



# Survival benefit of ICD implantation for primary prevention in dilated cardiomyopathy

Alimohammad Akrami<sup>1</sup>, Faezeh Dehghani Tafti<sup>1</sup>, Seyed Kazem Razavi Ratki<sup>2</sup>, Mohsen Mohammadi<sup>1</sup>,  
Mohammadtaghi Sarebanhassanabadi<sup>1</sup>, Maliheh Malekpoor<sup>1</sup>, Najmeh Ghiasi Hafezi<sup>1</sup>,  
Seyed Mostafa Seyed Hossaini Tezerjani<sup>1,\*</sup>

<sup>1</sup> Yazd Cardiovascular Research Center, Non-communicable Diseases Research Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup> Department of Radiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

**\* Corresponding Author:**

**Address:** Afshar Hospital, Jomhouri Blvd, Yazd, Iran. **Postal code:** 8917945556; **Tel:** +98 09133250347; **Email:** m.seydhossaini@gmail.com

**Article Information:**

Received: 06 Jun 2024; Revised: 04 Aug 2024; Accepted: 07 Aug 2024

DOI: 10.18502/cbj.v4i1.16224

## Abstract

**Objectives:** Dilated cardiomyopathy (DCM) represents a significant cause of heart failure unrelated to ischemic heart disease, posing a high risk of sudden cardiac death (SCD) due to low left ventricular ejection fraction (LVEF). This study evaluates the survival benefits of implantable cardiac defibrillators (ICDs) for primary prevention in DCM patients.

**Methods:** We enrolled 52 symptomatic non-ischemic cardiomyopathy patients (LVEF  $\leq$  35%, NYHA class II-III) eligible for ICD implantation in Afshar Hospital, Yazd, Iran, from 2014 to 2015. Exclusion criteria included those with ischemic indications or requiring cardiac resynchronization therapy. We divided patients into ICD recipients and those on a waiting list, collected the baseline data (age, functional class, LVEF), then followed up with patients to assess mortality rates.

**Results:** Among 45 patients, 64.5% received ICDs while 35.5% were on the waiting list. The mean age was  $57 \pm 13$  years, predominantly male (67.3%). The ICD group had a significantly lower mortality rate (17.3%) than the waiting list group (42.7%,  $p = 0.54$ ). Although age and functional class did not significantly predict outcomes, lower LVEF was a crucial factor for long-term survival. Despite some studies suggesting no survival benefit in non-ischemic heart failure, our findings highlight the efficacy of ICDs in reducing mortality among DCM patients.

**Conclusions:** ICD implantation in DCM patients substantially reduces all-cause mortality compared to those awaiting the procedure, underscoring the importance of timely ICD deployment for primary prevention in this population.

## Introduction

One of the final stages of various cardiovascular diseases is heart failure, which impacts many individuals globally. DCM is a category of heart failure that is not caused by ischemic heart disease<sup>1</sup>. DCM patients are at increased risk of death from pump failure and SCD. Low left ventricular EF, especially EF < 30% is the

most common risk factor for overall mortality from SCD<sup>2</sup>. The overall risk of SCD in heart failure patients is 6-9 times higher than in the general population. Among patients with mild to moderate heart failure symptoms (NYHA class II-III), SCD is the primary cause of death compared to those with NYHA class IV who primarily die from pump

