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Research Brief

Predictors for early mortality in patients with implantable cardiac defibrillator for heart failure with reduced ejection fraction

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ABSTRACT

Implantable cardioverter defibrillators (ICD) are recommended in heart failure with reduced ejection fraction (HFrEF) patients to reduce arrhythmic deaths. This study aimed to identify risk factors associated with mortality within one-year following the ICD. The data from our hospital's electronic database system was extracted for patients who were implanted ICD secondary to HFrEF between 2009 and 2019. Overall, 1107 patients were included in the present analysis. Mortality rate at one-year following the device implantation was 4.7%. In multivariate analysis; age, atrial fibrillation, New York Heart Association classification >2, blood urea nitrogen, pro-brain natriuretic peptide and albumin independently predicted one year mortality.

1. Introduction

Implantable cardioverter defibrillators (ICD) are recommended for both primary and secondary prevention to reduce arrhythmic events in patients with heart failure and reduced left ventricular ejection fraction (HFrEF).[1] The major contraindication for omitting ICD implantation in HF patients is the life expectancy of less than one-year. Understanding risk factors associated with early mortality despite ICD implantation is important for determining the group of patients that would benefit most from the device therapy. Our main objective was to identify predictors for early mortality (<one-year) in patients who died within the first year of ICD implantation.

2. Methods

The present research included patients with HFrEF who were implanted ICD in a tertiary center between January 2009 and January 2019. Diagnosis for HFrEF was made according to the ICD codes in the hospital electronic database system. Exclusion criteria were: i) age <18 years old, ii) ICD implantation in patients who had indications other than HFrEF such as channelopathies or structurally normal hearts and iii) absence of one-year mortality data. Implanted device settings and discharge medications were left at the discretion of the physician Delivered therapies were obtained from patients' reports or device interrogations that were recorded in the electronic database. The local ethics committee approved the study protocol.

3. Results

In total, 1107 patients were analyzed for the present study. Overall, 54 (4.7%) patients died within the first year following the device implantation. The median time to death was 8 (6–11) months in non-survivors during one-year follow-up. Patients who died within one-year were older and more likely to have diabetes,

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chronic renal failure, ischemic HF, atrial fibrillation (AF), ICD with single lead and New York Heart Association (NYHA) classification >2 (Table 1). In addition, they had lower hemoglobin and albumin levels and higher creatinine, blood urea nitrogen (BUN) and pro-brain natriuretic peptide (BNP) levels (Table 1). Finally, patients who died within one-year had lower left ventricle ejection fraction (LVEF) and higher LV end-diastolic diameters and more likely to have severe tricuspid regurgitation (Table 1). There were 49 patients (4.4%) with appropriate shocks and 14 patients (1.2%) with inappropriate shocks in the study population. In the inappropriate shock group, 85.7% were due to AF. In total, 384 ICD (34.6%) were implanted for primary prevention among all patients. In multivariate analysis; age, AF, NYHA classification >2, BUN, pro-BNP and albumin independently predicted one-year mortality (Table 2).

Mortality analysis of patients according to the year of ICD implantation is given in Fig. 1. The majority of patients who did not survive within one-year of implantation were not on triple therapy including beta blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers, and aldosterone receptor blockers, which were recommended by the current guidelines.

4. Discussion

Our mortality rate during the first year was lower compared to what was reported from randomized controlled trials (RCT)'s for the primary and secondary prevention trials, which ranged from 7% to 9% and 8%–11% respectively.[2,3] In the present analysis, a possible explanation for lower mortality rate could be that those RCT's were

Table 1
Comparison of demographic and clinical characteristics of patients according to 1-year mortality after ICD.

