Myocardial scar reduction after cardiac resynchronization therapy assessed by gated myocardial perfusion SPECT

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Received Aug 3, 2021; accepted Aug 3, 2021
doi:10.1007/s12350-021-02787-4

See related article, pp. 2571–2579

Heart failure is one of the major problems in cardiology. Patients who have ischemic or non-ischemic heart disease often encounter heart failure later in life. Gated-electrocardiogram myocardial perfusion single-photon emission computed tomography (GMPS) has previously shown its prognostic properties with post-stress ejection fraction (EF) and left ventricular volume.^{1,2} Decompensated heart failure sometimes indicates complete left bundle branch block, wide QRS duration, and left ventricular dyssynchrony.^{3–6} GMPS non-invasively describes dyssynchrony indices including histogram bandwidth (BW), phase standard deviation (PSD), and entropy using phase analytic software.⁷ Mechanical dyssynchrony or entropy of the left ventricle is an independent predictor of various causes of death and major adverse cardiac events.^{8,9} Cardiac resynchronization therapy (CRT) has shown a benefit in patients with severe heart failure (NYHA $\geq$ II) with optimal medical therapy, EF $\leq$ 35%, left bundle branch block, QRS duration $\geq$ 120 ms, and sinus rhythm.¹⁰

CRT improves mechanical dyssynchrony in patients with severe heart failure although its functional effect on myocardial perfusion including viability has not yet been

fully evaluated. Many echocardiographic studies have reported mechanical dyssynchrony by echocardiogram predicted functional recovery. Recently, some manuscripts reported an association between cardiac functional recovery and dyssynchrony indices including BW and PSD.^{4,11} Boogers et al has shown that BW 72.5° (sensitivity of 83% and specificity of 81%) and PSD 19.6° (sensitivity of 83% and specificity of 81%) are predictors of recovery in NYHA class by quantitative gated software (QGS). With different software (Emory Cardiac Toolbox), Henneman et al has reported BW 135° (sensitivity and specificity of 70%) and phase PSD 43° (sensitivity and specificity of 74%) with the same criteria of functional recovery. Interestingly, both authors calculated EF and left ventricular volume by dedicated software; however, their threshold of functional recovery was an improvement of NYHA functional class. Patients' symptoms, exercise capacity, and quality-of-life score were deemed to be appropriate to evaluate the effect of CRT.

Wang et al has documented left ventricular scar reduction (SR) assessed by GMPS using Emory Cardiac Toolbox after CRT. (xxxx, yy, zz-zz) Their patient population included 10% with prior myocardial infarction. They defined myocardial scar with less than 50% of maximal activity of Tc agent. Their unique findings not only refer to cardiac functional recovery after CRT but also to SR. Interestingly, SR group showed wider BW, PSD, and reduced wall thickening (RWT) than those in non-SR groups (Table 1). They found QRS duration (QRSd $\geq$ 162 ms) and RWT ($\geq$ 70.3%) were independent predictors of SR with multi-variate logistic regression analysis. Receiver operating curve analysis showed that the combination of QRSd and RWT developed the largest area under the curve predicting SR (Figure 1). This wide QRSd was also acceptable, which

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J Nucl Cardiol 2022;29:2580–2.
1071-3581/\$34.00

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Table 1. Comparison of functional changes after CRT between SR and non-SR groups

	SR (N = 22)	non-SR (N = 39)	P value
Echocardiography			
Δ LVEF, %	18.1 ± 12.4	9.4 ± 9.9	.007
Δ ESV, ml	− 91.6 ± 52.6	− 38.1 ± 46.5	< .001
Δ EDV, ml	− 90.8 ± 59.3	− 32.1 ± 52.6	< .001
Electrocardiography			
Δ HR, bpm	− 8.5 ± 13.7	− 4.1 ± 18.7	.288
Δ QRSd, ms	− 28.6 ± 16.7	− 14.3 ± 30.5	.021
Myocardial perfusion imaging			
Δ PSD, °	− 26.19 ± 18.42	− 5.8 ± 23	< .001
Δ BW, °	− 128.7 ± 82.8	− 25.2 ± 109	< .001
Δ RWT, %	− 19.6 ± 6.8	1.7 ± 9.2	< .001
Δ Scar, %	− 29.7 ± 18.9	− 4.2 ± 19.7	< .001

BW, bandwidth; EDV, end diastolic volume; ESV, end systolic volume; HR, heart rate; LVEF, left ventricular ejection fraction; PSD, phase standard deviation; QRSd, QRS duration; RWT, reduced wall thickening; SR, scar reduction

	Cutpoint	sensitivity	specificity	AUC	95% CI	p-value
QRSd, ms	≥ 162 ms	81.80%	56.40%	74.10%	67.5-80.8	<0.001
RWT, %	≥ 70.3%	86.40%	53.80%	68.10%	61-75.1	0.007
QRSd + RWT		68.20%	76.90%	77%	70.7-83.4	<0.001

QRSd, QRS duration; RWT, Reduced Wall Thickening.

Figure 1. ROC curve analysis of significant baseline parameters for predicting the development of scar reduction after CRT.

was more than 150 ms regarding CRT indication according to established guidelines.

How does improvement of mechanical dyssynchrony by CRT contribute to SR? Possible speculations are as follows: (1) mitochondrial function of hibernated but viable tissue would improve radioisotope uptake after CRT, (2) CRT may improve the microvascular or endothelial dysfunction which might be included in the present study. They used ^{99m}Tc -sestamibi in the present study, which was suitable for GMPS. However, ^{99m}Tc agent may not be sufficient to evaluate myocardial viability or scarring. Commonly, ^{201}Tl is useful in the evaluation of viable or non-viable tissue due to its high extraction fraction. Accurate diagnosis of hibernated myocardium in the scar tissue at resting perfusion should be evaluated by ^{18}F -fludeoxyglucose (FDG) positron emission computed tomography (PET). CRT does not increase myocardial blood flow at rest by myocardial perfusion PET study even in patients with functional recovery.¹² Therefore, SR would not be seen just after CRT, but potential functional reserve of hibernated myocardium expressed by RWT could enhance SR in the follow-up period. In addition, late gadolinium enhancement on magnetic resonance imaging to evaluate scar tissue could be appropriate for establishing a standard.

Finally, dyssynchrony indices are different among dedicated software due to their unique algorithms; therefore, interpretation of those parameters is sensitive.^{3,7,11,13} In conclusion, CRT may predict myocardial SR with potential functional reserve by RWT. Association between accurate myocardial viability assessed by ^{18}F FDG PET study and RWT by GMPS should be further evaluated in the future.

Disclosures

Naoya Matsumoto receives a lecture fee from Nihon Medipysics and Fujifilm Toyama Chemical. Naoya Matsumoto receives a scholarship funds from Fujifilm Toyama Chemical.

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