

QRS variation –index or percentage– to predict response to cardiac resynchronization therapy?

¿Índice o porcentaje de variación del QRS para predecir la respuesta a la terapia de resincronización cardíaca?

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To the Editor:

Cardiac resynchronization therapy (CRT) was created as a bridge to the heart transplantation, that is why no one knew at the beginning what it was going to represent *a posteriori* for cardiology and the patients; however, many publications describe the super-responders with an excellent quality of life and a NYHA (New York Heart Association)^{2,5} functional class I. There is still approximately a 30% of patients who do not respond well to the CRT, that is why, the reasons why CRT is not effective in this patients' subgroup are still being researched^{4,5}. In our opinion, and without disagreeing with many researchers who publish their results in this regard, we should look for what is failing in the CRT, in order not to wear ourselves out by describing variables that allow to recognize the response. Maybe, the identification of other type of indicators could allow us to modify the implantation procedure or the device programming, this way improving the response of those identified as possible non-responders.

Recently, I have carefully read the article “Cardiac resynchronization therapy: the QRS index as a response predictor” by Martínez López *et al*⁶, and I would like to point out some elements.

Maybe, the review of some articles quoted by these authors^{7,9}, in which the described formula is established as “index”, led Martínez López *et al*⁶ to named it that way again; but it could have been named “percentage” as well, as it is mathematically proven through its formula; given that, in this re-

search, what it is calculated is a proportion of the QRS narrowing. However, the way of naming this variable cannot be criticized, because an “index” can be a mathematical ratio that relates two variables, whose result can be understood in different ways¹⁰.

Some other aspects related to the objective, the study's design and the statistical analysis can be questionable topics. It is important to remind that the objectives of a research must be accurate, measurable and reachable, and they should not appear in any different way in the abstract and the article's body. It is not the same “to define the CRT positive response predictors” that “to determine the value of the QRS index as a CRT response predictor”.

It is also very important to take into account that “to go back into the past”, in order to look for the primary source of information, does not make the research retrospective, like it was defined by its authors⁶ in this case; because the starting point in the moment of the device implantation, with the patients monitoring and the data collection further in time (“electrocardiograms were made before the procedure, at 6th and 12th month after the implantation”) turn it into a prospective longitudinal research. Besides, in the method it is not clarified when was performed the follow-up echocardiogram, that allowed them to classify the patients according to the CRT response; neither it is mentioned in what derivation they measured the QRS for calculating the index; all that could represent a turn in the research. There are several publications proving that in the 12-lead electrocardiogram, there is one maxi-

mum and one minimum QRS, therefore some authors recognize the QRS dispersion variable as a CRT response predictor¹¹⁻¹³; one of those articles was published in this journal¹³.

Concerning the statistical analysis that is made in relation to the ROC (Receiver operating-characteristic) “to predict the CRT response”, it is probably a mistake to set it out in this way, because the area under the curve would provide the strength of the so-called QRS index to discriminate, not to predict. Perhaps, in a future analysis in the same line of research, with a greater number of cases, a correlation between the referred index and the CRT response could be applied, where they show, in addition to the graphic of the area beneath under the curve, others where they establish the cut-off point calculating the sensitivity and specificity; all this would facilitate the results’ interpretation and credibility to the readers.

On the other hand, during the reading of the article it is not clear which was the post-CRT moment for measuring the QRS duration variable; we just realize that it was not immediately after the implantation when we reach the limitations of the study. One of the factors contributing to this doubt is that in table 2⁶, where the authors describe the distribution of the echocardiographic and electrocardiographic variables according to the CRT response, the column that shows the value of the different variables in the total of the patients should have been entitled “pre- and post-CRT”, because there, the results of both moments of the research are summarized.

Finally, the conclusions of the study textually read: “A higher QRS index, that represents the decrease on this complex’s width, is related to a positive CRT response”; and it is important to remember, without detracting the local value of the discovery in this research, that “the decrease in the width” of the QRS is a variable that, since some years ago, has a proven relationship to a positive response to CRT¹⁴⁻¹⁹.

CONFLICT OF INTERESTS

None declared.

REFERENCES

1. Greenberg JM, Leon AR, Book WM, Hott BJ, DeLurgio DB, Langberg JJ, *et al.* Benefits of cardiac

resynchronization therapy in outpatients with indicators for heart transplantation. *J Heart Lung Transplant.* 2003;22(10):1134-40.

