ORIGINAL ARTICLE

Evaluating the Efficacy and Safety of Internal Cardioversion with Implantable Cardioverter Defibrillator Device for Atrial Fibrillation in Systolic Heart Failure Patients

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Background: Atrial fibrillation (AF) commonly observed in patients with heart failure and cardioversion was often needed to restore the sinus rhythm. Previously, there is no study evaluating usefulness of internal cardioversion with implantable cardioverter defibrillator (ICD) device. In this study, we aimed to compare the efficacy and long-term effects of internal cardioversion with ICD devices compared to conventional external cardioversion in patients with AF and heart failure.

Methods: Seventy patients with AF and heart failure who underwent electrical cardioversion were enrolled in the study. Forty patients (mean age 65.36 ± 10.37 , 35 male) were assigned to undergo internal cardioversion with approximately 35 J shocks delivered through the ICD electrode. Standard external cardioversion was performed for the remaining patients (30 patients; mean age 66.20 ± 11.89 ; 24 male) that were similar with regard to baseline, and electrocardiographic characteristics.

Results: Sinus rhythm was restored in 32 of 40 patients (80.0%) assigned to internal cardioversion compared with 25 of 30 patients (83.3%) assigned to external cardioversion ($P = 0.725$). We did not witness any serious complication during the procedure and hospitalization. On the follow-up, there was no statistically significant difference in recurrence of AF and incidence of major cardiovascular events between the internal and external cardioversion groups.

Conclusions: Internal cardioversion with ICD device is an effective and safe method to restore sinus rhythm in heart failure patients with AF.

Ann Noninvasive Electrocardiol 2016;21(2):181–188

atrial fibrillation; internal cardioversion; heart failure

Atrial arrhythmias and heart failure are commonly encountered together, and either condition predisposes to the other. The contribution of the atrial contraction to the cardiac performance in a normal heart is considered to be small, but the cardiac function is significantly affected by the development of atrial fibrillation (AF) in a

failing heart.^{1,2} Myocardial performance, exercise tolerance, and quality of life can be adversely affected by irregular ventricular response, poor control of ventricular rate, and loss of atrial systolic activity in patients with heart failure.³ In this way, patients with AF and signs of heart failure require urgent rate or rhythm control with often

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Conflict of Interest:

cardioversion. External electrical cardioversion is an effective method of converting AF to sinus rhythm.⁴

Patients with heart failure have a high risk of death, and implantable cardioverter defibrillator (ICD) are effective in preventing sudden cardiac death. Given that ICD devices are increasingly implanted in patients with heart failure, the prevalence of AF in heart failure patients with ICD has been increased. Previous studies demonstrated that invasive internal cardioversion with right atrium-coronary sinus catheters is valuable therapeutic option in patients in whom conventional external cardioversion failed.^{5,6} At the same time, internal cardioversion with ICD device seems to be efficacious in restoring sinus rhythm in patients with heart failure and AF. In addition, internal cardioversion with ICD device requires lower shock energy and obviates the need of general anesthesia. However, there is not sufficient evidence in the literature comparing the acute and long-term efficacy of internal cardioversion with ICD device compared to conventional external cardioversion in patients with heart failure. In this study, we aimed to compare the efficacy and long-term effects of internal cardioversion with ICD device compared to conventional external cardioversion in patients with AF and heart failure.

MATERIAL AND METHODS

Study Population

A subset of seventy patients with persistent AF and heart failure who underwent electrical cardioversion were enrolled in the study. Persistent AF was defined as an arrhythmic episode that lasts more than 7 days; AF duration was calculated according to both onset of symptoms, last electrocardiogram (ECG) in sinus rhythm, and ICD interrogation.⁷ All systolic heart failure patients had reduced left ventricle systolic function which was defined as ejection fraction of $\leq 35\%$. At admission, all patients underwent a complete assessment including medical history, clinical examination, a 12-lead ECG, two-dimensional and Doppler echocardiography, and blood tests (complete blood count, sodium, potassium, calcium; chloride, urea, creatinine, international normalized ratio [INR], thyroid hormones and fasting plasma glucose). Patients with electrolyte abnormalities, severe

renal and hepatic failure, thyroid dysfunction, contraindications to oral anticoagulation (OAC), INR < 2 in the least 4 weeks, thrombus in the left atrial appendage were excluded. The study protocol was approved by our institutional review board committee. Informed consent was received from each patient.

