Indian Heart Journal 75 (2023) 115–121

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Cardioverter-defibrillator reduces mortality risk in eligible ischemic and non-ischemic cardiomyopathy patients: Sub-analysis of the multi-center Improve SCA study

Balbir Singh [a, *], Yu-Cheng Hsieh [b, c], Yen-Bin Liu [d], Kuo-Hung Lin [e], Boyoung Joung [f], Diego A. Rodriguez [g, h], Alexandr R. Chasnoits [i], Dejia Huang [j], Shu Zhang [k], Janet E. O'Brien [l], Daniel R. Lexcen [l], Jeffrey Cerkvenik [l], Brian Van Dorn [l], Chi-Keong Ching [m]

[a] Department of Cardiology, Pan Max Hospital, New Delhi, India
[b] Cardiovascular Center, Taichung Veterans General Hospital, Taichung, Taiwan
[c] National Chung Hsing University School of Medicine, Taichung, Taiwan
[d] Division of Cardiology, Internal Medicine Department, National Taiwan University Hospital, Taipei, Taiwan
[e] Department of Cardiology, China Medical Center University Hospital, Taichung, Taiwan
[f] Cardiology Division, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea
[g] Instituto de Cardiología, Fundación Cardio Infantil, Centro Internacional de Arritmias, Bogotá, Colombia
[h] Universidad de la Sabana, Chía, Columbia
[i] Department of Roentgen-Endovascular Surgery, Republican Scientific and Practical Centre Cardiology, Minsk, Belarus
[j] Department of Cardiovascular Medicine, West China Hospital, Cardiology, Chengdu, China
[k] The Cardiac Arrhythmia Center, Fuwai Cardiovascular Hospital, Beijing, China
[l] Cardiac Rhythm Management, Medtronic Inc., Mounds View, Minnesota, USA
[m] Department of Cardiology, National Heart Centre of Singapore, Outram District, Singapore

ARTICLE INFO

Article history:
Received 27 July 2022
Received in revised form
9 January 2023
Accepted 29 January 2023
Available online 2 February 2023

Keywords:
Heart failure
Implantable cardioverter defibrillators
Sudden cardiac arrest
Sudden cardiac death
Ventricular arrhythmias

ABSTRACT

Background & Objective: Despite the burden of sudden cardiac arrest (SCA) worldwide, implantable cardioverter-defibrillators (ICDs) are underutilized, particularly in Asia, Latin America, Eastern Europe, the Middle East, and Africa. The Improve SCA trial demonstrated that primary prevention (PP) patients in these regions benefit from an ICD or a cardiac resynchronization therapy defibrillator (CRT-D). We aimed to compare the rate of device therapy and mortality among ischemic and non-ischemic cardiomyopathy (ICM and NICM) PP patients who met guideline indications for ICD therapy and had an ICD/CRT-D implanted.

Methods: Improve SCA was a prospective, non-randomized, non-blinded multicenter trial that enrolled patients from the above-mentioned regions. All-cause mortality and device therapy were examined by cardiomyopathy (ICM vs NICM) and implantation status. Cox proportional hazards methods were used, adjusting for factors affecting mortality risk.

Results: Of 1848 PP NICM patients, 1007 (54.5%) received ICD/CRT-D, while 303 of 581 (52.1%) PP ICM patients received an ICD/CRT-D. The all-cause mortality rate at 3 years for NICM patients with and without an ICD/CRT-D was 13.1% and 18.3%, respectively (HR 0.51, 95% CI 0.38–0.68, $p < 0.001$). Similarly, all-cause mortality at 3 years in ICM patients was 13.8% in those with a device and 19.9% in those without an ICD/CRT-D (HR 0.54, 95% CI 0.33–.0.88, $p = 0.011$). The time to first device therapy, time to first shock, and time to first antitachycardia pacing (ATP) therapy were not significantly different between groups ($p \geq 0.263$).

Conclusions: In this large data set of patients with a guideline-based PP ICD indication, defibrillator device implantation conferred a significant mortality benefit in both NICM and ICM patients. The rate of appropriate device therapy was also similar in both groups.

* Corresponding author. Pan Max Hospital, Max Super Specialty Hospital, Saket, New Delhi, 110017, India.
E-mail address: drbalbirs@gmail.com (B. Singh).

https://doi.org/10.1016/j.ihj.2023.01.010

Clinical trial registration: ClinicalTrials.gov ID: NCT02099721.

