Left Ventricular Ejection Fraction Predicts Severity of Posttraumatic Stress Disorder in Patients With Implantable Cardioverter-Defibrillators

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ABSTRACT

Background: Implantable cardioverter-defibrillators (ICD) have provided effective therapy for fatal arrhythmia. However, ICD patients are known to develop psychological problems, such as posttraumatic stress disorder (PTSD), if they have experienced potentially fatal arrhythmia and ICD shocks. Little is known about the factors influencing PTSD in ICD patients.

Hypothesis: Echocardiographic cardiac-function parameters might relate to psychological problems, especially PTSD, in ICD patients.

Methods: A total of 128 outpatients with ICD implantation completed the Impact of Event Scale Revised (IES-R) questionnaire as a measurement of PTSD. Demographic and clinical characteristic data were collected from medical records.

Results: The mean age of the ICD patients was 59 ± 16 years; 103 were male; and the mean left ventricular ejection fraction (LVEF) by echocardiography was $52.4\% \pm 18.3\%$. In the ICD patients, female sex and impaired LVEF were related to lower IES-R scores or led to PTSD ($P = 0.01$ and $P = 0.03$, respectively). Impaired LVEF also worsened 2 symptoms of PTSD, intrusion ($P = 0.02$) and hyperarousal ($P = 0.03$). In patients with LVEF $<35\%$, there was a significant negative correlation between LVEF level and IES-R score ($P = 0.045$).

Conclusions: This study showed that LVEF was related to the severity of PTSD, especially in the ICD patients with LVEF of $<35\%$. We should pay more attention to ICD patients with severely impaired left ventricular function to prevent psychological problems.

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Introduction

Implantable cardioverter-defibrillator (ICD) therapy is well established as an effective treatment for sudden cardiac death (SCD) in patients with fatal arrhythmia, and $>20\%$ of patients with coronary arterial diseases and congestive heart failure (CHF) undergo ICD implantation.^{1–3} Previous studies reported that 10% to 46% of ICD patients developed psychological problems, especially in the patients who recovered after SCD and experienced frequent ICD shocks

and/or inappropriate ICD shocks.^{4–6} Contributing factors for psychological problems in ICD patients were reported as female sex and age.^{7–9} These psychological problems might adversely affect the quality of life and increase mortality in ICD patients.^{10,11} However, limited data exist regarding influential factors on posttraumatic stress disorder (PTSD) in ICD patients, especially the influence of cardiac function. It was well known that left ventricular ejection fraction (LVEF) measured by echocardiography relates the severity of CHF and prognosis of patients with CHF.¹² Decreasing LVEF and severity of CHF based on the New York Heart Association (NYHA) functional class have also increased rates of depression in patients with myocardial infarction and CHF.^{13,14}

The aim of this study was to investigate the relationships between LVEF and psychological problems, especially PTSD, in the patients with ICD implantation.

Methods

Subjects

We recruited 179 consecutive outpatients with ICD implantation based on our previous study.⁹ The inclusion criteria were as follows: patients who (1) had undergone ICD implantation, (2) were age >18 years, (3) were judged capable of completing the survey physically and cognitively, and (4) were capable of understanding spoken and written Japanese. This study was approved by the Ethics Committee of the Kyushu University Graduate School of Medical Sciences and the Tokyo Metropolitan Hiroo Hospital (institutional review board approval number 258; approval date July 6, 2005). Written informed consent was obtained from all subjects before participation.

Measurements

This study was a cross-sectional multicenter study. We acquired demographic variables and clinical data from medical records. The obtained data included age, sex, purpose of ICD implantation (ie, primary or secondary prevention of fatal arrhythmias), frequency of fatal arrhythmia attacks, duration of ICD implantation, history of inappropriate shocks and CHF, echocardiographic data, predominant underlying heart diseases, targeted arrhythmias of ICD, and medications. Primary prevention of fatal arrhythmias refers to the use of ICD in patients who are at risk for, but have not yet had, an episode of sustained ventricular tachycardia (SVT), ventricular fibrillation (VF), or resuscitated cardiac arrest. Secondary prevention refers to prevention of fatal arrhythmias in patients who survived a prior SCD or SVT.

