Title: The mortality analysis of primary prevention patients receiving a cardiac resynchronization defibrillator (CRT-D) or implantable cardioverter defibrillator (ICD) according to guideline indications in the Improve SCA Study.

Short Title: Improve SCA mortality analysis according to guideline indications

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ABBREVIATIONS:

ICD = implantable cardioverter defibrillator

CRT-D = cardiac resynchronization therapy-defibrillator

ACC/AHA/HRS=American College of Cardiology Foundation, the American Heart Association, and the Heart Rhythm Society

ESC = European Society of Cardiology

LVEF = left ventricular ejection fraction

LBBB = left bundle branch block

NSVT = non-sustained ventricular tachycardia

PP = primary prevention

PVC = premature ventricular contraction

SCA = sudden cardiac arrest

SCD = sudden cardiac death

VF = ventricular fibrillation

VT = ventricular tachycardia

ABSTRACT

Background: Despite a proven mortality benefit in primary prevention (PP) patients, the utilization of implantable cardioverter-defibrillators (ICD) and cardiac resynchronization therapy-defibrillators (CRT-D) remains low in many geographies.

Purpose: The objective of this analysis was to examine the mortality benefit in PP patients by guideline-indicated device type: implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy-defibrillator (CRT-D).

Methods: Improve SCA was a prospective, non-randomized, non-blinded multicenter trial that enrolled patients from regions where ICD utilization is low. PP patient's CRT-D or ICD eligibility was based upon the 2008 ACC/AHA/HRS and 2006 ESC guidelines. Mortality was assessed according to guideline-indicated device type comparing implanted and non-implanted patients. Cox proportional hazards methods were used, adjusting for known factors affecting mortality risk.

Results: Among 2,618 PP patients followed for a mean of 20.8 ± 10.8 months, 1,073 were indicated for a CRT-D, and 1,545 were indicated for an ICD. PP CRT-D-indicated patients who received CRT-D therapy had a 58% risk reduction in mortality compared to those without implant (adjusted HR 0.42, 95% CI: 0.28-0.61, P<0.0001). PP patients with an ICD indication had a 43% risk reduction in mortality with an ICD implant compared with no implant (adjusted HR 0.57, 95% CI: 0.41-0.81, P=0.002).

Conclusions: This analysis confirms the mortality benefit of adherence to guideline-indicated implantable defibrillation therapy for PP patients in geographies where ICD therapy was underutilized. These results affirm that medical practice should follow clinical guidelines when choosing therapy for PP patients who meet the respective defibrillator device implant indication.

INTRODUCTION

Implantable cardioverter defibrillator (ICD) implantation for patients at risk of sudden cardiac arrest (SCA) has been well studied and is associated with a reduction in mortality and improved patient outcomes through multiple randomized controlled trials.(1-3) Recently, the Improve SCA study further confirmed the benefit of ICD/CRT-D implantation in primary prevention (PP) patients with additional risk factors including syncope, low ejection fraction (EF), non-sustained ventricular tachycardia (NSVT), and premature ventricular contractions (PVC). Importantly, this study demonstrated a 49% relative risk reduction in mortality among patients (with these additional risk factors) from regions around the world, including Asia, Latin America, Eastern Europe, the Middle East and South Africa that have been largely underrepresented in some of the landmark ICD studies.(4)

Despite the multitude of evidence of the beneficial effects of ICD therapy to prevent SCA, use of guideline-indicated ICD therapy remains low in many regions of the world.(5-8) While some of the patient barriers to life-saving device implantation have been preciously summarized (4), there is less known about practice patterns and the level of trust regarding guideline adherence in device choice. The guidelines provide clear recommendations on ICD or cardiac resynchronization therapy-defibrillator (CRT-D) implantation, However if they are slow to be adopted or are applied inconsistently, they fail to translate into improved patient care. Geographical variations in practice patterns, variations in patient population, and its impact on patient care has not been well characterized in many of the developing regions around the world, or well represented in landmark trials.