Abbreviations

ATP	antitachycardia pacing
CRT-D	cardiac resynchronization therapy defibrillator
ICD	implantable cardioverter defibrillator
ICM	ischemic cardiomyopathy
NICM	non-ischemic cardiomyopathy
NSVT	non-sustained ventricular tachycardia
PVC	premature ventricular contraction
SCA	sudden cardiac arrest
SCD	sudden cardiac death
VF	ventricular fibrillation
VT	ventricular tachycardia

1. Introduction

Implantable cardioverter defibrillators (ICDs) are the gold standard in the treatment of patients at high risk of ventricular tachyarrhythmias (ventricular tachycardia [VT], ventricular fibrillation [VF]) for both primary and secondary prevention (SP) of sudden cardiac death.[1–5] However, primary prevention (PP) ICD utilization remains low in some regions and varies greatly across geographies, due in part to the heterogeneous degree of reported benefit that ICDs confer to all PP patients.[6]

The Improve Sudden Cardiac Arrest (Improve SCA) trial was initiated in 2014 as an effort to collect data on understudied populations around the world. An initial report of the trial showed that the implant refusal rate among PP patients in these regions was 46.5%.[7] It was deemed that efforts to increase patient and physician awareness of SCA risk and ICD benefit would be important to address the gap between ICD-indicated patients and those that receive ICD therapy.[8,9]

Recent data from the DANISH trial on the efficacy of ICDs for PP of sudden cardiac death (SCD) in patients with non-ischemic cardiomyopathy (NICM) showed an overall reduction of SCD, but no significant reduction in all-cause mortality.[10] Studies since this publication have indicated that this data has affected a significant proportion of European practice in NICM PP ICD implantation.[11,12]

The Improve SCA study showed a mortality benefit despite the majority of the patients having NICM. This may provide an opportunity for new insight into the benefit of ICD therapy in NICM patients.[7] The current study will allow for further understanding of the current real-world mortality benefit of PP ICD implantation in patients with NICM. The aim of this analysis is therefore to compare the ICD benefit among the real-world cohort of ICM and NICM patients enrolled in the Improve SCA trial.

2. Material and methods

2.1. Study overview and enrollment

The previously published Improve SCA trial was a prospective, non-randomized, non-blinded, multi-center global study designed to evaluate the rate of ICD therapy for VT/VF in primary prevention patients with and without additional risk factors (PVC, Syncope, EF <25%, and NSVT) as compared to SP patients.[7,13] This study also compared the mortality rates between those implanted with a device (ICD/CRT-D) and those not implanted. Between March 26, 2014 and July 15, 2017, patients (n = 4222) were enrolled concurrently across regions where ICD utilization is low: Asia, South America, Eastern Europe, the Middle East, and Africa. All patients that were >18 years of age with a Class I indication for a single or dual-chamber ICD, or cardiac resynchronization therapy defibrillator (CRT-D) according to the ACC/AHA/HRS or ESC guidelines were eligible for participation.[4,5] Patients were then categorized as being either PP or SP.[14] Only PP patients that experienced a cardiomyopathy (ICM or NICM) were included in this analysis. This study was reviewed and approved by the ethics committee at each participating institution and followed the guidelines set forth by the Declaration of Helinski. Informed consent was obtained for all participating patients.

The decision to implant an ICD or CRT-D was left to the discretion of the patient and the physician. The reasons for refusal were documented for patients that chose not to undergo implantation and patients could select multiple reasons, which have been previously reported.[15]

2.2. Endpoints

Device therapy was used as a surrogate marker of SCA. The primary endpoints were, the risk of the time to the first appropriate VT/VF therapy including shock or anti-tachycardia pacing (ATP), the time to the first appropriate shock, the time to the first inappropriate shock, and the time to the first ATP, between ICM and NICM patients receiving ICD/CRT-D implantation for PP of SCA. The secondary endpoint was the risk of all-cause mortality in ICM and NICM patients receiving device therapy compared to those without implantation.

2.3. Statistics

All characteristics reported have been summarized using appropriate summary statistics. Variables on a continuous scale have been described as mean ± standard deviation. Categorical variables have been presented as percentages. Summary statistics have been reported with maximum of 1 decimal, as appropriate. The exposure time (months) has been computed from the date of implant to the date of last contact (follow-up visit, hospitalization, study exit, or death).

Survival curves were created using the Kaplan–Meier method, which does not adjust for other variables. Curves are ended when fewer than 20 patients are at risk. Hazard ratios were computed, and survival rates were compared using Cox proportional hazards methods. For the mortality analysis an adjustment was made for the baseline factors of age, sex, QRS duration, ICM, left bundle branch block (LBBB), NYHA Class, diabetes, LVEF, syncope, non-sustained ventricular tachycardia (NSVT), and premature ventricular contractions (PVCs). Multiple imputation was used to account for missing baseline factors. As implanted patients were generally less healthy at baseline, the aggregate effect of including these

variables was to decrease the hazard ratio between implanted and non-implanted patients. There was no adjustment for baseline factors for the other analyses. P-values are nominal, there was no adjustment for multiple comparisons. Analyses were performed with SAS® Version 9.4 (SAS Institute Inc.).