failure<sup>3</sup>. Therefore, patients with NYHA class II-II and an overall acceptable quality of life will take the greatest advantage of SCD prevention. Advancements in medical treatments, particularly using ICDs for primary prevention, reduce the incidence of SCD<sup>4</sup>. In the event of a cardiac arrest, every single minute is critical. ICDs can detect life-threatening heart rhythms and provide immediate treatment using rapid painless pacing or internal shock therapy. Numerous clinical trials have documented improved survival using ICDs in high-risk patients with LV dysfunction. Compared with conventional antiarrhythmic drugs, ICD therapy has been associated with a mortality reduction of about 23% to 55% due to a decrease in SCD<sup>6</sup>. There are two types of trials: primary prevention (prophylactic) trials in which the subjects have not experienced a life-threatening arrhythmia or symptomatic equivalent, and secondary prevention trials involving subjects who have had an aborted cardiac arrest or unexplained syncope with a high probability of ventricular tachyarrhythmia as the cause of the syncope<sup>7</sup>. SCD-HeFT trial enrolled both IHD and non-ischemic cardiomyopathy patients. For patients with IHD, primary prevention ICDs reduced total mortality after three years of follow-up by 20-59%. This reduction was sustained over eight years following. The non-ischemic patients in SCD-HeFT had a 3-year mortality reduction of 25%<sup>8</sup>. However, most trials in this setting are conducted among ischemic cardiomyopathies<sup>9</sup>. In the European Guidelines, ICD implantation is a class 1B recommendation for patients with non-ischemic heart failure and a class 1A recommendation for patients with ischemic heart failure<sup>10</sup>. Therefore, there is still a need for further investigation into the role of ICDs in primary prevention among dilated cardiomyopathy (DCM) patients, including treatment options such as timely painless pacing or internal shock therapy.

### Material and Methods

We enrolled 52 patients with non-ischemic cardiomyopathy who were eligible for ICD implantation between 2014 and 2015 in Afshar

Hospital, Yazd province of Iran. Symptomatic non-ischemic heart failure patients with LVEF  $\leq 35\%$ , NYHA class  $\geq II$ , and an indication of ICD implantation for primary prevention according to the latest guidelines were included. Exclusion criteria were evidence of ischemia based on imaging or angiography and indications for cardiac resynchronization therapy (CRT). We divided the patients into two groups: those who received ICD and those who were on a waiting list for ICD implantation. All patients filled out the informed consent. A questionnaire provided the baseline information (age, functional class, LVEF, and ICD type). We followed patients for about two years and evaluated the mortality rate in both groups. The ethics committee reviewed and approved the study protocol (ethic code: 6284). Statistical analysis results are expressed as mean  $\pm$  standard deviation (SD) for continuous variables. Continuous variables were compared between groups using a Student's t-test. Dichotomous variables are presented as percentages and were compared between groups via Fischer's exact test. A probability value of  $< 0.05$  was considered to indicate statistical significance. Data were analyzed using SPSS for Windows (version 21, Chicago, Inc.).

### Results

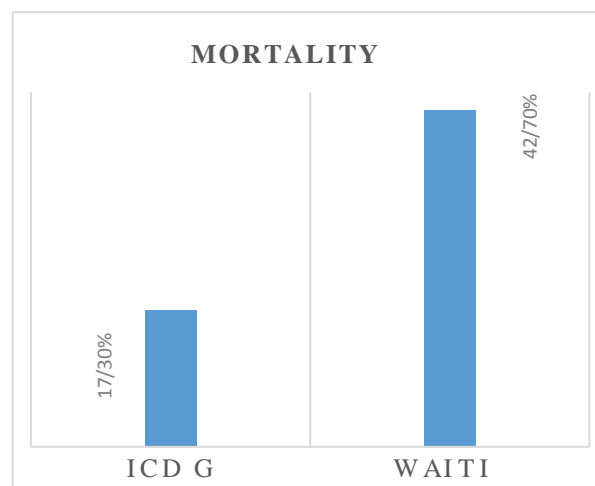
Among fifty-two patients who met our inclusion criteria, seven were excluded for missing data. The patients were predominantly male (67.3%). The mean age of participants was  $57 \pm 13$  years. Table 1 illustrates the clinical characteristics of participants. Twenty-nine patients (64.5%) received an ICD. Meanwhile, sixteen patients (35.5%) were on the waiting list for ICD implantation. Single-chamber ICDs (ICD-VR) and dual-chamber ICDs (ICD-DR) were chosen in 48.3% and 51.7% respectively. The LV ejection fraction was mostly between 20-30% in 48.2% of patients in the ICD group and was under 20% in 81.2% of patients waiting for ICD implantation. There was no significant difference in the NYHA class between the two groups. However, the waiting list group revealed a trend toward NYHA class III.