Posttraumatic stress disorder caused after distressing experiences such as fatal arrhythmias and/or ICD shocks was assessed using the Impact of Event Scale-Revised (IES-R) questionnaire.¹⁵ The IES-R consists of 22 questions with responses rated on a scale from 0 (not at all) to 4 (extremely), with respect to how distressing each item has been during the past week. Scale scores are calculated from 3 subscales, which reflect intrusion (8 items), avoidance (8 items), and hyperarousal (6 items) and show a high degree of intercorrelation.¹⁶ Good internal consistency and test-retest

values have been reported with the Japanese translation of the IES-R.¹⁷ The scoring of the IES-R questionnaire ranges from 0 to 88 points, and a cutoff value of ≥ 20 was used to indicate clinically significant levels of PTSD.¹⁸ The patients with ICD filled out the IES-R questionnaires in the outpatient ward, and well-trained nurses, who were blinded to the outcome of the questionnaire, supported the patients if they needed to help to complete the questionnaires.

Statistical Analysis

We assessed the Gaussian distribution of the data using a Kolmogorov-Smirnov test. In the independent samples, the *t* test, Mann-Whitney *U* test, and χ^2 test were used for assessing the differences of clinical characteristics between 2 groups. We used univariable analysis and multiple regression analysis to assess the relationships between clinical data and severity of PTSD, including its subscales. If the *P* value was <0.10 in univariable analysis, we regarded this variable as a confounder. The identified confounder was included in the multivariable regression analysis for adjustments. We also calculated the Pearson correlation coefficient and Spearman rank-order correlation between IES-R score and LVEF. All statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL). Results were presented as mean $\pm$ SD, number (percentage), correlation coefficient (*r*), or standardizing coefficient (β). A *P* value of <0.05 was considered significant, and a 2-sided test was used.

Results

Patient Characteristics

Fifty-one patients were excluded from the analyses. Twenty-one of 51 patients were the patients of the primary prevention. Nineteen of the 21 patients had no experiences of fatal arrhythmias nor inappropriate shocks by ICD, and thus they were excluded. The other 2 patients answered the IES-R questionnaire incompletely. In 30 patients with the secondary prevention, 28 patients answered the IES-R questionnaire incompletely and 2 patients were not measured with echocardiography. Finally, a total of 128 patients with ICD participated in this study.

Table 1 shows the clinical characteristics of the ICD patients. The mean age was 59 ± 16 years; 103 were male; and the mean duration of ICD implantation was 55 ± 41 months. Thirty-eight (29.7%) and 32 (25.0%) patients with an ICD had a history of inappropriate ICD shocks and CHF, respectively. The mean LVEF was $52.4\% \pm 18.3\%$. Ischemic heart disease was the most prevalent underlying heart disease, and VF was the most prevalent type of arrhythmia.

Posttraumatic Stress Disorder Measured by the Impact of Event Scale Revised Questionnaire

The mean IES-R score was 16.4 ± 17.4 points, and the average subscores were as follows: intrusion, 5.5 ± 6.8 ; avoidance, 6.5 ± 6.9 ; and hyperarousal, 4.4 ± 5.1 . We compared the clinical characteristics between 2 groups (higher and lower groups) divided by the median IES-R score (10.0 points; Table 2). Significant differences were observed in sex (*P* = 0.002) but not in other characteristics. With respect

Table 1. Clinical Characteristics (N = 128)

