Evaluating patients for CRT, what is relevant: identifying responders or estimating the amount of potential response?

KRT için hastaları değerlendirirken hangisi daha önemli: Yanıt verenlerin belirlenmesi mi, potansiyel yanıtın büyüklüğünün ölçülmesi mi?

Cardiac resynchronization therapy (CRT) is a very effective therapy for the group of patients with symptomatic heart failure (HF), low ejection fraction and a broad QRS complex. However, it is also very expensive, requires the appropriate team for selection, implantation and intensive follow-up and a substantial amount of individual patients show little improvement. Therefore, identifying the most appropriate candidate for CRT continues to be a challenge in heart failure clinics. Given the existing controversy, it has become clear that the potential benefit for the individual depends on a multitude of factors. First, there is the question whether the underlying substrate, resulting in HF, is amendable with electrical therapy. For this, there has to be some form of (intra-, inter- or atria-ventricular) dyssynchrony (1). Next, the implant procedure and lead placement has to be satisfactory and last, but not least, the myocardium, and the heart as a whole, should not have deteriorated too much and has to be able to improve its function after correcting the underlying electrical problem.

Technical improvements in the implant have led to significant progress in the deployment of this therapy, but we still have a long way to go in improving the identification of potentially correctable dyssynchrony mechanisms and in evaluating the relevant myocardial properties to predict the extent of reverse remodeling.

While several authors have investigated the assessment of scar burden and the viability of the myocardium as a predictor for response, these parameters should rather be used to estimate the amount of improvement one could expect rather than that they might identify the type or extent of dyssynchrony. For example, in patients with ischemic dilated cardiomyopathy, there was a direct relationship between (SPECT) viability and clinical response to CRT and between scar extent and no response (2). In another (MRI) study (3), there was a correlation between scar burden and changes in left ventricular (LV) volume at 6 months follow up. Dobutamine echocardiography has been used to study the relation between viability and the amount of response to CRT (4). Additionally, dobutamine echo was shown to be helpful in identifying the underlying dyssynchrony mechanism (5).

In this context, the article published in the March 2012 issue of the Anatolian Journal of Cardiology (6) presents interesting data from dobutamine echocardiography in coronary artery disease patients undergoing CRT. While the authors discuss myocardial viability, in reality, in this patient group, which has not necessarily been revascularised, they mainly assess segmental contractile reserve (7). The present study thus provides more evidence of the potential role of contractile reserve, and the status of the myocardium, in order to assess the expected amount of remodeling in a population with very advanced LV deterioration (8).

Some interesting conclusions can be drawn from the current paper (6). The most obvious is that, on group level, whether there is contractile reserve or not, patients importantly improve after CRT. However, the amount of response, assessed using different objective and clinical criteria, is depending on the amount of segments with preserved contractility/contractile reserve. Next, if a lot of improvement is to be expected, it will be already within 1 week, emphasizing again that it is mainly an acute electrical problem that is being addressed. However, CRT still improves the ventricle, even if there is no acute change and a lot of abnormal segments are present. The impact of this on the patient's quality of life and mortality as well as the underlying mechanisms, are still to be understood in more detail.

While this study reemphasizes the usefulness of contractile reserve and viability assessment for optimizing the selection of candidates that will benefit most from CRT, clinical reality, where cost, logistics and efficient patient flows are an issue, might limit the possibility for additional diagnostic tests in these patients. However, given the amount of evidence to show that imaging can add in predicting these individuals that will benefit most of CRT (rather than trying to identify responders per se), physicians implanting CRT devices should incorporate this in their clinical algorithm to prioritizes patients.

Maybe it is time to consider introducing some of these insights, apart from QRS width, in guidelines for the indications of CRT. It is always appealing to keep things simple, but complex pathophysiological settings such as heart failure with abnormal cardiac mechanics and a wide variety of myocardial abnormalities, cannot be oversimplified.

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Author Reply

When to take arms against a sea of troubles: CRT- still a challenging question

Aksilik denizine karşı ne zaman kuvvet toplamalıyız: CRT - hala meydan okuyan bir sorundur

Dear Editor,

The implantation of the biventricular device represents an initial expense and must be weighed against measures of short- and long-term efficacy with regards to survival, morbidity and quality of life (1).

