Development of Novel Algorithm for Quantitative Assessment of Left Ventricular Dyssynchrony Evaluated by ECG-gated Myocardial Perfusion SPECT Imaging: Award from 19th Meeting of the Japanese Society of Nuclear Cardiology

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Received: July 30, 2019/Revised manuscript received: July 31, 2019/Accepted: July 31, 2019

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Abstract

Cardiac resynchronization therapy (CRT) has been utilized for patients with advanced heart failure since 2004 in Japan. However, it has been regarded as the problem that about 30% of the patients with CRT show poor functional improvement. For the prediction of CRT response, the importance of the quantitative assessment of left ventricular (LV) dyssynchrony has been reported. Therefore, we developed novel algorithm for quantitative assessment of LV dyssynchrony with radionuclide imaging; ECG-gated myocardial perfusion SPECT imaging (NCVC method).

We applied “partial volume effect” in SPECT system for detecting regional systolic timing. Measuring the sequential change of regional myocardial counts in cardiac cycle, we determined “time to end-systole (TES)” which was the time from R-wave to maximum counts phase in each region. Then, we calculated maximum difference of TES between regions, named as “Dissynchrony Index (DI).”

For the verification of this NCVC methods, we evaluated the patients with CRT implantation. Responders showed significantly higher DI than non-responder, and also showed significant reduction of DI after CRT, however, non-responder did not show such reduction. Moreover, DI showed significant correlation to the index of LV dyssynchrony evaluated by “phase analysis” of commercially available software: QGS (quantitative gated SPECT). From these results, our novel algorithm “NCVC method” might be useful for CRT management; such as decision of indication and evaluation of therapeutic response similar with other software.

Keywords: Cardiac resynchronization therapy (CRT), ECG-gated myocardial perfusion SPECT, Left ventricular dyssynchrony, Partial volume effect

Cardiac resynchronization therapy (CRT) has been utilized as the established therapy reimbursed by health insurance for patients with advanced heart failure since 2004 in Japan. Although numerical studies have reported its effectiveness for the improvement of patients’ prognosis and quality of life (1, 2), about 30% of the patients with CRT show poor functional improvement (1, 3), in spite of compliance to the ACC/AHA heart failure guidelines (4, 5). Therefore, the prediction of CRT response was thought to be essential for the decision of its indication. Several reports revealed the usefulness of tissue Doppler imaging of echocardiography for prediction of CRT response, which enabled precise assessment of LV dyssynchrony by measuring regional time to peak velocity (6, 7).

In radionuclide imaging, ECG-gated myocardial perfusion SPECT (GMPS), which is able to examine LV myocardial perfusion and function simultaneously, has been thought to...
contribute to the quantitative assessment of LV dyssynchrony.  
“Phase analysis” technique of GMPS was reported as beneficial tool for the prediction of CRT response (8, 9). However, since this “phase analysis” has been unavailable in Japan for long time, we needed to develop our own original algorithm with GMPS for quantitative assessment of LV dyssynchrony.

In this study, we developed a new software program called “National Cerebral and Cardiovascular Center (NCVC) method”, which was applicable to the ordinary personal computers, to quantify the degree of LV dyssynchrony using GMPS data.

Concept and process of “NCVC method”

For developing NCVC method, we focused on “partial volume effect” of SPECT system for detecting regional systolic timing. Because GMPS data contains the information about regional wall thickening in a cardiac cycle, which is estimated by the change of regional wall counts based on the partial volume effect. Therefore, procedures of NCVC method were as follows.

① From acquired GMPS data, generating a polar map displaying myocardial pixel counts distribution as % peak activity for each ECG-gated frame (16 frames per cardiac cycle).
② Measuring “the mean value of % peak activity of 4 myocardial segments (anterior, lateral, inferior, and septum)” and “the maximum counts” of the polar map in each gated frame with quantitative perfusion SPECT (QPS) software (Figure 1A).
③ Those data were transferred to usual personal computer; then we calculated “the segmental mean value of absolute counts” of each gated frame by following formula: “segmental mean value of % peak activity” × “the maximum counts”.
④ Consequently, the segmental time-activity curves were generated by plotting the calibrated absolute counts of 16 gated frames, and were applied with the second-harmonic Fourier transform curve-fitting.
⑤ In each transformed time-activity curve, maximum count point was determined as the end-systolic (ES) point and then the interval from R-wave to the ES point was measured as time-to ES (TES) (Figure 1B).
⑥ Finally, the degree of LV dyssynchrony among the 4 myocardial segments was estimated using a following formula as a dyssynchrony index (DI): (Max.TES–Min.
TES) / R-R interval time × 100. An example of calculation of DI is shown in Figure 1C.