3. Results

3.1. Cohort characteristics

A total of 2429 PP patients from the Improve SCA study were included in this analysis.[7] In this cohort, 1848 were NICM PP patients indicated for ICD implantation, of which 1007 (54.5%) received either an ICD or CRT-D device. There were 581 ICM PP indicated patients, of which 303 (52.1%) received an ICD or CRT-D device (Fig. 1). Table 1 shows the baseline characteristics of the implanted patients in ICM and NICM groups, while Table 2 shows baseline characteristics for implanted and not implanted patients within each group. Patients were followed-up for an average of 20.8 ± 10.8 months.

3.2. Device therapy in implanted patients

A total of 1291 implanted patients (992 NICM and 299 ICM patients) were evaluated for the time to first ICD/CRT-D therapy for VT or VF episodes. Despite a numerical difference between groups, the statistical risk for time to the first device therapy, including appropriate shock and ATP, was not significantly different between ICM and NICM patients (HR 0.81, 95% CI 0.56–1.17, p = 0.263) (Fig. 2A). Similarly, the time to the first appropriate shock was not significantly different between the two groups despite the rate trending higher in NICM patients from 30 to 36 months (HR 0.89, 95% CI 0.57–1.39, p = 0.624) (Fig. 2B). The time to the first inappropriate shock trended higher in NICM versus ICM PP patients, but statistics revealed no significant difference between the two groups (HR 0.53, 95% CI 0.25–1.13, p = 0.099) (Fig. 2C). Lastly, the time to first ATP therapy was also not significantly different between the 2 groups (HR 0.83, 95% CI 0.52–1.31, p = 0.412) (Fig. 2D).

3.3. Device implantation on mortality

In ICM patients, those who were implanted with a defibrillator device had a lower risk of all-cause mortality compared to those without a device (adjusted HR 0.54, 95% CI 0.33–0.86, p = 0.011) (Fig. 3). Similarly, NICM patients who were implanted with a defibrillator device had a lower risk of all-cause mortality compared to those without a device (adjusted HR 0.50, 95% CI 0.38–0.68, p < 0.0001) (Fig. 3). The NICM group had a high rate of CRT-D implantation (55.9%), but there was no difference in mortality at 36 months between CRT-D (8.6%) and ICD (10.4%) patients in the NICM group (p = 0.26).

4. Discussion

In a contemporary cohort of patients (on current optimal medical therapy) in the aforementioned Improve SCA study, we saw one of the largest SCA relative risk reductions observed, with one of the lowest numbers needed to treat, highlighting ICD therapy in these regions is needed now more than ever.[7] Our data shows a significant mortality benefit in ICM and NICM PP ICD patients, and a non-significant difference in the rates of ICD therapy between ICM and NICM PP patients is also observed.

Sudden cardiac arrest continues to be a major cause of death in both ICM and NICM patients, and ICDs provide robust protection against SCA. As per the guidelines, ICD implantation is recommended as a secondary prevention measure for patients with LV dysfunction, and those who have survived serious ventricular arrhythmia irrespective of the aetiologies.[5,14] This indication