In the Editorial published on the Anatolian Journal of Cardiology and entitled "Evaluating patients for CRT, what's relevant: identifying responders or estimating the amount of potential response"(2) the author declares that identifying the most appropriate candidate for CRT "is also very expensive, requires the appropriate team for selection, implantation and intensive follow-up and a substantial amount of individual patients show little improvement".

Health care resources are, by now, limited all over the world. Therefore, clearly, the identification of the characteristics of the patient population most likely to benefit from cardiac resynchronization therapy (CRT) is of utmost importance and treatment strategy should target these patients for device implantation.

In the latest guidelines (3), great emphasis was placed on the impact of CRT on symptoms and exercise tolerance. Moreover, the NYHA class IV patients should now be ambulatory.

Great importance was given to the baseline electrocardiogram (ECG) - typical left bundle branch block (LBBB) pattern predicted a favorable outcome, while prolonged PR interval and right bundle branch block (RBBB) were the only predictors of a non-favorable outcome (4).

In the guidelines the role of echocardiography was not fully treated. In fact, the importance of echocardiography depends on its role during the follow-up.

As demonstrated by CARE-HF(4) and REVERSE (5), echo-monitoring revealed significant improvements in left ventricular (LV) size and function, LV ejection fraction, right ventricular function, left atrial size and mitral regurgitation in patients (NYHA class II) treated with CRT compared with implantable cardioverter-defibrillator only. Although these findings were consistent among all subgroups, the improvements in volumes were greatest in patients with a QRS width of ≥150 ms, in patients with LBBB, in patients with non-ischemic etiology and in female patients.

In our study (6), we demonstrated the prognostic and not only the diagnostic role of echocardiography. Patients with myocardial viability (MV) responded better than patients without MV with a significant improvement after the first week of following CRT (6).

We may have to change our point of view. Every day is very important when investing correctly our limited resources, and so great emphasis must be placed on the identification of responders to CRT- that is, on the category of patients who will benefit the most from resynchronization.

This, however, is a very challenging question, and perhaps future guidelines should also focus on the prognostic role of echocardiography.

Recently, on these lines, a very original work has appeared: Ciampi et al. (7) tried to use the Bowditch Treppe and Pressure/Volume relationship to identify the responders to CRT.

As in our study, also this article gave great importance to MV. In fact, as demonstrated in several papers, the presence of MV, instead of transmural scar tissue and fibrosis, plays an important role in identifying responders to CRT (8-10).

Patients with preserved contractility and myocardial viability show a favorable clinical outcome. Exercise and/or dobutamine stress echocardiography (DSE) is a sensible and specific test. It is not expensive and there are only a few contraindications. DSE is an important tool for the cardiologist and, according to the results of this study, it should be considered before the implantation of a biventricular device.

Progress in the pacing regards not only the prognostic and diagnostic tools, but also the implantation technique. Recently, Kassai et al. (11) described a new implantation method-as for the aortic valve, also for the ventricular lead a transapical approach was used.

This alternative approach is now reserved for cases of failure of coronary sinus lead implantation for resynchronization therapy.

The ventricular lead can be placed alternatively on the septum or on the free wall. In the first case it is used as a left univentricular pacing while in the latter as a biventricular pacing. In their work (11), recently published in Europace, transapical placement of LV endocardial pacing lead results as being an effective alternative strategy for cardiac resynchronization.

However we strongly agree with one of the final sentence reported in the Anatolian Journal of Cardiology Editorial (2): "maybe it is time to consider introducing some of these insights, apart from QRS width, in guidelines for the indications of CRT".

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ST-elevation myocardial infarction after acute carbon monoxide poisoning