Transthoracic Echocardiography

Echocardiographic studies were performed in the standard left lateral recumbent positions using a commercially available ultrasound system (Vingmed System Five GE ultrasound, Horten, Norway). Images were obtained using a 2.5–3.5 MHz transducer in the parasternal and apical views. Left ventricular end-diastolic (LVEDD) and end-systolic (LVESD) diameters were determined with M-mode echocardiography under two-dimensional guidance in the parasternal long axis view, according to the recommendations of the American Society of Echocardiography.⁸ Left and right atrial sizes were measured using Simpson's method in the apical four-chamber view at end systole. Left and right atrial volume indexes were calculated by dividing left and right atrial volume by body surface area. The severity of mitral regurgitation was graded in a semiquantitative fashion (0+, none; 1+, trace; 2+, mild; 3+, moderate; and 4+, severe) based on the size and geometry of the regurgitant jet.

Anticoagulation Protocol and Antiarrhythmic Therapy

Adequate anticoagulation defined as an INR level between 2.0 and 3.0. All patients received warfarin for at least 4 weeks before and 12 weeks after cardioversion. Patients who did not receive previous anticoagulation underwent transesophageal echocardiography to rule out the presence of left atrial thrombus. Additionally, anticoagulant therapy with unfractionated or low-molecular weight heparin was immediately initiated in these patients. Intravenous amiodarone was used as a bolus followed by a continuous intravenous infusion up to 24 hours in all patients (150 mg bolus, 1 mg/min for 6 hours, and 0.5 mg/min for 18 hours). Electrical cardioversion was planned after medical cardioversion failed to restore sinus rhythm. Maintenance dose of amiodarone is 100 or 200 mg either once or twice daily was avoided in

the presence of liver disease, thyroid dysfunction especially hyperthyroidism, or other side effects. In this situation, sotalol was preferred to maintain normal sinus rhythm (twice daily). Heart failure drugs prescription was guided by the current guidelines.⁹

Electrical Cardioversion

All cardioversions were performed in coronary care unit equipped with necessary devices for cardiopulmonary resuscitation after fasting for at least 8 hours. Pulse oximetry and heart rhythm were continuously monitored and blood pressure was regularly measured during the procedure. Oxygen supplementation and ventilation support were given if necessary. External (transcutaneous and transvenous) pacing systems were also available for all patients. Cardioversion was considered successful if patients were converted to sinus rhythm. Patients were discharged after a day.

In patients without ICD, agents used for sedation were midazolam (0.02–0.08 mg/kg) and propofol (2 mg/kg). The level of sedation was monitored and repeated administration was used to reach the optimal level. If necessary, flumazenil (0.5–1 mg i.v.) was administered to antagonize the effect of midazolam. Two paddles were used, one placed on the patient's anterior chest wall, the other in axillary position (anterolateral position). During continuous ECG monitoring, up to three R wave-synchronized biphasic external shocks were delivered to restore sinus rhythm (Cardiolife, TEC-5531K, Nihon Kohden Corporation, Tokyo, Japan). A maximum of four shocks at biphasic 200 J was applied. If atrial fibrillation persisted after two shocks, we repositioned the electrodes over the right lower sternal border and the left infrascapular area close to the spine (anteroposterior position). After an unsuccessful attempt, at least 1 min was allowed to elapse before the next shock.

In patients with ICD; adequate sensing and pacing parameters and electrical integrity (connections) between the leads and pulse generator were checked prior to cardioversion. All patients had Medtronic (Minneapolis, MN, USA) or Biotronik (Berlin, Germany) ICD device. Intravenous sedation consisted of midazolam and incremental dosages of midazolam (maximum; 0.1 mg/kg) were given according to previous studies.^{10,11} A maximum of three synchronized shocks at maximum available energy of ICD device was

applied. If the internal shock failed, external DCCV was performed at anteroposterior position. Complete device interrogation including atrial and ventricular pacing threshold, P-wave and R-wave amplitude, and battery status was performed after cardioversion. Device interrogation was repeated 1 hour and 1 day later after cardioversion.

