ONLINE FIRST

CARDIOLOGY JOURNAL

ISSN: 1897-5593

e-ISSN: 1898-018X

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DOI: 10.5603/cj.101837

Article type: Original Article

Submitted: 2024-07-31

Accepted: 2024-11-27

Published online: 2024-12-20

ORIGINAL ARTICLE

The impact of shock therapy on depression development and remote prognosis in cardiac resynchronization therapy recipients

Running title: **The impact of shock therapy on depression development**

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DOI:

10.5603/cj.101837

Date submitted:

31.07.2024

Date accepted:

27.11.2024

Abstract

Background: The aim of this study was to assess the incidence and clinical significance of depression in patients with cardiac resynchronization therapy with an implantable cardioverter-defibrillator (CRT-D). The study was also to evaluate the impact of shock therapy on depression development and long-term prognosis.

Methods: The prospective study encompassed 396 consecutive heart failure (HF) patients implanted with CRT-D. All patients completed the Beck Depression Inventory (BDI-II) and underwent a psychiatric examination at baseline. 221 patients free of depressive symptoms at baseline were included into the final analysis. The assessment of psychiatric status was routinely repeated every 6 months as well as after the shock delivery. The primary outcome was a composite endpoint of death or hospitalization for HF.

Results: During long-term observation (median 37.1 months) 52 (23.5%) patients suffered from an implantable cardioverter-defibrillator (ICD) shock, whereas 48 (21.8%) subjects developed depression. The incidence of new-onset depression was significantly higher in patients after shock delivery (Shock Group), CRT non-responders and subjects with atrial fibrillation. The risk for a composite endpoint was higher in the Shock Group than subjects without an ICD intervention: 57.7% vs. 25.4% and in patients with new-onset depression compared to the population free of this disorder: 62.5% vs. 24.9% (all $p < 0.001$). New-onset depression (HR 1.7) and an ICD shock (HR 2.1) were strong independent predictors of poor prognosis.

Conclusions: Depression is a common mental disorder in CRT-D recipients, that adversely affects long-term prognosis. Subjects suffering from ICD shocks and those with HF progression are at higher risk of experiencing depressive symptoms.

Keywords: depression, chronic heart failure, resynchronization therapy, implantable cardioverter-defibrillator, shock therapy

Introduction

Chronic heart failure (HF) is associated with a significantly increased prevalence of depression, anxiety and other mood disorders [1–4]. It is estimated that around 30–40% of HF patients are burdened with a concomitant depressive syndrome, and the severity of HF symptoms is associated with higher probability of development of mood disorders [2, 5]. According to previous studies, depression may deteriorate HF symptoms leading to even a 3-fold increase in mortality [6–9]. However, there are very poor data concerning the incidence of new-onset depression in patients with severe HF who were implanted with a cardiac resynchronization therapy defibrillator (CRT-D).

The beneficial effect of an implantable cardioverter-defibrillator (ICD) therapy on reducing the risk of sudden cardiac death (SCD) in patients with HF and significantly reduced left ventricular ejection fraction (LVEF) is incontrovertible [10, 11]. However, ICD shocks have also been reported to be associated with the increased mortality [12, 13]. Additionally, ICD interventions may potentiate psychological distress, impair daily activities and lead to reduced quality of life [14, 15]. Whereas, there are poor and conflicting data on the impact of ICD shocks on the development or deterioration of pre-existing depression [16, 17].

Therefore, the primary aim of this study was to assess the incidence and clinical significance of depression that developed in CRT-D recipients. The secondary aim was to evaluate the impact of ICD shocks on depression development and long-term prognosis.

Methods

A single-center, prospective, non-randomized study was conducted at the Department of Cardiology, Congenital Heart Diseases and Electrotherapy of the Silesian Center of Heart

Diseases (Zabrze, Poland). From January 2012 to December 2018 every HF patient admitted for the first-time CRT-D implantation was screened for potential participation in the study.