Akut karbon monoksit zehirlenmesi sonrası ST-yükselmeli miyokart enfarktüsü

Dear Editor,

Myocardial infarction (MI) is rarely reported in course of acute carbon monoxide poisoning (COP) (1). Pathogenesis of cardiac toxicity caused by carbon monoxide (CO) is rather complex. A 38-years-old male patient referred to our emergency department with altered consciousness, dyspnea and chest discomfort five hours after acute exposure to CO in a burning apartment. His arterial blood pressure was 145/95 mmHg, pulse rate was 142 beats/min with a regular rhythm. A 2/6 systolic murmur was audible along left sternal border. Electrocardiogram taken at admission showed ST segment elevation in precordial derivations (Fig. 1). After immediate oxygen supplementation with a flow rate of 6 L/min, arterial blood was obtained for analysis. In blood gas analysis, pH was 7.34; oxygen saturation was 86%, partial oxygen pressure was 75 mmHg, partial CO2 pressure was 42 mmHg, bicarbonate concentration was 16 mmol/L, and carboxyhemoglobin (COHb) saturation was 14%. 300 mg acetylsalicylate and 600 mg clopidogrel were administered to patient immediate before emergency angiography. Coronary angiography revealed total occlusion of proximal left anterior descending artery. Direct stent implantation was performed and TIMI 3 flow was restored with no residual obstruction (Fig. 2a, 2b and Video 1a, 1b. See corresponding video/movie images at www.anakarder.com). During procedure, tirofiban was initiated and continued for 72 hours after procedure. Twelve hours after admission, COHb level was 4% under 100% O2. Transthoracic echocardiography revealed an apicoseptal dyskinesia with an ejection fraction of 42%. Eight days after initial admission, he was discharged from hospital to be followed up in an outpatient basis.

When the balance between oxygen supply and demand to myocardium is disturbed, myocardial ischemia develops. CO not only replaces

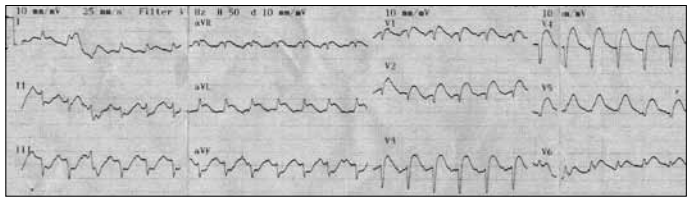

Figure 1. Electrocardiogram at the time of admission

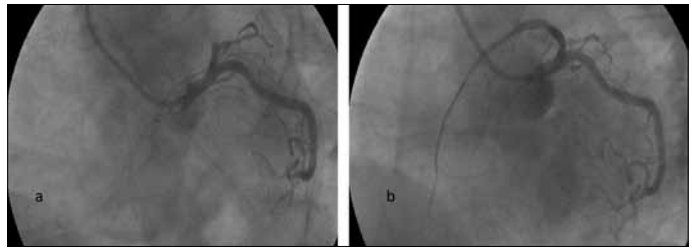

Figure 2. Selective coronary angiogram of left coronary artery in left anterior oblique caudal projection pre (a) and post (b) percutaneous coronary intervention

oxygen in hemoglobin (Hb) but also causes a shift in oxygen-hemoglobin dissociation curve so oxygen uptake in capillary level becomes harder. CO also inhibits mitochondrial function by formation of cytochrome a, a3-CO ligand; therefore disturbing intracellular respiration (2). Despite TIMI-3 flow was immediately restored after patient's admission to our facility, apicoseptal dyskinesia in left ventricular wall was nevertheless developed. This finding may imply CO has a more generalized toxic effect on myocardium or a limited toxicity localized at reperfused area (3). Even though blood oxygen concentration could be increased by administration of oxygen, tissue hypoxia is maintained as a result of inhibition of cellular respiratory functions induced by CO (2). Similarly, CO can trigger thrombus formation in vessels. Thrombotic tendency induced by CO was found to be related with increased platelet agreeability and polycythemia (4). Administration of 100% oxygen to patients with COP is usually adequate to achieve rapid recovery. Several approaches employ hyperbaric oxygen therapy in those with very high COHb levels or display cardiovascular dysfunction (5).

CO intoxication may cause acute MI in those with or without preexisting CAD, through aforementioned mechanisms. Careful consideration should be given to patients with COP. It is important to evaluate electrocardiogram and cardiac biomarkers in the first hours. Oxygen administration or hyperbaric oxygen therapy should be considered in patients with COP and cardiac toxicity. Emergent angiogram and reperfusion therapy is suitable in those with STEMI and demonstrable coronary obstruction.

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Video 1a-b: Selective coronary angiogram of left coronary artery in left anterior oblique caudal projection pre and post percutaneous coronary intervention

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