Follow-Up

The follow-up data were obtained by either clinical visits or hospital records. Follow-up appointments were scheduled at 1, 6, and 12 months after cardioversion and then every 6 months. Patients' complaints, rhythm, drug use, NYHA class, hospitalization for heart failure were assessed during each visit. Routinely, it also included a physical examination, a 12 lead ECG, complete blood count, thyroid function tests, liver, and kidney function tests, echocardiography and device interrogation. Cardiovascular clinical end points were defined as major adverse cardiac events (MACEs) if one of the following occurs during follow-up: (1) death, (2) nonfatal myocardial infarction, (3) life-threatening arrhythmias, such as sustained ventricular arrhythmia or ventricular fibrillation, and (4) hospitalization for heart failure.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation and categorical variables were expressed as percentages. Categorical variables were analyzed by chi-square test. Comparisons of continuous variables between the two groups were performed using the independent samples *t*-test. The occurrence of combined end points was analyzed by the Kaplan–Meier method and survival curves of the composite end points were compared using the log-rank test. Statistical analyses were performed using SPSS statistical software. A *P* value <0.05 was considered statistically significant.

RESULTS

Characteristics of Subjects

The study population consisted of 70 patients with the diagnosis of systolic heart failure (59 male, mean age 65 ± 10.3 years). Forty patients with ICD device were assigned to internal cardioversion and

Table 1. Characteristics of Patients Who Underwent Electrical Cardioversion for Atrial Fibrillation

	Internal Cardioversion	External Cardioversion	P Value
Number of patients	40	30	
Male gender, male (n, %)	35 (87.5%)	24 (80.0%)	0.107
Age (years, mean $\pm$ SD)	64.7 $\pm$ 9.10	66.20 $\pm$ 11.89	0.527
Hypertension (n, %)	36 (90.0%)	22 (73.3%)	0.112
Diabetes mellitus (n, %)	16 (40.0%)	10 (33.3%)	0.820
History of smoking (n, %)	14 (35.0%)	14 (46.7%)	0.458
Previous stroke or TIA (n, %)	6 (15.0%)	2 (6.7%)	0.199
CHA2DS2-VASC score, mean $\pm$ SD	3.47 $\pm$ 1.35	3.73 $\pm$ 1.51	0.455
NYHA class, mean $\pm$ SD	2.70 $\pm$ 0.46	2.60 $\pm$ 0.49	0.390
Body mass index (kg/m ²), mean $\pm$ SD	28.44 $\pm$ 2.33	29.55 $\pm$ 2.48	0.060
Underlying heart disease			
Ischemic cardiomyopathy (n, %)	21 (52.5%)	17 (56.7%)	0.973
Nonischemic cardiomyopathy (n, %)	15 (37.5%)	10 (33.3%)	
Valvular cardiomyopathy (n, %)	4 (10.0%)	3 (10.0%)	
Duration of current episode of AF (months), median	4.0 (1-24)	4.0 (1-9)	0.952
History of previous electrical cardioversion (n, %)	11 (27.5%)	6 (20.0%)	0.539
Medical therapy			
β -blocker (n, %)	36 (90.0%)	27 (90.0%)	0.913
RAAS blockage (n, %)	36 (90.0%)	26 (86.7%)	0.636
Digoxin (n, %)	38 (95.0%)	26 (86.7%)	0.288
Diuretic (n, %)	36 (90.0%)	22 (73.3%)	0.057
Warfarin (n, %)	36 (90.0%)	25 (83.3%)	0.429
Antiplatelet drug (n, %)	2 (5.0%)	4 (13.3%)	0.288

Table 2. Echocardiographic and Laboratory Characteristics in the Study Population

Parameters	Internal Cardioversion	External Cardioversion	P Value
Left ventricle end-diastolic diameter (cm), mean $\pm$ SD	6.4 $\pm$ 0.7	5.9 $\pm$ 0.8	0.035
Left ventricular ejection fraction (%), mean $\pm$ SD	29.8 $\pm$ 4.7	29.2 $\pm$ 6.1	0.630
Left atrial volume index (mL/m ²), mean $\pm$ SD	51.6 $\pm$ 18.2	47.2 $\pm$ 6.4	0.767
Right atrial volume index (mL/m ²), mean $\pm$ SD	51.3 $\pm$ 11.9	45.2 $\pm$ 8.1	0.045
Mitral regurgitation, mean $\pm$ SD	2.0 $\pm$ 0.7	1.3 $\pm$ 0.6	0.001
Tricuspid regurgitation, mean $\pm$ SD	1.5 $\pm$ 0.8	1.0 $\pm$ 0.5	0.020
Pulmonary artery pressure (mmHg), mean $\pm$ SD	40.4 $\pm$ 11.3	38.5 $\pm$ 10.8	0.576