The inclusion criteria were as follows:

1) a first-time CRT-D implantation according to the guidelines of the European Society of Cardiology [18,19]
2) age range of 18-80 years
3) signed informed consent

The exclusion criteria encompassed:

1) simultaneous participation in other clinical studies
2) a prior stroke or head injury with severe neurological deficit
3) epilepsy
4) Parkinson's disease
5) dementia, amnesic syndrome, delusional disorders or hallucinations
6) alcohol or drug abuse
7) already diagnosed (pre-existing) recurrent depressive or bipolar disorders
8) schizophrenia
9) inability to undertake follow-up (FU) visits

Out of 396 consecutive CRT-D patients recruited into the study as many as 233 subjects free of depression symptoms were eligible for further analysis. Among them 12 patients did not complete any FU visits (2 died before the first visit whereas 10 subjects were lost to FU), hence, 221 patients were included into the final analysis. Patients who experienced *de novo* depressive symptoms during long-term observation comprised the Depression Group, while the rest of the patients constituted the Depression-free Group. Moreover, the whole population was divided on account of an ICD shock — subjects who suffered from shock therapy were included into the Shock Group, whereas the others represented the Control Group.

Prior to CRT-D implantation, all patients had undergone a two-stage psychiatric evaluation. In addition to a psychiatric examination by one of two experienced psychiatrists (study co-investigators), every patient had to complete two self-report questionnaires: the Beck Depression Inventory (BDI) and the EQ-5D scale. The EQ-5D scale is a standardized measure of health status, consisting of the descriptive system and visual analogue scale. The EQ-5D descriptive system assesses five domains: self-care, mobility, usual activities, pain/discomfort and anxiety/depression. There are 3 statements concerning every domain and a patient is to indicate the most appropriate one in each of the 5 domains. Whereas the EQ-5D visual scale records a patient's self-rated health on an analogue scale (range from 0 – the worst imaginable health state, to 100 – the best imaginable health state). The BDI includes 21 questions concerning a patient's mental state during the previous week — a patient is to indicate one of four answers (range from 0 to 3) for each question.

Additionally, all patients underwent clinical assessment, including physical examination, 12-lead electrocardiogram (ECG) and transthoracic echocardiography (TTE) at enrollment.

Depression was diagnosed according to the criteria of the Diagnostics and Statistical Manual of Mental Disorders (DSM-IV) [20].

Routine follow-up visits were performed at 3 (± 1 week), 6 (± 2 weeks) and 12 months (± 2 weeks) after the procedure, and every 6 months (± 2 weeks) thereafter. The median follow-up was 37.1 months (range: 3.2–79.4 months). Every follow-up visit consisted of a history taken with NYHA (New York Heart Association) class re-assessment, physical examination and device check-up — data concerning CRT-D functioning, including pacing thresholds, occurrence of ventricular/supraventricular tachycardia, antitachycardia pacing or appropriate/inappropriate shocks were obtained during a device interrogation. Psychiatric evaluation including questionnaire completion was repeated during every follow-up visit.

Additionally, a standard transthoracic echocardiogram (TTE) was repeated at 12-month follow-up visit.

The primary endpoint was a major adverse cardiac event (MACE), defined as a composite of hospitalization for decompensated HF and all-cause mortality. Data on potential MACEs were collected during scheduled visits, *via* telephone calls from patients or their relatives, from hospital records and death certificates, as well as from records obtained from the insurer — the National Health Fund. The secondary endpoint was defined as the development of depression in patients with no history of depressive symptoms before the study enrollment.

Patients were considered to be CRT responders if a decrease of at least 1 NYHA class (clinical response) was observed or an increase in left ventricular ejection fraction (LVEF) of more than 5% (echocardiographic response) was documented 12 months after a CRT-D implantation.