2. Qiao Q, Ding LG, Hua W, Chen KP, Wang FZ, Zhang S. Potential predictors of non-response and super-response to cardiac resynchronization therapy. *Chin Med J (Engl).* 2011;124(9):1338-41.
3. Kolettis TM. How should we follow-up patients undergoing CRT? *Hellenic J Cardiol.* 2018;59(4):232-3.
4. Alraies MC, Buchanan K, Waksman R. CRT 2017 late-breaking trials. *Cardiovasc Revasc Med.* 2017;18(4):304-7.
5. Chatterjee NA, Heist EK. Cardiac Resynchronization Therapy-Emerging Therapeutic Approaches. *Curr Treat Options Cardiovasc Med [Internet].* 2018 [cited 14 Jan 2020];20(3):20. Available at: <https://doi.org/10.1007/s11936-018-0614-2>
6. Martínez López F, Castañeda Chirino O, Falcón Rodríguez R, Castro Hevia JA, Dorantes Sánchez M, Cruz Cardentey M, *et al.* Terapia de resincronización cardíaca: Índice del QRS como predictor de respuesta. *CorSalud [Internet].* 2019 [cited 14 Jan 2020];11(3):189-95. Available at: <http://www.revcorsalud.sld.cu/index.php/cors/article/view/486/911>
7. Rickard J, Popovic Z, Verhaert D, Sraow D, Baranowski B, Martin DO, *et al.* The QRS narrowing index predicts reverse left ventricular remodeling following cardiac resynchronization therapy. *Pacing Clin Electrophysiol.* 2011;34(5):604-11.
8. Rickard J, Cheng A, Spragg D, Cantillon D, Chung MK, Tang WH, *et al.* QRS narrowing is associated with reverse remodeling in patients with chronic right ventricular pacing upgraded to cardiac resynchronization therapy. *Heart Rhythm.* 2013;10(1):55-60.
9. Coppola G, Ciaramitaro G, Stabile G, DOnofrio A, Palmisano P, Carità P, *et al.* Magnitude of QRS duration reduction after biventricular pacing identifies responders to cardiac resynchronization therapy. *Int J Cardiol.* 2016;221:450-5.
10. Izar Landeta JM. Modelos matemáticos para la toma de decisiones. Ciudad de México: Instituto Mexicano de Contadores Públicos; 2019.
11. Wyndham CR, Smith T, Meeran MK, Mammana R, Levitsky S, Rosen KM. Epicardial activation in patients with left bundle branch block. *Circulation.* 1980;61(4):696-703.
12. Dilaveris P, Giannopoulos G, Synetos A, Aggeli C, Raftopoulos L, Arsenos P, *et al.* Effect of biventricular pacing on ventricular repolarization and

- functional indices in patients with heart failure: lack of association with arrhythmic events. *Europace*. 2009;11(6):741-50.
13. Chávez González E, Alonso Herrera A, Carmona Puerta R, Pérez Cabrera D, Ramos Ramírez RR, Gómez Paima W, *et al*. Dispersión del QRS como índice de disincronía en el bloqueo de rama izquierda y de sincronía tras la terapia de resincronización cardíaca, una variable de respuesta exitosa. *CorSalud* [Internet]. 2015 [cited 21 Jan 2020];7(2):106-16. Available at: <http://www.revcorsalud.sld.cu/index.php/cors/article/view/28/73>
 14. Sebag FA, Martins RP, Defaye P, Hidden-Lucet F, Mabo P, Daubert JC, *et al*. Reverse electrical remodeling by cardiac resynchronization therapy: Prevalence and clinical impact. *J Cardiovasc Electrophysiol*. 2012;23(11):1219-27.
 15. Bazoukis G, Naka KK, Alsheikh-Ali A, Tse G, Letsas KP, Korantzopoulos P, *et al*. Association of QRS narrowing with response to cardiac resynchronization therapy-a systematic review and meta-analysis of observational studies. *Heart Fail Rev* [Internet]. 2019 [Cited 21 Jan 2020]. Disponible en: <https://doi.org/10.1007/s10741-019-09839-5>
 16. Kaypakli O, Koç M, Gözübüyük G, Şahin DY. High left ventricular lead sensing delay predicts QRS narrowing and good response to cardiac resynchronization therapy. *Pacing Clin Electrophysiol*. 2016;39(12):1317-26.
 17. Bryant AR, Wilton SB, Lai MP, Exner DV. Association between QRS duration and outcome with cardiac resynchronization therapy: a systematic review and meta-analysis. *J Electrocardiol*. 2013; 46(2):147-55.
 18. Biton Y, Kutiyafa V, Cygankiewicz I, Goldenberg I, Klein H, McNitt S, *et al*. Relation of QRS duration to clinical benefit of cardiac resynchronization therapy in mild heart failure patients without left bundle branch block: The Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy Substudy. *Circ Heart Fail* [Internet]. 2016 [cited 22 Jan 2020];9(2): e002667. Available at: <https://doi.org/10.1161/CIRCHEARTFAILURE.115.002667>
 19. Zareba W, Klein H, Cygankiewicz I, Hall WJ, McNitt S, Brown M, *et al*. Effectiveness of cardiac resynchronization therapy by QRS morphology in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT). *Circulation*. 2011;123(10):1061-72.