	Patients with survival >1 year, ($n = 1053$)	Patients with survival ≤1 year ($n = 54$)	P value
Age, y	60.5 ± 14.4	67.6 ± 12.9	0.002
Male gender	836 (79.4%)	43 (79.7%)	0.966
Hypertension	516 (49.0%)	30 (55.6%)	0.348
Diabetes mellitus	313 (29.7%)	26 (48.1%)	0.004
Hyperlipidemia	398 (37.8%)	27 (50.0%)	0.072
Smoking	309 (29.3%)	12 (22.2%)	0.261
Chronic renal failure	212 (20.2%)	18 (33.3%)	0.020
Ischemic heart failure	807 (76.6%)	47 (87.0%)	0.095
Non-Ischemic heart failure	246 (23.4%)	7 (13.0%)	0.095
Chronic obstructive pulmonary disease	85 (8.1%)	4 (7.4%)	0.859
Coronary artery disease	771 (73.2%)	50 (92.6%)	0.002
Percutaneous coronary intervention	343 (32.6%)	18 (33.3%)	0.908
Coronary artery bypass grafting	267 (25.4%)	20 (37.0%)	0.056
Cerebrovascular accident	22 (2.1%)	2 (3.7%)	0.329
Atrial fibrillation	146 (13.9%)	26 (48.1%)	<0.001
NYHA classification >2	184 (17.5%)	34 (63.0%)	<0.001
Indication			
Primary	364 (34.6%)	20 (37.0%)	0.710
Secondary	689 (65.4%)	34 (63.0%)	0.710
Device types			
VVI-ICD	956 (90.8%)	53 (98.1%)	0.038
DDD-ICD	97 (9.2%)	1 (1.9%)	0.038
Out-hospital medication			
Beta-blockers	559 (53.1%)	23 (42.6%)	0.132
ACEIs or ARBs	808 (76.7%)	41 (75.9%)	0.892
Spironolactone	259 (24.6%)	9 (16.7%)	0.168
In-hospital mortality	0 (0.0%)	3 (1.8%)	0.003
Appropriate shock in 1-year	41 (4.4%)	8 (4.8%)	0.778
Inappropriate shock in 1-year	13 (1.4%)	1 (0.6%)	0.359
Laboratory variables			
Hemoglobin, g/dL	12.9 ± 1.9	12.2 ± 2.0	0.018
RDW, %	13.2 ± 1.2	13.0 ± 0.9	0.157
WBC, cells/μL	9.3 ± 4.5	9.3 ± 3.6	0.851
Platelet count, cells/μL	201.7 ± 64.7	212.3 ± 66.6	0.244
MPV, %	9.9 ± 1.6	10.1 ± 1.2	0.513
Creatinine, mg/dL	1.0 ± 0.3	1.1 ± 0.3	0.040
Urea, mg/dL	23.5 ± 13.9	33.9 ± 16.5	<0.001
TSH, U/L	1.5 ± 0.9	1.7 ± 1.0	0.558
AST, U/L	22.4 ± 6.3	23.0 ± 8.2	0.940
ALT, U/L	23.0 ± 9.9	21.8 ± 8.6	0.697
Glucose, mg/dL	108 (93–139)	122 (96–172)	0.079
Albumin, mg/dL	4.0 ± 2.4	3.4 ± 0.5	<0.001
Pro-BNP, pg/mL	474 (174–1079)	2513 (2019–3034)	<0.001
Echocardiography variables			
Ejection fraction, %	29.6 ± 7.0	27.2 ± 7.1	0.007
LVEDD, mm	58.4 ± 9.6	60.9 ± 7.4	0.040
LVESD, mm	45.0 ± 12.2	47.7 ± 9.9	0.087
TR ≥+3	80 (8.5%)	24 (14.5%)	0.020

Continuous variables are presented as mean (SD), nominal variables presented as frequency (%).
Abbreviations: NYHA, New York Heart Association; ICD, implantable cardioverter defibrillator; ACE, angiotensinogen converting enzyme; ARB, angiotensinogen receptor blocker; RDW, red cell distribution width; WBC, white blood cell; MPV, mean platelet volume; TSH, troid stimulating hormone; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BNP, brain natriuretic peptide; EF, ejection fraction; LVEDD, left ventricle end-diastolic diameter; LVESD, left ventricle end-systolic diameter; TR, tricuspid regurgitation.

Table 2
Univariate and multivariate Cox regression analyses for one-year mortality after ICD.

	Univariate analysis		Multivariate analysis	
	P value	HR (95% CI)	P value	HR (95% CI)
Age	0.001	1.037 (1.015–1.059)	0.024	1.031 (1.004–1.058)
Diabetes mellitus	0.006	2.123 (1.245–3.621)	–	–
Chronic renal failure	0.022	1.933 (1.098–3.404)	–	–
Ischemic heart failure	0.009	2.417 (1.246–4.687)	–	–
Coronary artery disease	0.044	1.292 (1.006–1.659)	–	–
Atrial fibrillation	<0.001	5.397 (3.164–9.206)	0.001	3.015 (1.604–5.668)
NYHA classification >2	<0.001	7.502 (4.317–13.035)	<0.001	3.305 (1.722–6.345)
Hemoglobin	0.007	0.846 (0.750–0.956)	–	–
Creatinine	0.043	1.929 (1.022–3.642)	–	–
Blood urea nitrogen	<0.001	1.028 (1.017–1.040)	0.032	1.012 (1.004–1.028)
Albumin	<0.001	0.315 (0.225–0.441)	0.027	0.527 (0.299–0.931)
Pro-BNP	<0.001	1.001 (1.001–1.002)	<0.001	1.001 (1.001–1.002)
Ejection fraction	0.019	0.956 (0.922–0.993)	–	–
TR ≥+3	0.021	2.240 (1.127–4.452)	–	–

Abbreviations: ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; TR, tricuspid regurgitation.