Categorical variables were expressed as number and percentage, whereas continuous parameters as mean ± standard deviation (SD). The comparative analysis between groups was performed with the Student t-test for continuous parameters, and the Chi-square or Fisher exact test, as appropriate, were used for dichotomous variables. The independent MACE predictors were identified with the multivariate Cox-regression model and expressed as hazard ratio (HR) with 95% confidence interval (CI). All parameters which differed significantly between patients who developed MACE and those free of MACE were considered covariates in the multivariate analysis. Cumulative proportions of patients free of MACE were plotted as Kaplan-Meier survival curves and compared with log-rank tests between different categories. P value < 0.05 was considered statistically significant. The software package Statistica (version 13.1, StatSoft Inc., Tulsa, OK, USA) was used for statistical analysis.

The Medical Ethics Committee of the Silesian Medical University approved the study protocol. The study was conducted according to the ethical guidelines of the Declaration of Helsinki.

Device settings

Pacing and antiarrhythmic settings of CRT devices were programmed identically in all patients. Pacemakers were set into DDD mode (except for patients with permanent atrial fibrillation [AF]) with a lower pacing rate of 50 beats per minute (bpm). Two detection zones were programmed for ventricular arrhythmias: ventricular tachycardia zone (VT > 170bpm) and ventricular fibrillation zone (VF > 214bpm). Pre-discharge settings were maintained throughout the whole follow-up period and no routine reprogramming was allowed unless clear indications occurred (for example: low CRT pacing or inappropriate ICD therapies due to AF).

Results

During long-term observation 52 (23.5%) patients had at least one high-energy ICD intervention. The incidence of AF was the only parameter that differed significantly between subjects from the Shock Group and those free of shock therapy: 59.6% vs. 41.4%, respectively ($p < 0.05$). Among 221 patients free of depression symptoms at baseline 48 (21.8%) developed depressive symptoms during long-term follow-up. The rate of new-onset depression was significantly higher in patients with AF, poorer CRT response and those with an increase of at least 1 NYHA class (all $p < 0.05$). Moreover, the risk of depression was increased 5-fold in subjects after an ICD shock compared to the population free of high-energy intervention ($p < 0.001$). The baseline characteristics of these groups were summarized in Tables 1 and 2.

According to the multivariate analysis only an ICD shock (HR 3.4) and increase in NYHA class by at least one class (HR 1.9) were independent predictors of depression development.

Patients who experienced MACE during long-term observation had significantly lower LVEF, higher NYHA class and were more often burdened with AF in comparison with patients free of MACE (all $p < 0.05$). Moreover, an ICD shock and new-onset depression were associated with significantly higher risk of MACE (both $p < 0.001$). Additionally, poorer prognosis was more likely in CRT non-responders and patients with severe mitral regurgitation (MR) (all $p < 0.05$). The baseline characteristics of these groups are shown in Table 3.

The risk for a composite endpoint was significantly higher in the Shock Group than in the Control Group: 57.7% vs. 25.4% ($p < 0.001$), as well as in patients with new-onset depression compared to the population free of this disorder: 62.5% vs. 24.9% ($p < 0.001$). However, the incidence of MACE was the highest in patients from the Shock Group with concomitant depression, as it was nearly a 3-fold increase in comparison with subjects from the Control Group: 70.0% vs. 25.4% ($p < 0.001$), and over a 3-fold increase when compared to patients free of an ICD shock and depression: 70.0% vs. 22.5%, respectively ($p < 0.001$). The data on clinical outcomes were presented in Tables 4 and 5 as well as in Figure 1.

The multivariate analysis demonstrated that an ICD shock (HR = 2.1), severe MR (HR = 1.8), new-onset depression (HR = 1.7) and AF (HR = 1.3) were the independent predictors for a composite endpoint in the analyzed population. The results of multivariate analysis are presented in Table 6.

Discussion

The main findings of the present study can be summarized as follows. Firstly, it was shown that depression is a common clinical problem amongst HF patients receiving CRT-D. Secondly, patients experiencing an ICD shock therapy are at the highest risk of depression

development. Thirdly, both depression and shock therapy portend significantly worse prognosis in CRT recipients.