Characteristics	Value
Age, y	59 ± 16
Male sex	103 (80.5)
Primary prevention	31 (24.2)
Frequency of attacks, n	1.6 ± 1.5
Duration of ICD implantation, mo	55 ± 41
History of inappropriate shocks	38 (29.7)
CHF	32 (25.0)
LVEF, %	52.4 ± 18.3
Underlying heart disease	
Ischemic heart disease	50 (39.1)
Cardiomyopathy	29 (22.7)
Brugada syndrome	22 (17.2)
None	8 (6.3)
Valvular disease	4 (3.1)
Others	15 (11.7)
History of arrhythmia	
VF	50 (39.1)
SVT	43 (33.6)
NSVT	19 (14.8)
Arrhythmia with syncope	9 (7.0)
Torsade de pointes	7 (5.5)
Medication	
Anticoagulant	62 (48.4)
β-Blocker	50 (39.1)
Diuretic	50 (39.1)
ARB	37 (28.9)
Ca channel antagonist	36 (28.1)
Warfarin	33 (25.8)
ACEI	22 (17.2)
Digitalis	4 (3.1)

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; Ca, calcium; CHF, congestive heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; NSVT, nonsustained ventricular tachycardia; SVT, sustained ventricular tachycardia; VF, ventricular fibrillation.
Data are presented as n (%) unless otherwise noted.

Table 2. Clinical Characteristics in the Patients Stratified by Median of IES-R Score

IES-R Groups	Higher	Lower	P Value
IES-R score, points	28.3 ± 17.0	3.7 ± 2.6	<0.001
Intrusion	9.9 ± 7.2	0.9 ± 1.1	<0.001
Avoidance	11.0 ± 6.8	1.6 ± 1.9	<0.001
Hyperarousal	7.5 ± 5.4	1.1 ± 1.2	<0.001
N	66	62	—
Age, y	56.7 ± 16.9	61.1 ± 15.9	0.14
Male sex	46 (69.7)	57 (91.9)	0.002
Primary prevention	18 (27.3)	13 (21.0)	0.42
Frequency of attacks, n	1.5 ± 1.3	1.7 ± 1.7	0.86
Duration of ICD implantation, mo	57.7 ± 44.4	52.2 ± 36.3	0.45
History of inappropriate shock	20 (30.8)	18 (29.0)	0.50
CHF	16 (24.2)	16 (25.8)	1.00
LVEF, %	52.4 ± 20.5	52.4 ± 15.6	0.80
History of arrhythmia			
VF	26 (39.4)	24 (38.7)	
SVT	19 (28.8)	24 (38.7)	
NSVT	12 (18.2)	7 (11.3)	
Arrhythmia with syncope	6 (9.1)	3 (4.8)	
Torsade de pointes	3 (4.5)	4 (6.5)	0.56
Medication			
Anticoagulant	31 (47.0)	31 (50.0)	0.86
β-Blocker	25 (37.9)	25 (40.3)	0.86
Diuretic	28 (42.4)	22 (35.5)	0.47
ARB	15 (22.7)	22 (35.5)	0.12
Ca channel antagonist	17 (25.8)	19 (30.6)	0.56
Warfarin	16 (24.2)	17 (27.4)	0.69
ACEI	11 (16.7)	11 (17.7)	1.00
Digitalis	3 (4.5)	1 (1.6)	0.62

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; Ca, calcium; CHF, congestive heart failure; ICD, implantable cardioverter-defibrillator; IES-R, Impact of Event Scale Revised questionnaire; LVEF, left ventricular ejection fraction; NSVT, nonsustained ventricular tachycardia; SVT, sustained ventricular tachycardia; VF, ventricular fibrillation.

Data are presented as n (%) unless otherwise noted.

to the patients with primary and secondary prevention, there were no significant differences in IES-R score (primary, 21.2 ± 21.4 points, vs secondary, 14.8 ± 15.8 points; $P = 0.20$).

As shown in Table 3, the IES-R scores significantly related to female sex ($\beta = 0.21$, $P = 0.02$) and LVEF ($\beta = -0.18$, $P = 0.048$). Neither primary prevention, duration of diagnosis of

arrhythmia and ICD implantation, history of inappropriate shock, nor CHF related to IES-R scores. With regard to the factors affecting the symptoms of PTSD, female sex related significantly to severe intrusion ($\beta = 0.22$, $P = 0.01$) and avoidance ($\beta = 0.21$, $P = 0.02$) and tended to relate with the severity of hyperarousal ($\beta = 0.15$, $P = 0.099$); and primary prevention significantly related to intrusion ($\beta =$