**Table1.** Clinical characteristics of participants

	Patient with ICD N:29	Patient in waiting list N:16
Mean age (years)	58±14	56±11
ICD type (%)		
VR	14(48.3%)	-
DR	15(51.7%)	-
LVEF (%)		
>30-35	2(6.8%)	0(0.0%)
20-30	14(48.2%)	3(18.7%)
<20	13(44.7%)	13(81.2%)
NYHA class N (%)		
Class II	10(34.5%)	4(25.0%)
Class III	11(37.9%)	11(68.7%)
Class IV	8(27.6%)	1(6.3%)
Follow-up period (months)	28 ± 10	23 ± 14
Mortality rate (%)	5(17.3%)	7(42.7%)

The mean follow-up period for the entire group was 27 months. 42.7% of patients on the waiting list died during this period (Figure 1). The rate of mortality in patients with ICD was 17.3% (P-

value: 0.54). Age and functional class were not significant predictive covariates (P-value >0.05) but Left ventricular function significantly did affect long-term survival.

**Figure1.** Comparison of mortality rate between both groups

## Discussion

As we know, ICD is superior to antiarrhythmic drugs in increasing overall survival<sup>1</sup>. Large published trials have proven the critical role of ICDs in different diseases<sup>12</sup>. However, most of these trials are conducted in ischemic cardiomyopathies, with less investigation into non-ischemic dilated cardiomyopathies<sup>11</sup>. In the European Guidelines, ICD implantation is a class 1B recommendation for patients with non-ischemic heart failure and a class 1A recommendation for patients with ischemic heart failure<sup>10</sup>. Therefore, this study aimed to evaluate the survival benefit of ICD for primary prevention in

DCM patients who received ICDs and who remain on a waiting list for ICD implantation. In this study, at a projected follow-up period of 27 months, freedom from death remained near 82.7%, demonstrating the reliability of the ICD in terminating sudden cardiac death. During this time 42.7% of patients on the waiting list died. Some retrospective studies showed that the use of ICD in patients waiting for heart transplantation could reduce overall mortality by 36% to 49%, which is in concordance with our results<sup>13</sup>. The DANISH trial showed that in patients with systolic heart failure not

caused by ischemic heart disease. There is no survival benefit of ICD in terms of decreasing total mortality<sup>9</sup>. However, patients with a high predicted relative likelihood of SCD seemed to benefit from ICD implantation. Some trials concluded that younger patients would get the highest survival benefit after ICD implantation<sup>14-15</sup>. Nevertheless, in our study, age was not a determining factor for total mortality (P-value: 0.3). Maybe our results are due to the low number of patients older than 68 years old in our trial. Patients on the waiting list group had significantly lower LVEF (<20%, P-value<0.05) without significant differences in the NYHA class. These results showed selection bias. Although lower EF is considered a determining risk factor for SCD, unfortunately, these patients are deprived of ICD implantation. Maybe this is because of the idea that they would have lower survival. But in different trials, NYHA class IV, not LVEF is a contributing factor to death<sup>16-17</sup>.