It was demonstrated that over 20% of CRT-D recipients suffer from new-onset depression after a device implantation. According to available research the current study is the first to assess the prevalence of new-onset depression in a CRT-D population. The vast majority of published studies reported the incidence of depression in HF population at the moment of an ICD/CRT-D implantation or irrespectively of the presence of a high-energy device, whereas findings herein strictly concern patients with no history of depression before a CRT-D implantation [2, 3, 5, 21]. Moreover, it is of great importance, that the diagnosed depression was in a two-step protocol – first, a self-reported patient questionnaire was to be completed and secondly the diagnosis was further verified clinically by a psychiatrist, whereas the majority of previous studies used a self-reported survey as the only diagnostic tool for depression diagnosis [15, 21]. Owing to this, the present results seem to be more precise, as the prevalence of depression might be stacked when it is assessed only on the basis of self-reported tests [5]. According to previous data depression affects between 20% and 65% HF patients [2, 3, 5, 21]. The present results are mainly consistent with these reports, however they are closer to the upper threshold, as apart from 163 (41.2%) already depressed patients not included into the study, newly diagnosed depressive syndrome was indicated in 48 (12.1% of the whole population) patients after a device implantation. The high risk of depression development in patients with severe HF should not be surprising, as symptomatic HF was reported to be the single most important clinical correlate of depression and anxiety [22]. Moreover, higher NYHA class is associated with worse psychological functioning and impaired quality of life (QoL) [4,21]. Additionally, ICD\CRT-D recipients may have some concerns about the risk of receiving an unexpected shock therapy or device-related social and professional restrictions, that might increase psychological distress [14, 22].

There are conflicting data on the impact of ICD shocks on depression development. Luyster et al. reported that a high-energy ICD therapy, apart from poor social support and worse physical functioning, were associated with significantly higher risk of depression [23]. The consistent results were provided by Johansen et al. as they demonstrated a strong impact of ICD shocks on depression and anxiety development. They also found symptomatic HF to be the most powerful predictor of psychological distress in ICD recipients [22]. Moreover, Jacq et al. observed that the risk of depressive symptoms correlated significantly with the number of shocks [24]. On the contrary, no association between ICD shocks and depressive symptoms was observed in a prospective study including 308 ICD recipients [25]. In addition, Pedersen et al., demonstrated that symptomatic HF and type D personality, but not high-energy ICD therapy, predicted persistent depression after an ICD implantation [16].

The current study found that exposure to shocks has a negative impact on psychological state, resulting in over a 3-fold increased risk of new-onset depression. It seems reasonable and intuitive that patients who have experienced an ICD shock are more anxious and prone to be depressed than those who had no shock. An ICD therapy is sudden, painful and unpredictable; therefore, it might be expected to contribute to mental health disorders. The anticipation of receiving another shock can further increase psychological distress and promote depressive symptoms. Besides, concerns about shock delivery might also lead to limitations in daily functioning and social withdrawal both resulting in higher risk of depression occurrence [4, 14].

The present study demonstrated that both depression and ICD shock are strong independent predictors of worse prognosis in CRT-D recipients. Although ICDs and CRT-Ds improve long-term survival in severe HF patients, shocks have been found to significantly increase long-term mortality [13, 26–28]. According to the vast majority of the studies both appropriate and inappropriate interventions portend poor prognosis, however, those for

ventricular arrhythmias are associated with more deleterious effects [13, 26–28]. It is still questionable, whether shocks are only a marker of the severity of HF or whether they potentiate the risk because of direct myocardial stunning [26]. Powell et al. reported no adverse impact of inappropriate shocks for sinus tachycardia or non-arrhythmic reasons (oversensing, noise, artifacts) on outcomes [13]. Moreover, antitachycardia pacing was demonstrated to be associated with over a 2-fold increased risk of death [29]. These findings might support the hypothesis, that an ICD shock is rather a marker of a more advanced disease.

