Analysis of Cardiac Dyssynchrony – An Unsolved Issue! How to improve selection and response to Cardiac Resynchronization Therapy?

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Short Editorial regarding the article: Relationship of Electromechanical Dyssynchrony in Patients Submitted to CRT With LV Lead Implantation Guided by Gated Myocardial Perfusion Spect

The authors Nascimento et al., 1 published an important work demonstrating the value of myocardial perfusion scintigraphy (SPECT-Gated) to identify cardiac dyssynchrony (CD) and with posterior implantation of left ventricle (LV) electrode in the area with higher dyssynchrony, with favorable correlation with clinical results and cardiac function. The study raises important issues in the attempt to reduce non-respondent rate (30-40%). These high rates are due to implants in very advanced or irreversible phases of the disease or to positioning of the LV electrode in areas with fibrosis or due to absence of dyssynchrony.

All the current directives take the indication of cardiac resynchronization therapy (CRT) in consideration, based on electrical dyssynchrony criteria, in detriment of mechanical dyssynchrony criteria. The Echo CRT study confirmed the unfavorable results in patients submitted to CRT in absence of CD, minding it may be a deleterious therapy.

Occurrence of CD is the pathophysiological base of CRT. Over 1/3 of patients with left branch blockade (LBB) may not suffer from CD, particularly those with QRS < 150 ms. 2 That number is higher in the other intraventricular conduction disorders. Thus, new techniques which may improve the selection of those patients and allow for implanting electrodes in the regions with a higher level of contraction delay are welcome.

However, several aspects deserve special attention. This work encompasses a subgroup of patients, from an ongoing multicentric VISION-CRT global study, which must bring a definitive answer on the value of perfusion scintigraphy in the selection of patients for CRT, thus helping to select the location to position the electrode in the coronary sinus. 3

Several imaging methods were and have still been described as important ones to identify and quantify CD. All of them show both advantages and disadvantages, and their studies, are mostly unincentric and performed with small populations and show non-reproducible results, with no direct correlation with relevant outcomes, such as mortality or, even, substitutive outcomes, such as response to CRT.

Echocardiogram has classically become the standard and most used method, given its low cost, easy accessibility and repetition, when necessary for pacemaker (PC) reprogramming, however, in virtue of the lack of standardization of the best methodology, of the high intra- and inter-observer variability, of the need for a proper acoustic window and, mainly, due to the lack of favorable results in multicentric studies, such as PROSPECT trial, its trustworthiness and applicability were caused to decrease. 5

New echocardiographic techniques emerged and have evolved in that sense, such as Speckle-tracking, the Septal Flash, the Apical Rocking and the 3D-echocardiogram, some of which already showing initial evidence of correlation with better prognosis after CRT, as shown in the study by Hoke and Bax J. 6 on PREDICT–CRT 7 and on TARGET 8 studies. As disadvantages, they are always dependent observers and, up to the moment, have not show favorable results in large series.

Myocardial perfusion scintigraphy has appeared in the last decade, with the phase analysis technique, as an additional method for CD analysis. Its advantage lies on lower intra- and inter-observer variability, on high reproducibility and on allowing three-dimensional LV contraction analysis, also having the possibility of joint analysis of ischemia and fibrosis, however, it adds more costs than echocardiogram, radiation, higher acquisition time, lower possibility of repetitions for PC comparisons and reprogramming. Also, the benefits of its use in large series still require confirmation. Variations on protocols and cut-off values related to better evolution are also under discussion. 9 This method may present difficulty of analysis in cardiac segments with poor tissue perfusion, overestimating areas with extensive scarring, mainly, in dilated hearts and hearts with fine walls. 9-11

Magnetic resonance imaging has allowed a good assessment of CD and an excellent analysis of the cardiac function and its areas with fibrosis, the disadvantage being the long time of the exam, auditory noises, difficulty for claustrophobia, impossibility of use for patients with old PC who are going to be submitted to “up-grading”, high costs, lower availability and analyses of results achieved only in small series. 10,11