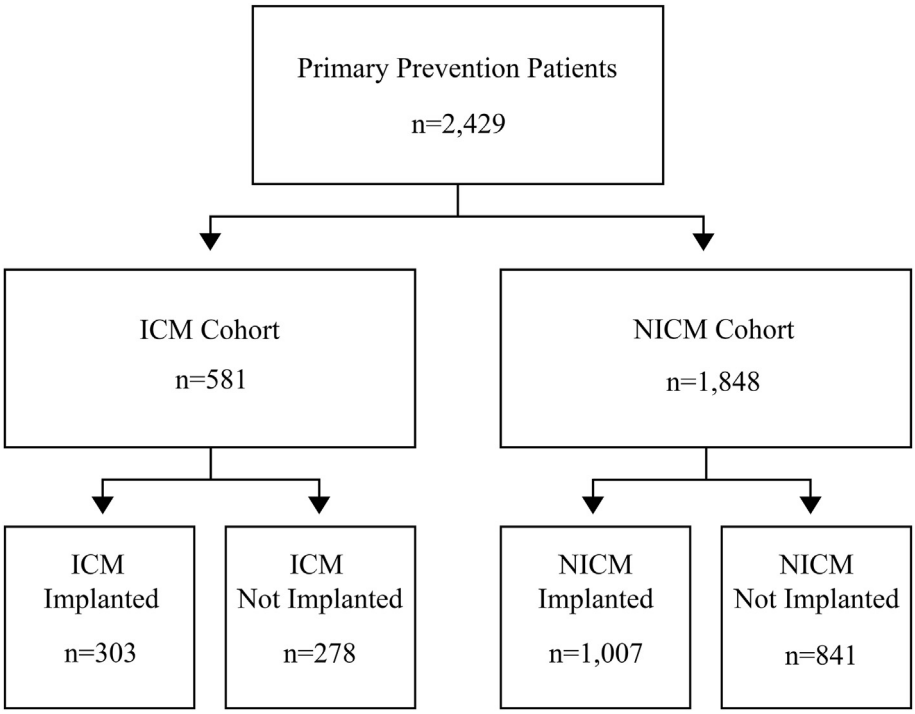

Fig. 1. Summary of PP patients included in the analysis. A total of 2429 PP patients were enrolled in the study. Patients were split into 2 groups based on whether their cardiomyopathy was ischemic or non-ischemic. The groups were further subdivided based on ICD/CRT-D implant status. ICM = ischemic cardiomyopathy; NICM = nonischemic cardiomyopathy.

Table 1
Baseline characteristics of the NICM and ICM PP patients of the Improve SCA study in this analysis.

Variable	ICM Implanted N = 303	NICM Implanted N = 1007	P value
Age (years)	64.5 ± 11.0	60.0 ± 11.7	<0.0001
Male (%)	85.5%	70.9%	<0.0001
QRS duration (ms)	122.7 ± 33.7	136.0 ± 35.9	<0.0001
LBBB (%)	20.1%	35.0%	<0.0001
NYHA Class III/IV (%)	45.9%	63.6%	<0.0001
Diabetes (%)	40.9%	25.7%	<0.0001
LVEF (%)	26.8 ± 5.4	26.1 ± 5.7	0.0549
NSVT (%)	33.0%	38.5%	0.0812
PVCs (%)	45.9%	54.1%	0.0117
Syncope (%)	11.9%	7.7%	0.0251
Hypertension (%)	50.5%	34.7%	<0.0001
Myocardial Infarction (%)	100.0%	4.3%	<0.0001
CRT-D Implanted %	34.0%	55.9%	<0.0001
Device chambers (%):			<0.0001
Single	44.2%	32.0%	
Dual	21.8%	12.1%	
Triple	34.0%	55.9%	
Anti-arrhythmics[a]	35.0%	47.1%	0.0002
Beta blockers	72.3%	72.2%	0.9776
ACE Inhibitors - Angiotensin II Receptor Blockers	72.6%	71.8%	0.7833
Diuretics	82.2%	86.2%	0.0837

ACE = angiotensin-converting enzyme, CRT-D = cardiac resynchronization therapy-defibrillator, ICD = implantable cardiac defibrillator, ICM = ischemic cardiomyopathy, LBBB = left bundle branch block, LVEF = left ventricular ejection fraction, ms = milliseconds, NICM = nonischemic cardiomyopathy, NSVT = nonsustained ventricular tachycardia, NYHA = New York Heart Association, PVC = premature ventricular contractions.
[a] Excluding beta blockers.

Table 2
Baseline characteristics of all PP patients.

Variable	ICM Implanted N = 303	NICM Implanted N = 1007	ICM Not Implanted N = 278	NICM Not Implanted N = 841
Age (years)	64.5 ± 11.0	60.0 ± 11.7	62.0 ± 12.1	57.1 ± 13.8
Gender Male (%)	85.5%	70.9%	87.1%	74.1%
QRS duration (ms)	122.7 ± 33.7	136.0 ± 35.9	112.4 ± 27.5	117.0 ± 30.8
LBBB (%)	20.1%	35.0%	14.4%	19.5%
NYHA Class III/IV (%)	45.9%	63.6%	37.4%	50.9%
Diabetes (%)	40.9%	25.7%	42.5%	24.8%
LVEF (%)	26.8 ± 5.4	26.1 ± 5.7	27.7 ± 5.2	26.5 ± 6.1
NSVT (%)	33.0%	38.5%	18.7%	26.9%
PVCs (%)	45.9%	54.1%	46.0%	45.3%
Syncope (%)	11.9%	7.7%	3.2%	3.6%
Congestive Heart Failure	35.3%	44.1%	24.5%	41.5%
Hypertension (%)	50.5%	34.7%	43.9%	35.1%
Myocardial Infarction (%)	100.0%	4.3%	100.0%	6.4%
CRT-D Implanted	34.0%	55.9%		
Anti-arrhythmics[a]	35.0%	47.1%	32.0%	39.6%
Beta blockers	72.3%	72.2%	83.5%	80.4%
ACE Inhibitors - Angiotensin II Receptor Blockers	72.6%	71.8%	71.9%	72.7%
Diuretics	82.2%	86.2%	84.9%	84.2%