The association between depression and unfavorable remote prognosis in HF populations has been already widely reported. In contrast to earlier studies, the prevalence and impact of depression was assessed in a homogenous population of first-time CRT-D recipients, nevertheless the present findings were generally consistent with previous results [8, 16, 30]. Depressed patients are less likely to comply with medical treatment, furthermore the adherence to therapy is proportional to the severity of depression [5, 16]. Moreover, depression leads to social withdrawal contributing to limitations in daily activities. Therefore, patients with depressive symptoms less often participate in cardiac rehabilitation and show worse compliance with secondary prevention lifestyle interventions [5, 16]. Besides, patients who suffer from depression might have a tendency to avoid medical visits and might be less willing to look for help if any medical complications arise [5, 16].

There are some findings to date, indicating that remission from depression may exert a beneficial effect on prognosis in HF population [31, 32]. It might be expected, that better compliance to complex medical treatment, sleep disorders reduction and increased physical activity might be the main factors that influence positively the remote outcomes in this population. Hence, it seems crucial to assess psychological co-morbidities in every HF patient, not only with indications for a high-energy device implantation. However, it should

be emphasized that repeated re-assessments of mental status are required, especially in case of HF deterioration or after an ICD shock [19]. Once the depression is diagnosed, a patient should receive psychological support and medical therapy ought to be administered under strict and constant psychiatric supervision [19]. Management of depression is complex and burdened with a high rate of failure, therefore, further studies are needed to establish the most effective treatment regimen of depression in severe HF patients.

Conclusions

Depression is a common mental disorder in CRT-D recipients, affecting over 20% of patients after a device implantation. Subjects suffering from ICD shocks, as well as those with HF progression are at significantly higher risk of experiencing depressive symptoms. Apart from repeated depression screening, every effort should be made to avoid factors contributing to depression, as it adversely affects long-term outcomes in the HF population.

Limitations of the study

The present study has several limitations. Firstly, the results were derived from a single-center, non-randomized, prospective, observational study, with all the shortcomings associated with such data. Secondly, although patients with new-onset depression were offered antidepressive treatment, only slightly over 50% of them agreed to take antidepressants. Hence, the Depression Group was not homogenous, as it consisted of patients with treated as well as untreated depression. However, because of a small number of participants this population could not be divided into patients taking antidepressants and those who declined psychiatric treatment.

Conflict of interests:

Tomasz Podolecki, MD, PhD – received consultant fees from Abbott, Boehringer-Ingelheim and AstraZeneca

Robert Pudlo, MD, PhD - no conflict of interests reported

Michał Mazurek, MD – received consultant fees from Medtronic, Biotronik, St Jude Medical, Boston Scientific

Monika Kozieł-Siołkowska, MD – no conflict of interests reported

Joanna Boidol, MD – no conflict of interests reported

Oskar Kowalski, MD– received consultant fees from Medtronic, Biotronik, St Jude Medical, Boston Scientific

Radosław Lenarczyk, MD, PhD – consultant and lecture fees: Abbott, Boston Scientific; European Union's Horizon 2020 research and innovation programme under grant agreement no 847999; PROFID-EHRA Project

Zbigniew Kalarus, MD, PhD – received company sponsored speaker’s bureau from Pfizer, Eli Lilly, Boehringer-Ingelheim, Abbott, Bayer; received consultant fees from Abbott

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Figure 1. Kaplan-Meyer curves of cumulative survival without MACE (Major Adverse Cardiac Events)