Table 3. Predictors for Worsening of PTSD Estimated by Univariable Analysis

Variable	Subscales							
	IES-R		Intrusion		Avoidance		Hyperarousal	
	β	<i>P</i> Value	β	<i>P</i> Value	β	<i>P</i> Value	β	<i>P</i> Value
Age	0.02	0.82	−0.02	0.84	0.00	0.97	0.09	0.33
Female sex	0.21	0.02	0.22	0.01	0.21	0.02	0.15	0.099
Primary prevention	0.15	0.08	0.21	0.02	0.12	0.17	0.10	0.29
Frequency of attacks	0.01	0.91	0.04	0.73	−0.02	0.82	0.02	0.82
Duration of ICD implantation	−0.01	0.87	−0.05	0.55	0.01	0.93	0.01	0.89
History of inappropriate shock	−0.04	0.63	−0.05	0.57	−0.03	0.71	−0.04	0.70
CHF	0.06	0.52	0.06	0.51	−0.05	0.61	0.18	0.045
LVEF	−0.18	0.048	−0.19	0.03	−0.09	0.34	−0.23	0.009

Abbreviations: CHF, congestive heart failure; ICD, implantable cardioverter-defibrillator; IES-R, Impact of Event Scale Revised questionnaire; LVEF, left ventricular ejection fraction; PTSD, posttraumatic stress disorder.

Table 4. Predictors for Worsening of PTSD Estimated by Multiple Regression Analysis

Variable	Subscales							
	IES-R		Intrusion		Avoidance		Hyperarousal	
	β	<i>P</i> Value	β	<i>P</i> Value	β	<i>P</i> Value	β	<i>P</i> Value
Female sex	0.22	0.01	0.23	0.008	0.21	0.02	0.17	0.056
Primary prevention	0.14	0.10	0.19	0.03	—	—	—	—
CHF	—	—	—	—	—	—	0.10	0.29
LVEF	−0.19	0.03	−0.20	0.02	—	—	−0.21	0.03

Abbreviations: CHF, congestive heart failure; IES-R, Impact of Event Scale Revised questionnaire; LVEF, left ventricular ejection fraction; PTSD, posttraumatic stress disorder.

0.21, $P = 0.02$). Complication of CHF significantly related to severity of hyperarousal ($\beta = 0.18$, $P = 0.045$). Moreover, decreasing LVEF significantly related to the severity of intrusion ($\beta = -0.19$, $P = 0.03$) and hyperarousal ($\beta = -0.23$, $P = 0.009$). When adjusted for confounding factors, as shown in Table 4, female sex related to IES-R scores ($\beta = 0.22$, $P = 0.01$), greater severity of intrusion ($\beta = 0.23$, $P = 0.008$), and avoidance ($\beta = 0.21$, $P = 0.02$) and tended to relate to the severity of hyperarousal ($\beta = 0.17$, $P = 0.056$); and primary prevention significantly related to the severity of intrusion ($\beta = 0.19$, $P = 0.03$). Interestingly, LVEF levels were significantly related to IES-R scores ($\beta = -0.19$, $P = 0.03$), greater severity of intrusion ($\beta = -0.20$, $P = 0.02$), and hyperarousal ($\beta = -0.21$, $P = 0.03$). However, the complication of CHF did not relate to severity of hyperarousal after the adjustment. Then, we examined the correlation between LVEF levels and IES-R scores. There was a significant negative correlation between LVEF levels and IES-R scores ($r = -0.36$, $P = 0.045$) in the patients with LVEF <35% (Figure 1).

