Intrathoracic Impedance Changes Reflect Reverse Left Ventricular Remodeling in Response to Cardiac Resynchronization Therapy in Chronic Heart Failure Patients

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Summary

Intrathoracic impedance monitoring has been reported to be useful for prediction of worsening chronic heart failure (CHF). However, it has not revealed the relation between changes in intrathoracic impedance and improvement of cardiac function in CHF patients with cardiac resynchronization therapy (CRT) implantation. Therefore, we investigated whether intrathoracic impedance change reflects reverse left ventricular (LV) remodeling in response to CRT in patients with CHF. The study subjects consisted of 29 CHF patients (23 males, mean age 64 ± 12 years) with CRT-defibrillator (CRT-D) implantation. The patients were divided into two groups based on whether the Opti-vol Fluid Index® reached over 60 ohms (group A, n = 7) or not (group B, n = 22) within 6 months of observation after CRT-D implantation. Levels of plasma B-type natriuretic peptide (BNP) were measured, and LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LV ejection fraction (LVEF) were evaluated before and 6 months after CRT-D implantation. In group B, BNP (556 ± 88 pg/mL versus 330 ± 70 pg/mL, P < 0.05), LVEDV (177 ± 18 mL versus 149 ± 14 mL, P < 0.01), and LVESV (128 ± 14 mL versus 100 ± 12 mL, P < 0.01) were significantly decreased 6 months after CRT-D implantation. LVEF (28 ± 2% versus 35 ± 2%, P < 0.01) was significantly increased after CRT-D implantation. On the other hand, no significant changes were detected in any parameters in group A. These data showed intrathoracic impedance changes reflected reverse LV remodeling in response to CRT in patients with CHF. Therefore, the monitoring of changes in intrathoracic impedance is useful for predicting CRT responders in patients with CHF. (Int Heart J 2012; 53: 249-252)

Key words: Chronic heart failure, Cardiac resynchronization therapy, Reverse remodeling, Intrathoracic impedance monitoring

Cardiac resynchronization therapy (CRT) has been actively adapted to chronic heart failure (CHF) patients who are refractory to conventional therapies, and many patients have received the benefits of CRT, such as improvement of cardiac function and their prognosis.1-3) However, the responses of CRT have not been promised in all CHF patients, and indeed about 30% of patients with CRT implantation have not responded.1,4) Moreover, it is difficult to predict responders for CRT, and there is no useful criterion in conventional parameters.5) Therefore, it is important to continuously monitor cardiac function even after CRT implantation to avoid the worsening of CHF.

Recently, it has been shown that intrathoracic impedance monitoring is useful for detecting pulmonary congestion and CHF worsening earlier than the appearance of symptoms and elevation of plasma levels of B-type natriuretic peptide (BNP).6,7) However, few reports have observed a relationship between the changes in intrathoracic impedance and cardiac function including left ventricular (LV) volume change on CRT.

Therefore, in the present study we investigated whether the changes in intrathoracic impedance reflect reverse LV remodeling in response to CRT in patients with CHF.

Methods

Study subjects and implanted devices: The subjects were 29 patients (23 males, mean age 64 ± 12 years) who had received CRT with defibrillator (CRT-D) implantation at our hospital. Eligible criteria for CRT were New York Heart Association (NYHA) class III/IV symptoms of heart failure despite receiving optimal medical therapy, an LV ejection fraction of 35% or less, and QRS duration of 120 msec or more.

The implanted devices were selected based on their ability to perform intrathoracic impedance monitoring (Concerto® or Consulta®, from Medtronic Inc., Minneapolis, MN, USA). The optimization of atrioventricular delay and interventricular interval was performed soon after CRT-D implantation, but additional optimization had not been performed until first analysis 6 months after CRT-D implantation. Intrathoracic impedance between the right ventricular lead and device case was...
automatically measured daily by the device, and reference impedance was set up based on the trend of changes in intrathoracic impedance. Lung congestion was defined as being present when the accumulated impedance under reference impedance (Opti-vol Fluid Index\textsuperscript{6}) reached over 60 ohms.\textsuperscript{6}

**Study design and evaluation of clinical parameters:** Patients were followed-up in our hospital for 6 months after discharge, and the Opti-vol Fluid Index was continuously monitored during the follow-up period. Plasma levels of BNP were measured before and 6 months after CRT-D implantation. An experienced echocardiologist blindly measured LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LV ejection fraction (LVEF) before and 6 months after CRT-D implantation.

The study subjects were divided into 2 groups according to whether the Opti-vol Fluid Index had reached over 60 ohms (group A, $n = 7$) or not (group B, $n = 22$) within 6 months of observation after CRT-D implantation. We compared these parameters and the occurrence of hospitalization due to CHF worsening and fatal arrhythmia requiring appropriate shock therapy between the two groups during the 6 month observation period. Written informed consent was obtained from all study subjects. The study protocol was approved by the ethics committee of Fukushima Medical University.