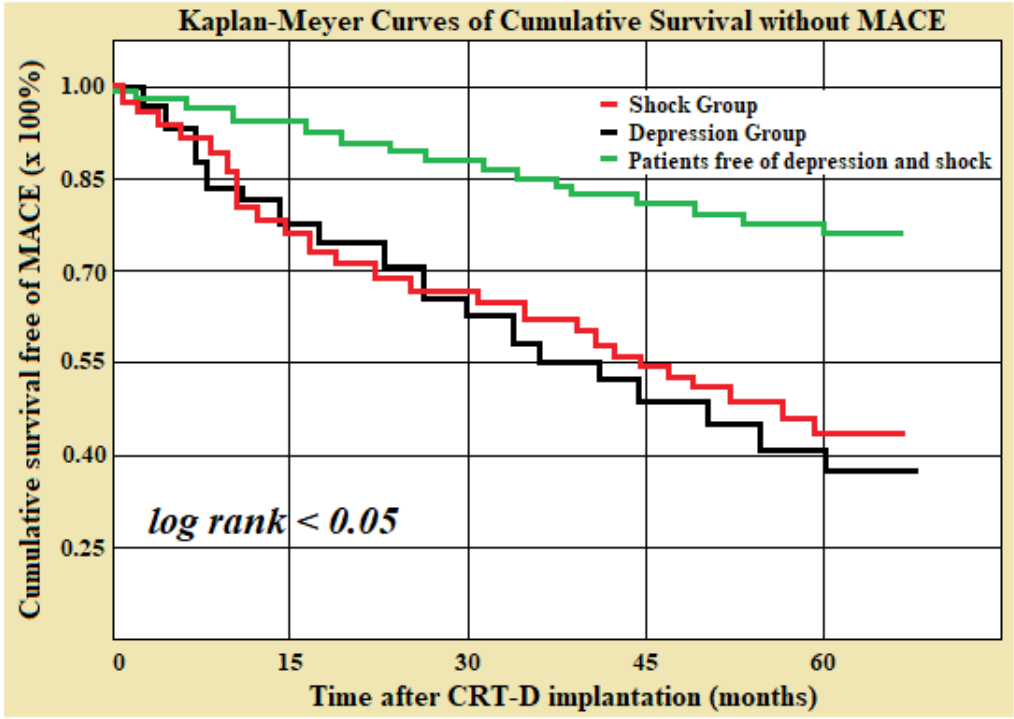
Kaplan-Meyer Curves of Cumulative Survival without MACE
Cumulative survival free of MACE (x 100%)
1.00
0.85
0.70
0.55
0.40
0.25
0
15
30
45
60
Time after CRT-D implantation (months)
Shock Group
Depression Group
Patients free of depression and shock
log rank < 0.05

Table 1. The baseline characteristics of the Shock Group and Control Group

Parameter	Shock Group (n = 52)	Control Group (n = 169)	P-value
Male – no. [%]	40 (76.9)	133 (78.7)	NS
Age (years)	65.6 ± 10.6	64.2 ± 12.9	NS
Ischaemic CHF – no. [%]	36 (69.2)	119 (70.4)	NS
NYHA class	2.66 ± 0.45	2.56 ± 0.53	NS
Diabetes mellitus – no. [%]	23 (44.2)	71 (42.0)	NS
Arterial hypertension – no. [%]	28 (53.9)	100 (59.2)	NS
AF total – no. [%]	31 (59.6)	70 (41.4)	< 0.05
COPD – no. [%]	7 (13.5)	19 (11.2)	NS
Hypothyroidism – no. [%]	8 (15.4)	24 (14.2)	NS
QRS duration (ms)	157.3 ± 14.3	160.9 ± 13.9	NS
LVEF [%]	26.4 ± 7.8	27.3 ± 8.9	NS
LVEF < 20% - no. [%]	13 (25.0)	31 (18.3)	NS
Moderate MR – no. [%]	19 (36.5)	57 (33.7)	NS
Severe MR – no. [%]	8 (15.4)	20 (11.8)	NS
CRT pacing [%]	95.11 ± 6.47	96.25 ± 5.62	NS
CRT responders – no. [%]	38 (73.1)	142 (84.0)	NS
Beta-blocker – no. [%]	49 (94.2)	164 (97.0)	NS
ACE-I/ARB – no. [%]	46 (88.5)	154 (91.1)	NS
Loop diuretics – no. [%]	47 (90.4)	152 (89.9)	NS