Abbreviations are the same as in Table 1.
[a] Excluding beta blockers.

remains free from controversy. However, ICD use for primary prevention in NICM has generated debate due to the heterogeneity of results from major trials.[10,16]

4.1. Past trials showed contradicting results using ICDs for PP in NICM patients

The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), which enrolled patients with both ICM and NICM with an LVEF <35% and NYHA class II or III symptoms, demonstrated an all-cause mortality benefit with ICD in both ICM and NICM patients.[17] This has been the guideline recommendation for ICD therapy in patients with LVEF <35%, class II- III symptoms and on optimal medical management.[5]

In the recent DANISH trial, there was no benefit with ICD on mortality in patients with NICM in the PP setting, leading to controversy on the use of ICD for PP in NICM. Several reasons may have attributed to a benefit not being observed: this was a contemporary trial, pharmacotherapy use has improved over the last few decades which may have brought about a reduction in SCD, the rates of death were higher in older patients (over 68 years), and the limited cohort of patients (n = 556) were enrolled from only one geography (Denmark).[10]

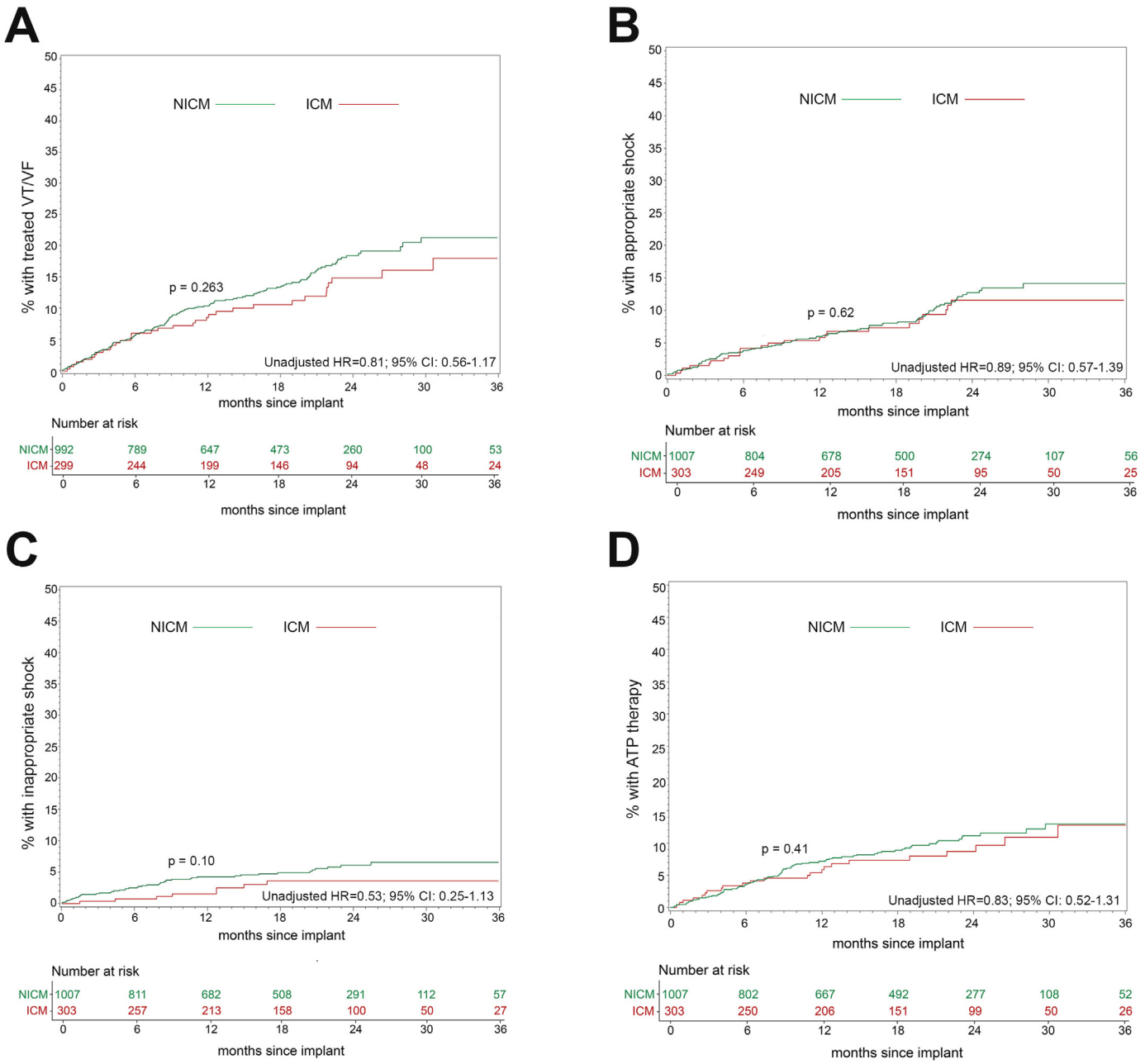

Fig. 2. Time to first device therapy in NICM and ICM patients. **(A–D)** Kaplan–Meier plots depicting time to: first ATP therapy or appropriate shock **(A)**, appropriate shock only **(B)**, inappropriate shock only **(C)**, or ATP therapy only **(D)**. NICM and ICM patients depicted by green and red lines, respectively. Tables represent the number still at risk at that specific time-point. P-values generated by comparing NICM to ICM. Hazard ratios are for ICM/NICM. ATP = antitachycardia pacing; CI = confidence interval; HR = hazard ratio; other abbreviations same as in Fig. 1.