Demonstrate of NCVC method with clinical cases

For the evaluation of clinical utility of NCVC method for the management of CRT, we analyzed thirty-three patients (25 males and 8 females, 58 ± 16 years) with chronic heart failure, who were scheduled for implantation of CRT device. Furthermore, the study patients were classified into two groups based on LV functional response to CRT, 18 responders and 15 non-responders. The responders were defined as those with improvement of LVEF >10% and/or percent reduction of LVESV >10% during the 6-month follow-up. In pre-CRT state, responders showed significantly higher DI than non-responders (25.9 ± 22.2 vs. 10.8 ± 8.9, P=0.01) (Figure 2). And 6 months after the implantation of CRT, DI decreased significantly in responders (25.9 ± 22.2 to 13.6 ± 10.9, P<0.05), while no significant change was observed in non-responders (10.8 ± 8.9 to 15.1 ± 13.9) (10).

Further development of NCVC method: analysis with 20-segment model and comparison with phase analysis in commercially available software

From the results described above, we made further development of algorithm applying 20-segment model for precise LV dyssynchrony analysis. The basic concept and procedures were same with 4-segment model which was previously described. Moreover, we evaluated “coefficient of variance (CV)” as a parameter of LV dyssynchrony, in addition to DI. In these indices, DI suggests the time lag of systolic phase between myocardial segments, and CV suggests the heterogeneity of systolic phase in a whole heart.

We demonstrated this method with same subjects with 4-segment model, and not only DI but also CV were significantly higher in responders than non-responders. Furthermore, we compared these DI and CV to indices of phase analysis in QGS program, and significant correlation between two methods were observed. (Figure 3) (presented at Society of Nuclear Medicine 58th Annual Meeting; SNM 2011. Unpublished data.)

Discussion

We have developed novel algorithm for quantitative assessment of LV dyssynchrony by GMPS. Firstly, we demonstrated this method with 4-segment model, clinical

![Figure 2](image-url)

**Figure 2** Comparison of dyssynchrony index (DI) at baseline between responders (white bar) and non-responders (gray bar). Pre-CRT DI was significantly higher in responders than in non-responders (P=0.01).

![Figure 3](image-url)

**Figure 3** Comparison between NCVC method and phase analysis in QGS.

A: Comparison of dyssynchrony index (DI) between 2 methods.
B: Comparison of coefficient of variance (CV) between 2 methods.

PA: phase analysis

\[ r=0.60, P=0.0003 \]
\[ Y=2.149 + 0.62X \]

\[ r=0.55, P=0.0012 \]
\[ Y=0.11 + 0.61X \]
utility for CRT management was implied. Then, we upgraded to 20-segment model, and not only DI, but also CV were thought to be useful for decision of CRT indication. Furthermore, these indices were comparable to those by phase analysis in commercially available software.

From these results, NCVC method was thought to be useful not only for the CRT indication but for the evaluation of CRT therapeutic effect. Moreover, the advantages of NCVC method are: 1. available in ordinarily PC, 2. regardless of file format. If GMPS data contains information of sequential counts during cardiac cycle, NCVC method can assess LV dyssynchrony quantitatively by usual PC, which results in reduction of cost and broad data availability, compared to “phase analysis” in commercially available software.

However, as a result that “phase analysis” has been installed in several cheap software, phase analysis was getting major in assessment of LV dyssynchrony rather than our NCVC method, and our challenge has not achieved to widely clinical use and product commercialization.

Conclusion

NCVC method, which was novel algorithm for assessing LV dyssynchrony, might be useful for CRT management, such as decision of indication and evaluation of therapeutic response.

Acknowledgments

None.

Sources of funding

None.

Conflicts of interest

All authors have nothing to declare related to this study.

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