Imaging exams such as cardiac tomography arise as a perspective of combined use of several methods, aiming, besides CD analysis, at the identification of the anatomy of the coronary sinus, allowing to opt for the best surgical technique, such as lateral mini-thoracotomy, video-thoracoscopy or endocardial LV electrode implantation by transeptal puncture when necessary, due to the absence of tributary veins proper for its positioning in the regions with the highest degree of delay.
Some issues seem defined: the importance of cardiac dyssynchrony as a first therapeutic target in cardiac resynchronization, the need for its identification, quantification and localization, the relevance of an ideal electrode positioning in the LV, in fibrosis-free areas with higher ventricular contraction delay. Confirmation for the data mentioned previously in multicentric studies, correlated with better prognosis outcomes, should clarify an effervescent area in artificial heart stimulation and it may cause such techniques to become widespread in medical guidelines and implemented in clinical practice. Thus, the study at hand shows positive perspectives in search for better results in cardiac resynchronization therapy.

References

1. Nascimento EA, Wiefels Reis CC, Ribeiro FB, Alves CR, Silva EN, Ribeiro ML, Mesquita CT. Relação entre dissincronismo elétrico e mecânico em pacientes submetidos a TRC com implante do eletrodo de VE orientado pela cintilografia GATED SPECT. Arq Bras Cardiol. 2018; 111(4):607-615.

2. Ruschitzka F, Abraham WT, Singh JP, Bax JJ, Borer JS, Brugada J, et al. Cardiac-resynchronization therapy in heart failure with a narrow QRS complex. N Engl J Med. 2013;369(15):1395-405.

3. Sillanmäki S, Lipponen JA, Tarvainen MP, Laitinen T, Hedman M, Hedman et al. Relationships between electrical and mechanical dyssynchrony in patients with left bundle branch block and healthy controls. J Nucl Cardiol. 2018 Feb 08:1-12.

4. International Atomic Energy Agency (IAEA). IAEA Annual Report 2013. Vienna (Austria); 2013. [Cited in 2017 Feb 09] Available from: <https://www.iaea.org/About/Policies/GC/GC58/GC58Documents/English/gc58-3-att1_en.pdf>.

5. Chung ES, Leon AR, Tavazzi L, Sun JP, Nihoyannopoulos P, Merlino J, et al. Results of the predictors of response to CRT (PROSPECT) trial. Circulation. 2008; 117(20):2608-16.

6. Höke U, Bax JJ, Delgado V, Ajmone Marsan N. Assessment of left ventricular dyssynchrony by three-dimensional echocardiography: Prognostic value in patients undergoing cardiac resynchronization therapy. J Cardiovasc Electrophysiol. 2018; 29(5):780-7.

7. Stankovic I, Prinz C, Ciarka A, Darabani AM, Kotrle M, Aarones M, et al. Relationship of visually assessed apical rocking and septal flash to response and long-term survival following cardiac resynchronization therapy (PREDICT-CRT). Eur Heart J Cardiovasc Imaging. 2016; 17(3):262-9.

8. Khan FZ, Virdee MS, Palmer CR, Pugh PJ, O’Halloran D, Elsik M, et al. Targeted left ventricular lead placement to guide cardiac resynchronization therapy: the TARGET study: a randomized, controlled trial. J Am Coll Cardiol. 2012; 59(17):1509-18.

9. Romero-Farina G, Aguadé-Bruix S. Analysis of ventricular synchrony: A complex puzzle. J Nucl Cardiol. 2018 Mar 13. [Cited in 2018 June 10]. Available from: https://doi.org/10.1007/s12350-018-1252-5.

10. Sassone B, Nucifora G, Mele D, Valzania C, Bissignani G, Boriani G; for Task Force on Imaging of Italian Association of Arrhythmias and Cardiac Stimulation (AIAC). Role of cardiovascular imaging in cardiac resynchronization therapy: a literature review. J Cardiovasc Med (Hagerstown). 2018;19(5):211-22.

11. Reis CCW, Nascimento EAD, Dias FBR, Ribeiro ML, Wanderley APB, Batista LA, Mesquita CT. Aplicabilidade da cintilografia miocárdica de perfusão na avaliação do sincronismo cardíaco. Arq Bras Cardiol imagem cardiovasc. 2017; 30(2):54-63.