The German Device Registry (DEVICE), a nationwide, prospective registry with one-year follow-up investigating 5451 patients receiving device implantations in 50 German centers, supports the recently published results of the DANISH trial. Like the DANISH trial, the influence of increased age may also play a role in limiting the potential beneficial effect of ICD therapy.[10,18] This age factor in PP NICM device benefit was further shown in the meta-analyses of randomized controlled trials proposed by Barakat et al.[19]

The DANISH trial rapidly changed physician attitudes regarding ICD indications in the NICM PP patient population and clinical trials did not provide conclusive evidence concerning the benefit of prophylactic ICDs in patients with severe NICM.[12,20] Recently conflicting results in terms of all-cause mortality and mortality from certain subgroups of SCD, in patients with NICM were obtained by systematic review, analysis, and meta-analysis of previous trials.[21,22]

4.2. Improve SCA trial, while having a more diverse cohort, reinforces results from the landmark SCD-HeFT trial

The sub-analysis of the Improve SCA trial presented here provides further understanding of the current, real-world benefit on

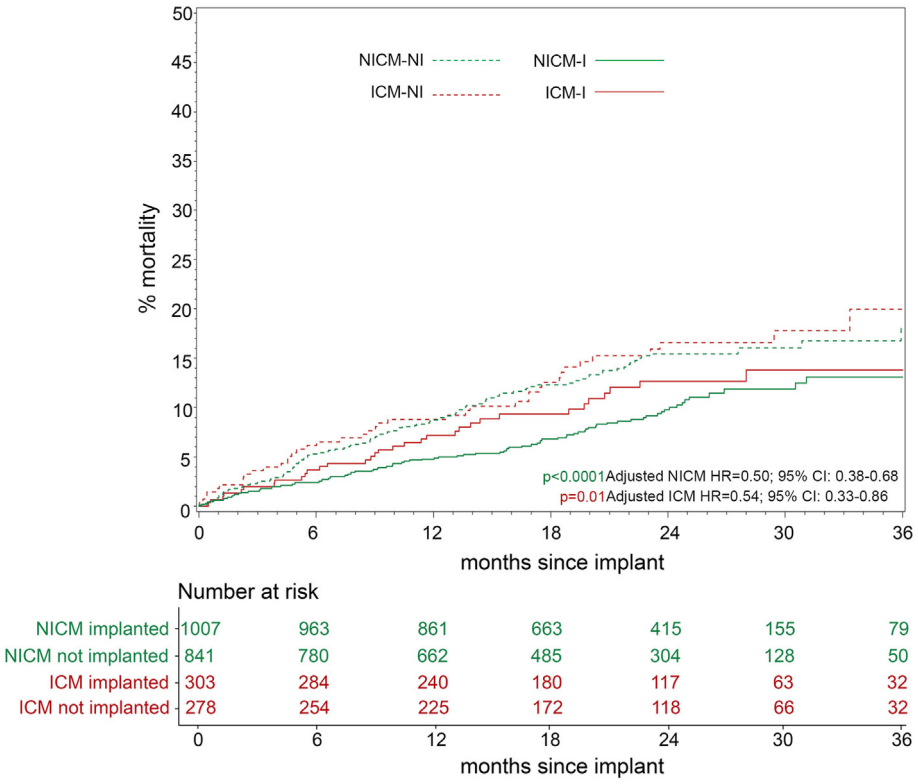

Fig. 3. Effect of ICD/CRT-D implantation status on mortality in both NICM and ICM patients. Kaplan–Meier plot to compare mortality between ICD implanted (solid line) and non-implanted (dashed line) NICM (green) and ICM (red) patients. Table below represents the number still at risk at that specific time-point. P-values generated by comparing implanted vs not implanted in ICM and NICM groups. Hazard ratios are implanted/not implanted for NICM and ICM. NICM/ICM-NI = NICM/ICM not implanted; NICM/ICM-I = NICM/ICM implanted; other abbreviations same as in previous figures.

