The QRS narrowing index for easy and early identification of responder to cardiac resynchronization therapy

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The rationale for cardiac resynchronization therapy (CRT) in patients with heart failure (HF) is based on the possibility of inducing substantial left ventricular reverse remodeling. It is well known that some of these patients don't benefit from this therapy (the so-called non-responders) [1,2]. No better predictors of a positive answer to CRT than pre-CRT QRS duration (QRSd) were found [3,4].

The aim of our study was to identify a parameter for an easy and early identification of responders to CRT. In this regard, according to Rickard et al., we identified and observed QRS index (QI), as an expression of electrical remodeling after CRT, and its relation with anatomic reverse remodeling, ecocardiographically assessed at six months [5].

We enrolled 39 patients who underwent CRT implantation. The following inclusion criteria were applied: New York Heart Association (NYHA) functional classes II–IV, left ventricular ejection fraction (LVEF) $\leq$ 35% and pre-CRT QRSd > 120 ms.

The procedure was performed according to the current technique. The pre- and post-CRT ECGs were the last ECG recorded prior to and after CRT implantation, respectively. QRS morphologies were classified in two categories: left bundle branch block (LBBB) and non-LBBB, which included right bundle branch block (RBBB) and nonspecific intraventricular conduction delay (NSIVCD). QI was defined as the relative reduction of the post-CRT QRSd and was determined through the following formula: QI = [(QRSd post CRT − QRSd pre CRT) / QRSd pre CRT] × 100 with a negative value corresponding to a higher reverse remodeling [5]. All patients were followed up at 1, 3, 6 and 12 months. At 6 months, patients were classified as responders to reverse remodeling if left ventricular end-systolic volume (LVESV) decreased by >10% from baseline according to Yu criteria [6]. Atrioventricular interval optimization was performed, if possible, soon after the implantation; interventricular interval optimization was performed at six months, only in the case of non-responders.

Among 39 patients, 26 (66%) were considered responders to CRT with a significant QRS narrowing and QI decrement compared to non-responders ones (127 ± 17 vs 141 ± 17 msec, P < 0.01; −14 ± 7 vs −6.8 ± 7%, P < 0.004, respectively). In univariate analysis, the presence of ischemic cardiomyopathy (19.2% in responders vs 30.7% in non-responders, P < 0.003) was associated with non responders to CRT (P = 0.004), while no statistically significant differences were found for atrial fibrillation (7.6% vs 23%) and glomerular filtration rate. No significant differences between responders and non-responders were found for pre-CRT QRSd and pre-CRT LVEF, LVESV and LVEDV. Both groups, responders and non-responders, showed an increase of post-CRT LVEF, which was higher among responders both as absolute value (32 ± 7 vs 22 ± 4%, P < 0.0001) and as an index of variation between pre- and post-CRT (8.7 ± 8 vs 0.3 ± 3%, P0.0005).

Using multivariate analysis we found that QI could be a short-term predictor of response to CRT [Odds ratio di 1.5 (1.1–2.1), P = 0.03]. Spearman correlation analysis showed that QI was positively correlated with Yu index (Fig. 1). Because of the small sample size it is not possible to identify a cut-off value of QI but in our population this value was empirically considered about −10% (Fig. 2).

Even if twenty years have passed since CRT was introduced, the number of responders to this therapy and how to get to an early identification of responders is still a matter of discussion. In our study, we identify responders, according to Yu criteria [6]. After CRT, LVEF improved in both categories, with a higher increase in responders. However, we registered an increase of left ventricular function in all patients who underwent CRT, independently from baseline LVEF and LVESV. This evidence stands for the absolute benefit of biventricular stimulation in patients with HF and overt left ventricular dysfunction. Besides this, in our population we observed a better outcome, in terms of response to CRT, in patients with LBBB [2].

However, the main unsolved problem is a fast identification of possible non-responders in order to provide, soon after the procedure, all the measures to obtain the best result from CRT. We chose QI because of its immediate availability and reproducibility. At 6 months follow-up, 66% of our population was responder to CRT, having shown signs of reverse remodeling; an improvement of ≥1 in NYHA functional class was registered in all patients and none of responders was admitted to the hospital at one year follow-up. Our study is important because it shows not only an association between QRSd reduction and responders but also between responders and QI (Figs. 1–2). Moreover it demonstrates the relation between QI and Yu index that is another example of the strong relationship between electrical and anatomic remodeling [6]. This suggests the possible role of QI as a fast and easy to obtain parameter for an early prediction of CRT response. In this way we could optimize the device or drug therapy during or soon after implantation looking for a possible reduction of non-responder population considering a different position or pacing configuration of the left catheter during implantation, echocardiographic optimization of the interventricular interval or a best titration of drug therapy.