ACE-I/ARB — angiotensin converting enzyme inhibitor/angiotensin receptor blocker; AF — atrial fibrillation; CHF — chronic heart failure; COPD — chronic obstructive pulmonary disease; CRT — cardiac resynchronization therapy; LVEF — left ventricle ejection fraction; MR — mitral regurgitation; NYHA — New York Heart Association

Table 2. The baseline characteristics of the Depression Group and Depression-free Group

Parameter	Depression Group (n = 48)	Depression-free Group (n = 173)	P-value
Male – no. [%]	38 (79.2)	135 (78.0)	NS
Age (years)	65.6 ± 10.1	64.3 ± 12.4	NS
Ischemic CHF – no. [%]	33 (68.8)	122 (70.5)	NS
NYHA class at baseline	2.64 ± 0.51	2.57 ± 0.44	NS
Change in NYHA class:			
improved by at least 1 class – no. [%]	20 (41.7)	114 (65.9)	< 0.05
worsened by at least 1 class – no. [%]	12 (25.0)	14 (8.1)	< 0.05
Diabetes mellitus – no. [%]	22 (45.8)	72 (41.6)	NS
Arterial hypertension – no. [%]	26 (54.2)	102 (59.0)	NS
AF total – no. [%]	30 (62.5)	78 (45.1)	< 0.05
ICD shock – no. [%]	30 (62.5)	22 (12.7)	< 0.001
COPD – no. [%]	5 (10.4)	21 (12.1)	NS
Hypothyroidism – no. [%]	9 (18.8)	23 (13.3)	NS
QRS duration (ms)	160.1 ± 11.4	157.6 ± 13.5	NS
LVEF [%]	26.7 ± 9.0	27.2 ± 8.6	NS
LVEF < 20% – no. [%]	9 (18.8)	35 (20.2)	NS
Moderate MR – no. [%]	18 (37.5)	58 (33.7)	NS
Severe MR – no. [%]	5 (10.4)	23 (13.3)	NS
CRT pacing [%]	92.8 ± 8.1	96.9 ± 7.4	< 0.05
CRT responders – no. [%]	31 (64.6)	149 (86.1)	< 0.05
Beta-blocker – no. [%]	46 (95.8)	167 (96.5)	NS
ACE-I/ARB – no. [%]	43 (89.6)	157 (90.8)	NS

Loop diuretics – no. [%]	44 (91.7)	155 (89.6)	NS

ACE-I/ARB — angiotensin converting enzyme inhibitor/angiotensin receptor blocker; AF — atrial fibrillation; CHF — chronic heart failure; COPD — chronic obstructive pulmonary disease; CRT — cardiac resynchronization therapy; ICD — implantable cardioverter-defibrillator; LVEF – left ventricle ejection fraction; MR — mitral regurgitation; NYHA — New York Heart Association

Table 3. The baseline characteristics of patients who experienced MACE and those free of MACE

Parameter	MACE Group (n = 73)	MACE-free Group (n = 148)	P-value
Male – no. [%]	59 (80.8)	114 (77.0)	NS
Age (years)	65.9 ± 8.9	63.9 ± 11.7	NS
Ischemic CHF – no. [%]	53 (72.6)	102 (68.9)	NS
NYHA class	2.77 ± 0.39	2.49 ± 0.48	< 0.001
Diabetes mellitus – no. [%]	35 (47.9)	59 (39.8)	NS
Arterial hypertension – no. [%]	43 (58.9)	85 (57.4)	NS
AF total – no. [%]	44 (60.3)	57 (38.5)	< 0.05
ICD shock – no. [%]	30 (41.1)	22 (14.9)	< 0.001
COPD – no. [%]	9 (11.8)	17 (11.5)	NS
Hipothyroidism – no. [%]	12 (12.3)	20 (13.5)	NS
Depression de novo – no. [%]	30 (41.1)	18 (12.2)	< 0.001
QRS duration (ms)	160.4 ± 11.5	159.7 ± 12.8	NS
LVEF [%]	25.1 ± 9.2	28.1 ± 8.7	< 0.05
LVEF < 20% – no. [%]	22 (30.1)	22 (14.9)	< 0.05