30 patients without ICD to external cardioversion groups. There were no significant differences between the 2 groups in age, male/female ratio, body mass index, underlying heart disease, New York Heart Association functional class, left ventricular ejection fraction, duration of the current episode of AF, history of previous electrical or pharmacological cardioversion, and time of first onset of AF in this study. However, it was observed that left ventricle end-diastolic diameter, right atrial volume index, mitral and tricuspid regurgitation were greater in internal cardioversion group than in external cardioversion group. The baseline characteristics, medications and echocardiographic features of both groups were demonstrated in Tables 1 and 2.

Results of Cardioversion

Sinus rhythm was restored in 32 of 40 patients (80.0%) assigned to internal cardioversion compared with 25 of 30 patients (83.3%) assigned to external cardioversion ($P = 0.725$). A successful cardioversion record obtained from ICD device was demonstrated in Figure 1. The first shock was successful in 25 of 32 patients (78.1%) in the internal cardioversion group, and in 21 of 25 patients (84%) in the external cardioversion group. This difference was not significant ($P = 0.355$). Internal cardioversion was unsuccessful in eight patients; while external cardioversion was effective in restoring sinus rhythm in three patients who failed by internal cardioversion. In the

Figure 1. A successful cardioversion record obtained from ICD device.

remaining five patients both internal and external cardioversion were ineffective among patients assigned to internal cardioversion. Transient sinus bradycardia and nodal rhythm occurred after internal cardioversion in four patients and external cardioversion in three patients. There were neither instances of persistent atrioventricular block nor requirement for transient pacing in patients without ICD device. In patients with ICD device, mean ventricular thresholds were 0.93 V (range: 0.5–2.0 V) before the cardioversion. After the procedure, values were not significantly changed over 24 hours (mean: 1.03, range: 0.5–2.5, $P = 0.107$). Battery status and lead impedance were also unchanged in all patients after the cardioversion.

Recurrences of Atrial Fibrillation

On the follow-up, 23 of 40 patients (57.5%) in the internal cardioversion group and 21 of 30 patients (70.0%) in the external cardioversion group remained in sinus rhythm ($P = 0.143$). There was no significant difference in the recurrence rate of AF between the 32 patients in whom sinus rhythm initially was restored by internal cardioversion and the 25 patients in whom sinus rhythm was restored by external cardioversion (Table 3). Kaplan–Meier analyses showed no statistically significant difference in recurrence of

atrial fibrillation between the internal and external cardioversion groups ($P = 0.274$) (Fig. 2).

Follow-Up

Through two years follow-up, 31 (44.3% of 70 patients) adverse events had occurred. In the follow-up, there were 3 (4.3%) deaths, 3 (4.3%) patient with nonfatal myocardial infarction, 4 (5.7%) patient with life-threatening arrhythmia, and 21 (30.0%) patients with hospitalization for heart failure (Table 3). Long-term outcomes were similar in the internal cardioversion group compared with the external cardioversion group. Kaplan–Meier analyses showed no statistically significant difference in freedom from adverse events between the internal and external cardioversion groups ($P = 0.751$) (Fig. 3).

DISCUSSION

Our study demonstrated that internal cardioversion with ICD device had a similar efficacy in converting AF to sinus rhythm when compared to classical external cardioversion. As a result, it can be performed safely and efficiently in heart failure patients with ICD.

Heart failure has been shown to be associated with an increased risk to develop several supraventricular arrhythmias. Augmented atrial load, atrial

Table 3. Results of Cardioversion and Follow-Up

Parameters	Internal Cardioversion (n = 40)	External Cardioversion (n = 30)	P Value
Successful cardioversion, n (%)	32 (80.0%)	25 (83.3%)	0.584
First successful cardioversion, n (%)	25 (62.5%)	21 (70.0%)	0.355
Sinus rhythm on follow-up, n (%)	23 (57.5%)	21 (70.0%)	0.143
AF recurrence time, months (median)	6.5 (1–22)	6.2 (2–28)	0.824
Major adverse cardiac events			0.131
Death, n (%)	3 (7.5%)	0	
Nonfatal myocardial infarction, n (%)	1 (2.5%)	2 (4.0%)	
Life-threatening arrhythmias, n (%)	4 (10.0%)	0	
Hospitalization for heart failure, n (%)	5 (29.4%)	9 (30.0%)