**Statistical analysis:** All clinical data and information from each CRT-D device were evaluated and analyzed. Continuous data are reported as means ± standard deviation, and categorical data are shown as percentages. The Wilcoxon signed rank test was used to compare the changes in clinical parameters between pre-CRT-D implantation and 6 months after CRT-D implantation in each group. Fisher's exact probability test was used to compare the presence of hospitalization due to CHF worsening and fatal arrhythmias between the 2 groups.

### Results

**Baseline characteristics of study subjects:** The Table shows the baseline characteristics of the study subjects. The study population consisted of 29 patients (23 males, mean age 64 ± 12 years) who presented symptoms according to NYHA class III/IV. In total, 20 (69%) patients had nonischemic heart disease etiology. A majority of the patients received the optimal medical therapy, as evidenced by 93% usage of \(\beta\)-blockers and 93% usage of angiotensin-converting enzyme inhibitors (ACEI)/angiotensin II receptor blockers (ARB).

**Changes in BNP and echocardiographic parameters:** The plasma level of BNP was significantly decreased 6 months after CRT-D implantation compared to that before CRT-D implantation in group B (556 ± 88 pg/mL to 330 ± 70 pg/mL, \(P < 0.05\)) (Figure 1). However, BNP did not change in group A (491 ± 155 pg/mL to 452 ± 204 pg/mL).

Among the echocardiographic parameters, LVEF was significantly increased 6 months after CRT-D implantation compared to that before CRT-D implantation in group B (28 ± 2% to 35 ± 2%, \(P < 0.01\)) (Figure 2). However, LVEF did not improve in group A (28 ± 2% to 30 ± 3%). Figure 3 shows the changes in LVEDV and LVESV after CRT-D implantation. LVEDV and LVESV in group B were significantly reduced 6 months after CRT-D implantation (LVEDV: 177 ± 18 mL to 149 ± 14 mL, \(P < 0.01\); LVESV: 128 ± 14 mL to 100 ± 12 mL, \(P < 0.01\)). However, in group A, LVEDV and LVESV did not improve after CRT-D implantation (LVEDV: 165 ± 17 mL to 168 ± 22 mL, LVESV: 119 ± 13 mL to 116 ± 17 mL).
Comparisons of rehospitalization rate due to worsening CHF:
There were two patients (29%) with hospitalization due to CHF worsening in group A, but no hospitalized patients in group B ($P < 0.05$, Figure 4). The number of patients with ventricular arrhythmias requiring appropriate shock therapy was not different between the 2 groups (1 (14%) in group A versus 2 (9%) in group B).

**DISCUSSION**

In the present study, LV reverse remodeling, defined as an improvement of LVEF and reduction of LV volume, was observed in patients after CRT-D implantation in whom the OptiVol Fluid Index had not reached over 60 ohms during the 6 month observation period. Accordingly, changes in intrathoracic impedance reflect LV function and remodeling in response to CRT in CHF. In addition, the monitoring of changes in intrathoracic impedance may be useful for predicting CRT responders in patients with CHF.

CRT is a well established treatment for patients who suffer from severe heart failure despite undergoing optimal medical treatment. Several studies have demonstrated that CRT improves exercise capacity, quality of life, NYHA functional class, and mortality in CHF patients with impaired LV systolic function and intraventricular conduction delay.\(^1\)\(^2\)\(^3\) Despite these impressive results, about 30% of patients with CRT implantation do not respond to such therapy.\(^1\)\(^2\) None of the established CRT selection criteria, such as NYHA class, QRS duration, and parameters obtained from echocardiography can adequately predict the short or long-term response to CRT.\(^4\)\(^5\) On the other hand, LV reverse remodeling after CRT implantation appears to be a strong predictor of patient outcomes.\(^6\)\(^7\) Therefore, it is very important to continuously observe changes in cardiac function and LV volume after CRT implantation.

Intrathoracic impedance is calculated as the impedance of a subthreshold electrical impulse between the right ventricular lead and device case and reflects fluid retention in the intrathoracic space, especially the lungs.\(^8\) According to this, monitoring of intrathoracic impedance has been clinically used to detect early decompensation and to adjust medical treatment in CHF patients with CRT-D. On the other hand, animal studies demonstrated changes in intrathoracic impedance are directly correlated to changes in LV filling pressure.\(^9\)\(^10\) Hence, besides pulmonary fluid accumulation, the impedance measured between the right ventricular lead and device case may depend on the amount of blood in the ventricular cavity.

It has been reported that changes in intrathoracic impedance are able to detect pulmonary congestion and edema earlier than the appearance of symptoms and other clinical parameters such as elevation of plasma BNP levels.\(^11\)\(^12\)\(^13\) The present study has demonstrated for the first time that monitoring of intrathoracic impedance is useful for predicting reverse LV remodeling and rehospitalization due to worsening CHF. Intrathoracic impedance monitoring provides additional helpful information regarding the condition of the patient for the management of CHF in the early phase.

Limitations of the present study were that it was a retrospective study and the low number of study subjects. Thus, a prospective study with a larger patient population is needed in the future.

**Conclusions:** The results indicated that intrathoracic impedance changes reflected reverse LV remodeling in response to CRT in patients with CHF. Therefore, the monitoring of changes in intrathoracic impedance is useful for predicting CRT responders among patients with CHF.

**REFERENCES**