all-cause mortality of PP ICD implantation in patients with NICM. The Improve SCA trial has some unique features: a) it was carried out in China, India, Brazil and many east European countries which were never a part of major randomised trials, and it provides real world data of ICD usage in this population, b) a large number of patients (n = 4222) were recruited in this trial, c) the proportion of patients with NICM was much higher than ICM, which is a pattern in most of the countries that recruited patients, d) the usage of beta blockers and ACE/ARB inhibitors was high.

This subset analysis has specifically looked at the cohort of patients with ICM and NICM with a PP indication for ICD therapy. There was no significant difference in the time to first appropriate shock and both groups had significant mortality reductions with ICDs. The mortality reduction observed was even greater in the NICM group. The results are similar to the SCD-HeFT trial published in 2005 wherein the NICM subgroup had a relative and absolute survival benefit similar to the ICM subgroup (NICM HR: 0.73; 5-year mortality rate 21% in the ICD group and 28% in the placebo group, with an absolute mortality difference of 7%). Thus, results of our contemporary study analysis reinforce the results of the SCD-HeFT trial and support the guideline recommendation of PP in all patients with reduced ejection fraction (Table 1).[17]

The cohort of patients with NICM includes diverse diseases, including familial cardiomyopathy due to LMNA (lamin A/C gene) mutation and sarcoidosis, which clearly have high incidence of sudden death, and some others which may have significant scarring. Our results do not support the DANISH trial results which may be attributed to a diversely different global population cohort.[10]

4.3. Study limitations

This is a post hoc analysis of a non-randomized trial with the use of defibrillator therapy in patients with guideline-based indications. The device implantation was left to the discretion of physician/patient leading to collection of real-world data and not all patients were followed-up for the full 3 years. Lack of randomization leaves uncontrolled variability in patient management and concomitant therapy. Also, only Medtronic devices were implanted, and an assessment that includes all possible manufacturers may be a more accurate representation of the population.

The rate of CRT-D implantation was higher in the NICM group than in the ICM group, which might have affected the results, specifically the mortality rate due to improved LVEF from added CRT therapy. Several baseline characteristics differed between ICM and NICM patients, which may also affect the results. However, to control for this potential bias, we adjusted the mortality analysis to account for baseline characteristics that would most likely have an impact on mortality.

5. Conclusions

In this large global data set of patients with LVEF <35% and a guideline-based ICD indication of PP, we found that implantation of a defibrillator provided mortality benefit for both ICM and NICM PP patients, and the time to first appropriate VT/VF therapy was not significantly different between groups. Thus, NICM PP patients in our cohort benefited from implantable defibrillator therapy as

much as ICM patients and should be strongly considered for an implantable defibrillator.

What is already known?

The Improve SCA trial demonstrated that PP patients, in regions where ICDs are underutilized, benefit from implantable defibrillator therapy.

What this study adds?

This sub-analysis of the Improve SCA trial specifically shows the benefit of implantable defibrillator therapy for both ICM and NICM PP patients in underrepresented regions. This provides more clarity to clinicians in these regions when determining treatment for NICM PP patients.

Author disclosures

Drs Singh, Liu, Rodriquez, Chasnoits, Zhang and Ching have received steering committee fees from Medtronic and participated as principal investigators in the Improve SCA trial. Drs Hsieh and Huang were principal investigators in the Improve SCA and has received speaker fees from Medtronic. Dr Huang also received speaker fees/consulting fees from Boston Scientific and Abbott. Dr Rodriguez has received proctor/lecture fees from Boston Scientific, proctorship fees from Biosense Webster and Abbott. Dr Zhang has received speaker fees/consulting fees from Boston Scientific, Medtronic, Abbott, and Biotronik. Ms. O'Brien, Dr Lexcen, Mr. Cerkvenik, and Mr. Van Dorn are employees of Medtronic. Dr Ching has received honoria from Abbott, Biotronik, Boston Scientific and Medtronic. Dr. Joung has served as a speaker for Bayer, BMS/Pfizer, Medtronic, and Daiichi-Sankyo, and received research funds from Medtronic and Abbott.