Figure 2. Proportion of patients remaining in sinus rhythm after successful internal cardioversion (23 patients) and external cardioversion (21 patients). Kaplan–Meier analyses showed no statistically significant difference in recurrence of atrial fibrillation between two groups ($P = 0.274$).

dilatation, local conduction disturbances, and some degree of atrial fibrosis are important key factors to create a substrate of atrial tachyarrhythmias.¹² In all atrial tachyarrhythmias, AF is the most common sustained cardiac arrhythmia. An excessive ventricular rate, loss of atrial contraction, and an irregular ventricular filling time increase the risk for progressive ventricular dysfunction. As a consequence, AF can lead to heart failure, and heart failure can lead to AF.¹³ In patients with

Figure 3. Kaplan–Meier analysis demonstrating no statistically significant difference in major adverse cardiac events between internal and external cardioversion groups ($P = 0.751$).

AF and heart failure, rhythm control has been presumed to be advantageous. Although several trials did not support a routine strategy of rhythm control in patients with AF, this was based on the following theoretical benefits of sinus rhythm over AF: (i) regulation of the ventricular rate improves hemodynamics, (ii) atrial contractile function is restored, (iii) tachycardiomyopathy is prevented or reversed, and (iv) functional status and quality of life improves.¹⁴

ICD implantation rates are growing rapidly both for primary and secondary prevention of sudden cardiac death in patients with heart

failure.¹⁵ Consequently, a significant proportion of patients with heart failure and ICD present with atrial arrhythmias. Termination of atrial arrhythmias by means of external cardioversion is indicated in many patients with ICD device. It was discovered that lower energy with biphasic shocks was a safe choice for atrial arrhythmia termination in patients with implanted pacemaker or cardioverter-defibrillator systems.¹⁶ Although a prospective study suggested that external cardioversion in patients with AF and implanted cardiac devices may be safe and effective, several cases of interaction between pacemaker systems and external cardioversion procedures have been reported resulting in device failure.¹⁷⁻¹⁹ Studies evaluating the underlying mechanism indicated that the electrical current cause thermal burn at the electrode-endocardial interface.²⁰

Previously, it was demonstrated that low-energy internal cardioversion with electrodes placed on right atrium and coronary sinus was a useful means of restoring sinus rhythm in patients with AF refractory to external cardioversion.²¹ In another study, it was found that shocks delivered to the thorax in conventional fashion were not effective in restoring sinus rhythm, an attempt at internal cardioversion might be appropriate.²² Our findings suggested that, conversion to sinus rhythm could be achieved with using an easier method by using the implanted device. Furthermore, internal cardioversion with ICD device can decrease necessary energy level to convert atrial arrhythmias to sinus rhythm. Shock energy required for AF termination was significantly lower with internal cardioversion than external cardioversion (35 J vs 200 J). It is anticipated that low energy delivered by the internal cardioversion can reduce the risk for interference with the ICD programming as well as the risk for endocardial damage. In addition to the obviating the need for an extensive anesthesia, this method was less time consuming and clearly associated with lesser pain; therefore increasing the patient comfort by means of a similar safety and efficacy with the conventional method.

Despite our promising results, our study had some limitations. First, the main limitation of our study was the small number of patients. Second, patients were not randomized to receive cardioversion in our cross-sectional study. Third, we did not evaluate optimal energy level and maximal provided energy by the device had been used to convert AF to sinus rhythm. As a

result, further studies are needed to determine optimal cardioversion threshold. Finally, we did not evaluated level of myocardial damage in both groups. However, according to several studies, it is anticipated that low energy levels with internal cardioversion cause lesser myocardial damage than with external cardioversion.^{23,24}

CONCLUSION

According to our results, internal cardioversion was an effective and safe method to restore sinus rhythm in patients with heart failure and ICD device. In addition, the procedure which reduced the risk for endocardial damage and obviated the need for deep anesthesia can be performed easily in clinical practice.

DISCLOSURES

On behalf of all the authors, the corresponding author states that there are no conflicts of interest.

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