## Limitations

## References

1. Wang K, Xu X, Qi Y, et al. Comparison of the benefit of primary prevention implantable cardioverter-defibrillator therapy in ischemic versus nonischemic dilated cardiomyopathy. *Authorea*. 2020.
2. Halliday BP, Cleland JG, Goldberger JJ, et al. Personalizing risk stratification for sudden death in dilated cardiomyopathy: the past, present, and future. *Circulation*. 2017; 136(2):215-231.
3. Sun WP, Li CL, Guo JC, et al. Long-term efficacy of implantable cardiac resynchronization therapy plus defibrillator for primary prevention of sudden cardiac death in patients with mild heart failure: an updated meta-analysis. *Heart Fail Rev*. 2016; 21(4):447-53.
4. Pezawas T, Grimm M, Ristl R, et al. Primary preventive cardioverter-defibrillator implantation (Pro- ICD) in patients awaiting heart transplantation. A prospective, randomized, controlled 12-year follow-up study. *Transpl Int*. 2015; 28(1):34-41.
5. Clementy N, Challal F, Marijon E, et al. Very high rate programming in primary prevention patients with reduced ejection fraction implanted with a defibrillator: Results from a large multicenter controlled study. *Heart Rhythm*. 2017; 14(2):211-217.
6. Algalarrondo V, Perault R, Bories MC, et al. Prophylactic implantable cardioverter defibrillators for primary prevention: From implantation to heart transplantation. *Arch Cardiovasc Dis*. 2018; 111(12):758-765.
7. Connolly SJ, Hallstrom AP, Cappato R, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. AVID, CASH and CIDS studies. Antiarrhythmics vs Implantable Defibrillator study. Cardiac Arrest Study Hamburg. Canadian Implantable Defibrillator Study. *Eur Heart J*. 2000; 21(24): 2071-8.
8. Ursaru AM, Petris AO, Costache II, et al. Comparable Efficacy in Ischemic and Non-Ischemic ICD Recipients for the Primary Prevention of Sudden Cardiac Death. *Biomedicines*. 2021; 9(11):1595.
9. Køber L, Thune JJ, Nielsen JC, et al. Defibrillator implantation in patients with nonischemic systolic heart failure. *N Engl J Med*. 2016; 375(13):1221-30. Ponikowski P, Voors AA, Anker SD. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2016;37(27): 2129-200.
10. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016; 37(27):2129-2200.
11. Kolodziejczak M, Andreotti F, Kowalewski M, et al. Implantable cardioverter-defibrillators for primary prevention in patients with ischemic or nonischemic cardiomyopathy: a systematic review and meta-

The present study was a single-center study. Moreover, the sample size was small. In addition, it would be better if we had a longer follow-up period.

## Conclusion

In conclusion, DCM patients with ICD implantation compared to those on a waiting list had a reduction in the risk of all-cause mortality.

## Ethical statements

The ethics committee reviewed the study protocol in 2018 and sent the approval letter with a delay in 2024. Ethic code: IR.SSU.MEDICINE.REC.1403.102432.

## Authors contributions and Conflicts of Interest

None

## Funding

None

## Acknowledgments

None Declared

- analysis. *Ann Intern Med.* 2017; 167(2):103-111.
- 12.Pathak RK, Sanders P, Deo R. Primary prevention implantable cardioverter-defibrillator and opportunities for sudden cardiac death risk assessment in non-ischaemic cardiomyopathy. *Eur Heart J.* 2018;39(31):2859-2866.
- 13.Da Rosa MR, Sapp JL, Howlett JG, et al. Implantable cardioverter-defibrillator implantation as a bridge to cardiac transplantation. *J Heart Lung Transplant.*2007; 26(12):1336-9.
- 14.Santangeli P, Di Biase L, Russo AD, et al. Meta-analysis: age and effectiveness of prophylactic implantable cardioverter- defibrillators. *Ann Intern Med.* 2010; 153(9):592-9.
- 15.Golwala H, Bajaj NS, Arora G, et al. Implantable cardioverter- defibrillator for nonischemic cardiomyopathy: an updated meta-analysis. *Circulation.* 2017;135(2):201-203.
- 16.Dagres N, Hindricks G. Risk stratification after myocardial infarction: is left ventricular ejection fraction enough to prevent sudden cardiac death? *Eur Heart J.* 2013;34(26):1964-71.
- 17.Al-Khatib SM, Fonarow GC, Joglar JA, et al. Primary prevention implantable cardioverter defibrillators in patients with nonischemic cardiomyopathy: a meta-analysis. *JAMA cardiol.* 2017;2(6):685-688.