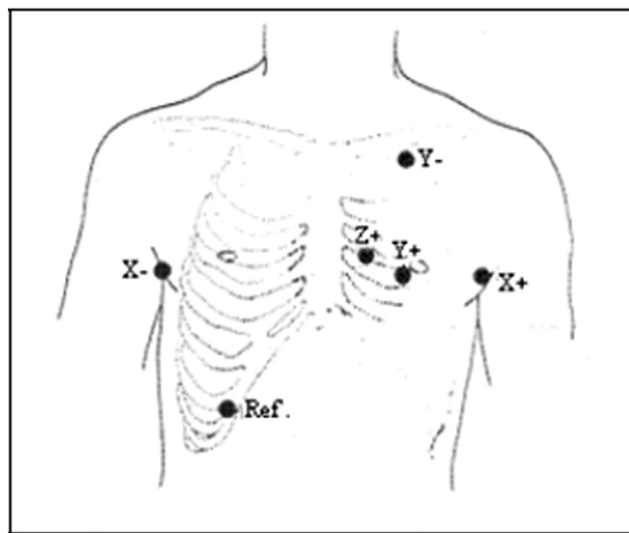


Fig. 1. Orthogonal lead system. Seven electrodes are placed on the chest to record signals in the horizontal plane (*x* axis, electrodes + *X* and – *X* in the left and right midaxillary line, fourth intercostals space), frontal plane (*y* axis, electrodes + *Y* in the standard V3 position and – *Y* in the superior aspect of the manubrium) and sagittal plane (*z* axis, electrodes + *Z* in the standard V2 position and – *Z* immediately posterior to + *Z*). The seventh electrode (*ref*) is placed in the right hypochondrium. (Of note electrode – *Z* is not shown in the picture).

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