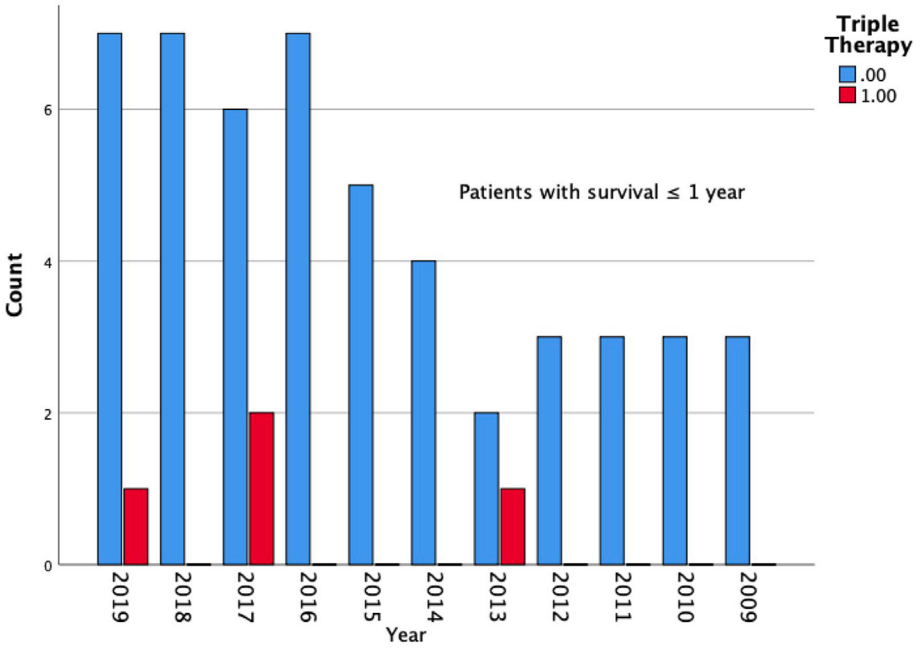

Fig. 1. Mortality analysis of patients who died within one-year following İmplantable cardioverter defibrillators (ICD).

mostly conducted during the first decade of 2000; while, our data were extracted majorly from patients that were implanted ICD in the second decade. Our findings indicated that older age is a predictor for mortality during the first year.

Although current guidelines do not recommend withholding ICD therapy on the basis of age, several prior reports demonstrated increased rate of mortality in the first year among older patients.[4,5] It is possible that elderly patients more likely to die from non-arrhythmic death as the burden and the prognosis of comorbid conditions accumulate as age increases.

Atrial fibrillation is considered as a strong adverse prognostic marker in patients with HFrEF.[6] Almost half of our patients who died at one-year had AF. Presence of AF might indicate more advanced diseases with extensive atrial and ventricular remodeling.[7] Furthermore, AF exacerbates HF symptoms, increases hospitalizations and might cause ischemic stroke.[6]

In our study, we found that BUN levels were independent predictor of mortality in patients with HFrEF receiving ICD. Several reports demonstrated that in patients with HF, BUN exhibited greater impact on mortality compared to creatinine and glomerular filtration rate (GFR).[8,9] It was suggested that BUN represented not only impaired renal functions but also fluctuations in fluid volume, neurohormonal activities and hemodynamics.

Finally, we found that patients with low albumin level were at high risk for one-year mortality. It is known that advanced HF is a pro-inflammatory state characterized by high plasma concentration of various cytokines. This conditions lead to higher muscle and fat consumption and reduced energy intake caused by diminished appetite and decreased intestinal absorption.[10]

Another important data from our study was the fact that considerable number of patients were not taking HF medications that were recommended in guidelines. We believe that increasing awareness of both clinicians and patients for the importance of opting guideline-directed medical therapy is of utmost importance to improve outcomes. An important limitation of our study was the lack of data regarding the cause of death.

5. Conclusions

In patients who had HFrEF and implanted ICD, older age, presence of AF, NYHA classification >2, elevated BUN and pro-BNP levels along with reduced albumin levels predicted mortality within one-year following device implantation.

Declaration of competing interest

All authors declare that they do not have conflict of interest.

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None.

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