Moderate MR – no. [%]	28 (38.4)	48 (32.4)	NS
Severe MR – no. [%]	15 (20.6)	13 (8.8)	< 0.05
CRT pacing [%]	93.36 ± 9.69	96.5 ± 7.38	< 0.05
CRT responders – no. [%]	51 (69.9)	129 (87.2)	< 0.05
Beta-blocker – no. [%]	71 (97.3)	142 (96.0)	NS
ACE-I/ARB – no. [%]	65 (89.0)	135 (91.2)	NS
Loop diuretics – no. [%]	67 (91.8)	132 (89.2)	NS

ACE-I/ARB — angiotensin converting enzyme inhibitor/angiotensin receptor blocker; AF – atrial fibrillation; CHF — chronic heart failure; COPD — chronic obstructive pulmonary disease; CRT — cardiac resynchronization therapy; LVEF — left ventricle ejection fraction; MR — mitral regurgitation; NYHA — New York Heart Association

Table 4. Twelve-month and long-term prognosis in the Depression Group and Depression-free Group

Parameter	Depression Group (n = 48)	Depression-free Group (n = 173)	P-value
12-month follow-up			
Mortality – no. [%]	3 (6.3)	8 (4.6)	NS
DHF – no. [%]	7 (14.6)	13 (7.5)	NS
MACE – no. [%]	9 (18.8)	18 (10.4)	NS
Long-term follow-up			
Mortality – no. [%]	10 (20.8)	19 (11.0)	0.074
DHF – no. [%]	24 (50.0)	31 (17.9)	< 0.001
MACE – no. [%]	30 (62.5)	43 (24.9)	< 0.001

DHF — hospitalization for decompensated heart failure; MACE — major adverse cardiac event

Table 5. Twelve-month and long-term prognosis in the Shock Group and Control Croup

Parameter	Shock Group (n = 52)	Control Group (n = 169)	P-value
12-month follow-up			
Mortality – no. [%]	4 (7.7)	7 (4.1)	NS
DHF – no. [%]	7 (13.5)	13 (7.7)	NS
MACE – no. [%]	10 (19.2)	17 (10.1)	0.077
Long-term follow-up			
Mortality – no. [%]	10 (19.2)	19 (11.2)	NS
DHF – no. [%]	23 (44.2)	32 (18.9)	< 0.001
MACE – no. [%]	30 (57.7)	43 (25.4)	< 0.001

DHF — hospitalization for decompensated heart failure; MACE — major adverse cardiac event

Table 6. The independent predictors of major adverse cardiac events - Cox-regression model

Parameter	Hazard ratio ± 95% CI	P-value
Depression	1.72 (1.37–2.07)	< 0.05
NYHA class	1.44 (0.83–2.06)	NS
Atrial fibrillation	1.28 (1.05–1.51)	< 0.05
Severe MR	1.79 (1.18–2.40)	< 0.05
LVEF	0.98 (0.95–1.01)	NS
CRT pacing	0.99 (0.97–1.01)	NS
ICD shock	2.11 (1.63–2.59)	< 0.001
CRT non-response	1.49 (0.78–2.21)	NS

CI — confidence interval; CRT — cardiac resynchronization therapy; ICD — implantable cardioverter-defibrillator; LVEF — left ventricle ejection fraction; MR — mitral regurgitation; NYHA — New York Heart Association