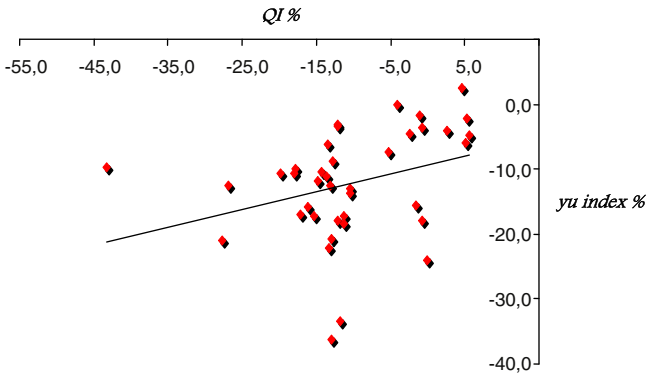

Fig. 1. Spearman correlation analysis.

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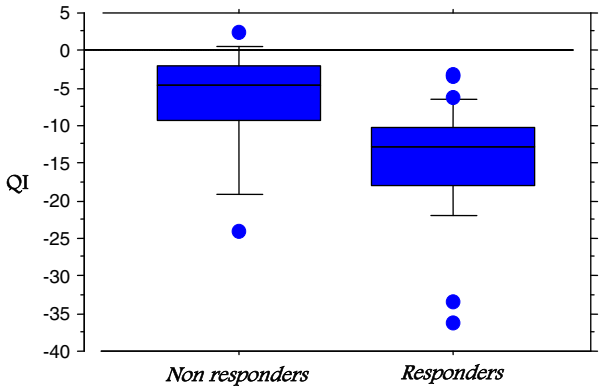

Fig. 2. Box plot value of QI in patients responders and not.

Further evaluations with a larger population are requested to validate this association.

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Multi-level vascular aneurysms and polycystic kidney disease

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A 71-year-old patient with previous bypass surgery in 2007 was admitted to the Emergency Department in 2012 complaining of typical chest pain at rest. His coronary risk factors included a metabolic syndrome, a history of smoking and hypertension. The patient was known for multiple aneurysms located on the abdominal aorta (3.5 cm), the left anterior descending (LAD) (2 cm) and right (1.5 cm) coronary artery. These aneurysms were discovered fortuitously on a CT scan performed in 2006 in the work-up of polycystic kidney disease. At that time, the diagnosis of Kawasaki disease or any other vasculitis was ruled out.

Upon admission physical examination was unremarkable. The ECG was consistent with an old inferior myocardial infarction, and demonstrated no ischemic ST-segment changes; on blood analysis only a minor Troponin I raise was found. Echocardiography demonstrated global left ventricular dysfunction (EF 39%), a 1.3 cm pericardial effusion predominantly at the apex without right ventricular compression.

Workup included cardiac MRI and cardiac CT (both performed without contrast medium because of severe renal failure), which showed an increase of the mid LAD aneurysm from 2 cm to 5.8 cm (Figs. 1 and 2). This aneurysm presented now with partial rupture and thrombus formation towards the pericardial effusion. The aneurysm on the right coronary artery had remained unchanged. The patient was discussed within the "heart team" but because of its high risk, surgery was not considered. A coronary angiography and potential percutaneous treatment was scheduled but unfortunately the patient deteriorated rapidly and died in cardiogenic shock before this could be undertaken.

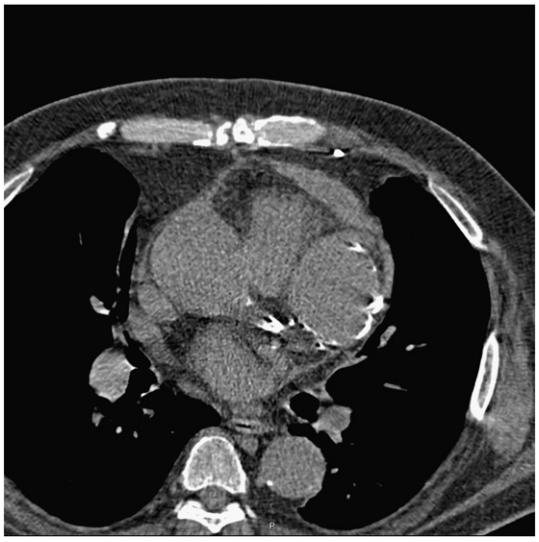

Fig. 1. Cardiac CT shows the main pulmonary artery, the aorta, the left main coronary and a 5.8 cm mid LAD aneurysm.

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