Rethink RethinQ? Papillary muscle dyssynchrony and functional mitral regurgitation

RethinQ çalışmasını yeniden düşünelim mi? Fonksiyonel mitral yetersizliği ve papiller kas dissenkronisi

Cardiac resynchronization therapy (CRT) benefits patients with moderate to severe heart failure and wide QRS complex, but the RethinQ trial showed no clinical benefit in patients with QRS duration less than 130 ms despite concomitant presence of mechanical dyssynchrony assessed by standard echocardiographic parameters (1). This context lends importance to the clinical relevance of the study by Tigen et al. (2). The authors looked into the relationship between papillary muscle dyssynchrony (PMD) assessed by echocardiography and degree of "functional" mitral regurgitation in patients with nonischemic cardiomyopathy with low ejection fraction. Prior studies have demonstrated that mitral regurgitation is associated with increased mortality in these patients (3-5) and an intriguing study demonstrated that CRT reduces mitral regurgitation in heart failure patients (6) potentially by reducing intraventricular dyssynchrony that may play a role in the development of mitral regurgitation (7).

In the current study, the authors found that in consecutively enrolled nonischemic cardiomyopathy patients with both wide and narrow QRS duration, PMD was associated with greater degrees of mitral regurgitation, a finding that has been consistently demonstrated in heart failure patients with wide QRS duration (6-9). A novel aspect of the study is describing for the first time the relationship between PMD and mitral regurgitation in patients with narrow QRS duration. In this subset comprising 55 patients, subjects with PMD showed greater degree of mitral regurgitation as measured by regurgitant volume and effective regurgitant orifice area; this difference in mitral regurgitation was not seen between subjects with and without septal-lateral wall dyssynchrony. This suggests that not all types of dyssynchrony produce similar physiologic consequences. This leads to the intriguing possibility that perhaps a subset of narrow QRS heart failure patients may benefit from resynchronization therapy targeted at patients with significant functional mitral regurgitation and/or PMD.

Alas, the study is only a hypothesis-generating study and one should be cautious about extending the reported association as a causal relationship, as the authors at times suggest. A further correlation between the level of dyssynchrony and its effect on the severity of mitral regurgitation would have been supportive. Also, nonischemic cardiomyopathy patients with more than mild degree of mitral regurgitation versus those with mild regurgitation, not only demonstrate greater PMD but also have more advanced degrees of diastolic dysfunction (shorter deceleration time and isovolumic relaxation time) so teasing out the role of myocardial dysfunction versus timing of regional contraction will be important in further defining the mechanistic basis of mitral regurgitation. Follow-up studies need to determine whether available CRT modalities can alleviate papillary muscle dysfunction in narrow QRS heart failure patients and whether such an approach reduces functional mitral regurgitation. If such is the case, a targeted randomized trial may be worthwhile to determine if CRT that relieves mitral regurgitation in heart failure patients with narrow QRS will favorably impact clinical outcomes. In light of the finding that not all types of dyssynchrony produce similar physiologic results, there is need to understand timing of regional contraction on a 3-dimensional, rather than 2-dimensional basis as is currently done and also recognize that potential resynchronization therapy of the future may need to be flexible in being able to change activation timing of specific regions, a challenge that may not be met by current means of pacing from the right ventricle and coronary sinus.

While the current study is intriguing, it leaves several more questions unanswered: What is the prevalence and severity of mitral regurgitation in patients with papillary muscle dyssynchrony and non-ischemic dilated cardiomyopathy? Is there a difference in morbidity and mortality as it relates to severity of mitral regurgitation? Is there a relationship between medical therapy and morbidity/mortality, and severity of mitral regurgitation? How do these patients compare with patients who have a prolonged QRS duration? This paper has engendered several thought-

Address for Correspondence / Yazışma Adresi: Raymond Q. Migrino, MD, Medical College of Wisconsin-CVM E5100, 9200 W. Wisconsin Avenue Milwaukee WI 53226, USA
Phone: 001 414 9556737 Fax: 001 414 4566203 E-mail: rmigrino@mcw.edu

©Telif Hakkı 2009 AVES Yayıncılık Ltd. Şti. - Makale metnine www.anakarder.com web sayfasından ulaşılabilir.
©Copyright 2009 by AVES Yayıncılık Ltd. - Available on-line at www.anakarder.com

provoking questions whose answers may impact our understanding of and make us rethink how we treat heart failure.

Amitoj Marwaha, Ashvin Patel, Raymond Q. Migrino
Division of Cardiovascular Medicine, Medical College of Wisconsin, Wisconsin University, Milwaukee, WI, USA

References

1. Beshai JF, Grimm RA, Nagueh SF, Baker JH, 2nd, Beau SL, Greenberg SM, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. New EnglJ Med 2007; 357: 2461-71.
2. Tigen K, Karaahmet T, Gürel E, Çevik C, Otahbachi M, Pala S, et al. Papillary muscle dyssynchrony as a cause of functional mitral regurgitation in non-ischemic dilated cardiomyopathy patients with narrow QRS complexes. Anadolu Kardiyol Derg 2009; 9: ???
3. Blondheim DS, Jacobs LE, Kotler MN, Costacurta GA, Parry WR. Dilated cardiomyopathy with mitral regurgitation: decreased survival despite a low frequency of left ventricular thrombus. Am Heart J 1991; 122 (3 Pt 1): 763-71.
4. Junker A, Thayssen P, Nielsen B, Andersen PE. The hemodynamic and prognostic significance of echo-Doppler-proven mitral regurgitation in patients with dilated cardiomyopathy. Cardiology 1993; 83: 14-20.
5. Koelling TM, Aaronson KD, Cody RJ, Bach DS, Armstrong WF. Prognostic significance of mitral regurgitation and tricuspid regurgitation in patients with left ventricular systolic dysfunction. Am Heart J 2002; 144: 524-9.
6. Kanzaki H, Bazaz R, Schwartzman D, Dohi K, Sade LE, Gorcsan J, 3rd. A mechanism for immediate reduction in mitral regurgitation after cardiac resynchronization therapy: insights from mechanical activation strain mapping. J Am Coll Cardiol 2004; 44: 1619-25.
7. Soyama A, Kono T, Mishima T, Morita H, Ito T, Suwa M, et al. Intraventricular dyssynchrony may play a role in the development of mitral regurgitation in dilated cardiomyopathy. J Card Fail 2005; 11: 631-7.
8. Ypenburg C, Lancellotti P, Tops LF, Bleeker GB, Holman ER, Pierard LA, et al. Acute effects of initiation and withdrawal of cardiac resynchronization therapy on papillary muscle dyssynchrony and mitral regurgitation. J Am Coll Cardiol 2007; 50: 2071-7.
9. Ypenburg C, Lancellotti P, Tops LF, Boersma E, Bleeker GB, Holman ER, et al. Mechanism of improvement in mitral regurgitation after cardiac resynchronization therapy. Eur Heart J 2008; 29: 757-65.