Funding

The trial was sponsored by Medtronic Inc.

Acknowledgments

The authors gratefully thank trial coordinators and principal investigators at each of the enrolling centers as well as Thomas Holmes, PhD for his help with manuscript preparation.

References

1. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346(12):877–883.
2. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med*. 1996;335(26):1933–1940.
3. Priori SG, Blomstrom-Lundqvist C. 2015 European Society of Cardiology Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death summarized by co-chairs. *Eur Heart J*. 2015;36(41):2757–2759.
4. Epstein AE, Dimarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: executive summary. *Heart Rhythm*. 2008;5(6):934–955.
5. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death–executive summary: a report of the American college of cardiology/American heart association task force and the European society of cardiology committee for practice guidelines (writing committee to develop guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death) developed in collaboration with the European heart rhythm association and the heart rhythm society. *Eur Heart J*. 2006;27(17):2099–2140.
6. Chia YMF, Teng TK, Tan ESJ, et al. Disparity between indications for and utilization of implantable cardioverter defibrillators in asian patients with heart failure. *Circ Cardiovasc Qual Outcomes*. 2017;10(11).
7. Zhang S, Ching CK, Huang D, et al. Utilization of implantable cardioverter-defibrillators for the prevention of sudden cardiac death in emerging countries: Improve SCA clinical trial. *Heart Rhythm*. 2020;17(3):468–475.
8. Kadakia RS, Link MS, Dominic P, Morin DP. Sudden cardiac death in non-ischemic cardiomyopathy. *Prog Cardiovasc Dis*. 2019;62(3):235–241.
9. Ganga HV, Maan A, Kevin Heist E. Should primary prevention ICDs still Be placed in patients with non-ischemic cardiomyopathy? A review of the evidence. *Curr Cardiol Rep*. 2018;20(5):31.
10. Kober L, Thune JJ, Nielsen JC, et al. Defibrillator implantation in patients with nonischemic systolic heart failure. *N Engl J Med*. 2016;375(13):1221–1230.
11. Higgins AY, Bjerre J, Parzynski CS, et al. Comparison of mortality and readmission in non-ischemic versus ischemic cardiomyopathy after implantable cardioverter-defibrillator implantation. *Am J Cardiol*. 2020;133:116–125.
12. Haugaa KH, Tilz R, Boveda S, et al. Implantable cardioverter defibrillator use for primary prevention in ischaemic and non-ischaemic heart disease-indications in the post-Danish trial era: results of the European Heart Rhythm Association survey. *Europace*. 2017;19(4):660–664.
13. Zhang S, Singh B, Rodriguez DA, et al. Improve the prevention of sudden cardiac arrest in emerging countries: the Improve SCA clinical study design. *Europace*. 2015;17(11):1720–1726.
14. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American college of cardiology/American heart association task force on practice guidelines (writing committee to revise the ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices) developed in collaboration with the American association for thoracic surgery and society of thoracic surgeons. *J Am Coll Cardiol*. 2008;51(21):e1–e62.
15. Singh B, Zhang S, Ching CK, et al. Improving the utilization of implantable cardioverter defibrillators for sudden cardiac arrest prevention (Improve SCA) in developing countries: clinical characteristics and reasons for implantation refusal. *Pacing Clin Electrophysiol*. 2018;41(12):1619–1626.
16. Masri A, Hammadah M, Adelstein E, Jain S, Saba S. Implantable cardioverter defibrillator in non-ischemic cardiomyopathy: a meta-analysis of randomized controlled trials. *Cardiovasc Diagn Ther*. 2017;7(4):397–404.
17. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med*. 2005;352(3):225–237.
18. Frommeyer G, Andresen D, Ince H, et al. Can we rely on Danish? Real-world data on patients with nonischemic cardiomyopathy from the German Device Registry. *Heart Ves*. 2019;34(7):1196–1202.
19. Barakat AF, Saad M, Elgendy AY, et al. Primary prevention implantable cardioverter defibrillator in patients with non-ischaemic cardiomyopathy: a meta-analysis of randomised controlled trials. *BMJ Open*. 2017;7(6), e016352.
20. Forleo GB, Solimene F, Pisano EC, et al. Long-term outcomes after prophylactic ICD and CRT-D implantation in nonischemic patients: analysis from a nationwide database of daily remote-monitoring transmissions. *J Cardiovasc Electrophysiol*. 2019;30(9):1626–1635.
21. Gimbel JR, Mackall J. Does anyone really believe the results of the Danish trial?-implanting an ICD in nonischemic cardiomyopathy patients. *Pacing Clin Electrophysiol*. 2017;40(5):459–462.
22. 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.