Discussion

This study showed that impairment of left ventricular function in terms of decreased LVEF related to subjective distress caused by traumatic events such as history of SCD and/or near-fatal arrhythmias and inappropriate and/or appropriate shocks by ICD (i.e., PTSD) and its symptoms. The patients with decreased LVEF should be followed up carefully for potential psychological problems, in addition to female patients and those with complications of CHF.^{8,9} There are some underlying mechanisms indicating that impaired cardiac function increases the severity of PTSD in ICD patients. One previous study reported that physical disability and performance assessed by the Short Physical Performance Battery test were related to severity of PTSD.¹⁹ Limited physical activity also existed in ICD patients with impaired cardiac function due to skeletal-muscle hypoperfusion and resulted in the worsening of PTSD in ICD patients with low LVEF levels.²⁰ Other possible underlying mechanisms were impaired central nervous system (CNS) caused by impaired cardiac function. It has been reported that patients with PTSD have a structural organic brain abnormality, particularly in the hippocampus, which regulates psychological stress.^{21–23} A meta-analysis also reported that the severity of PTSD increased with a reduction of hippocampal volume.²⁴ Because impaired cardiac function was reported to relate to the circulatory system (including cerebral perfusion),^{25,26} we consider that the ICD patients with impaired cardiac function also have CNS hypoperfusion, which is one of the causes of cerebral atrophy.^{27,28} In addition, previous magnetic resonance imaging studies have reported that the hippocampus, frontal cortex, and insular cortex were injured in patients with severe cardiac dysfunction.^{29,30} These reports concluded that brain hypoperfusion caused by impaired cardiac function was a critical factor resulting in temporal lobe and cerebral dysfunction. Based on these reports, the ICD patients with impaired cardiac function might develop more psychological problems because of brain atrophy caused by CNS hypoperfusion.

Figure 1. Correlation between LVEF and IES-R scores in patients with ICD, showing (A) patients with LVEF <35%, (B) patients with LVEF 35%–49%, and (C) patients with LVEF ≥50%. Abbreviations: ICD, implantable cardioverter-defibrillator; IES-R, Impact of Event Scale Revised questionnaire; LVEF, left ventricular ejection fraction.

Early intervention in patients with ICD implantation might reduce psychological problems. It has been reported that early recognition and intervention prevented psychological problems in ICD patients.³¹ An educational psychology-based telephone intervention program delivered by expert cardiovascular nurses within the first 8 weeks after ICD implantation had a significant and sustained influence on physical and psychosocial outcomes at 6 and 12 months.³¹ The authors concluded that the intervention programs for

ICD recipients should be implemented after hospitalization, addressing both physical and psychological problems and including both information and skill acquisition. Kohn et al also reported that cognitive behavioral therapy was associated with decreased depression, decreased anxiety, and increased adjustment for ICD recipients, particularly among those patients receiving shocks.³¹ One psychoeducational intervention reduced anxiety and depressive symptoms early after ICD implantation, lowered the probability of depressive symptoms at 1 year, and decreased disability days and calls to providers.³¹ Our results showed that the characteristics of female sex and low LVEF levels (especially LVEF <35%) were useful indicators for early recognition of psychological problems.

Study Limitations

There were some limitations in this study. First, we did not examine the personalities of the ICD patients. It has been reported that the type D personality has a significant effect on psychological problems.³² Second, 80.5% of patients with an ICD in this study were male. We could not deny that there was selection bias in this study, but we believe that the differences of these patients (ie, age and frequency of shocks) did not confound the outcome in this study because the characteristics did not affect the IES-R score. The present study was not a case-control study, but it was a natural distribution of ICD patients. Third, we could not obtain echocardiographic data and IES-R questionnaire scores on the same date. There was a time discrepancy of up to 1 month between LVEF testing and IES-R questionnaire administration in this study. Finally, the ICD patients with lower LVEF were more medicated with β -blockers, warfarin, anticoagulants, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and diuretics than those with a higher LVEF (data not shown). We could not deny potential psychological adverse effects of those medicines, but we did not include the regression analysis in this study because the medications, such as β -blockers and diuretics, show multicollinearity to the cardiac function, which distorts the outcome.

Conclusion

Levels of LVEF were a useful predictor of the severity of PTSD, especially in ICD patients with LVEF <35%. We should focus more on ICD patients with severely impaired left ventricular function to control psychological problems. The ICD patients may benefit physically and psychologically from improvement of cardiac function, as measured by echocardiography (ie, LVEF). We believe their quality of life would improve through interventions aimed to increase cardiac function.

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