The Improve SCA study presents a unique opportunity to gain greater insight into practice patterns, and patient outcomes as a result of the device choice according to guideline

recommendations. The objective of this analysis was to evaluate the mortality benefit for PP patients within the Improve SCA study population who received the device that they were indicated for (CRT-D or ICD).

METHODS

Study Design

The study design and results of the Improve SCA Study have been previously described.(4, 9) Briefly, the Improve SCA Study (ClinicalTrials.gov ID: NCT02099721) was a prospective, non-randomized, non-blinded, multicenter global study enrolling ICD-indicated patients designed to assess the rate of ventricular tachycardia (VT) and ventricular fibrillation (VF) in implanted patients, and to compare mortality between implanted and non-implanted patients. Patients were enrolled from geographies in which clinically indicated ICD utilization is low including: Asia, Latin America, Eastern Europe, the Middle East, and South Africa. Patients at least 18 years of age with a class I indication for an ICD, or indicated for CRT-D according to current clinical guidelines were eligible for study participation.(10, 11) The decision to implant or not implant an ICD or CRT-D was determined by the patient and physician (it was not dictated by the study). The study protocol was approved at each participating institution and each patient provided written informed consent prior to enrollment.

For this post hoc analysis, the Improve SCA PP patient cohort were classified as CRT-D-indicated (based on the 2015 practice guidelines from the European Society of Cardiology [ESC]) or ICD indicated (based on the class 1 indication from the 2008 American College of Cardiology Foundation, the American Heart Association, and the Heart Rhythm Society guidelines [AHA/ACC/HRS]).(12, 13)

Class I indications for CRT include left ventricular ejection fraction (LVEF) ≤ 35%, left bundle branch block (LBBB) with a QRS ≥150 ms, NYHA Class II, III, or ambulatory with Class IV symptoms. Class II indications for CRT include LVEF ≤ 35%, with LBBB QRS 120-149 ms or non-LBBB QRS ≥ 150 ms, and NYHA Class II, III, or ambulatory Class IV, or non-LBBB 120-149 with NYHA III or IV. (Table 1)

Class 1 indications for ICD therapy were based on the 2008 AHA/ACC/HRS guidelines. PP includes patients who are at risk but have not yet had an episode of VT, VF or resuscitated cardiac arrest.(12)

Analysis Endpoints

The aim of this post hoc analysis of the Improve SCA study(4) was to assess the mortality outcome of guideline-indicated PP patients who received a CRT-D or ICD device vs those who did not. Secondary analyses were done to examine the survival benefit in patients with Class I or Class II indication for CRT-D.(14)

Statistical Analysis

Means are reported as mean ± standard deviation. 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 (HR) were computed, and survival rates were compared using adjusted Cox proportional hazards methods. The baseline pre-specified factors used for adjustment were age, sex, QRS duration, ischemic cardiomyopathy, left bundle branch block, 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. Subgroup analysis was not pre-specified. Groups were chosen based on

common cut-offs (e.g., 65 years for age). P-values are nominal, there was no adjustment for multiple comparisons.

RESULTS

Patient Characteristics

There were 2,696 PP patients in the Improve SCA study (4). A total of 78 patients were excluded from this analysis due to missing baseline QRS duration, leaving 2,618 analyzable patients. Of these analyzed PP patients, 1,073 met indication for CRT-D therapy (394 with a Class 1 indication, and 679 with a Class II indication). The remaining 1,545 patients met indication for an ICD implantation (Figure 1). The majority of the PP patient cohort had non-ischemic cardiomyopathy and were taking guideline-directed medications (at the baseline visit) for high blood pressure, arrhythmias, and heart failure. The mean follow-up was 21.5 ± 10.1 months.

CRT-D Indicated Patients

Of the CRT-D indicated patients, 54% received a CRT-D implantation, 11% received an ICD, and 34% had no implant at all. Patients with a Class II indication for CRT-D were more likely to receive an ICD (98%) or no implant, than Class I indicated CRT-D patients.

Among all CRT-D indicated patients, differences across baseline characteristics were observed between those who received a CRT-D (n=582) vs an ICD (n=125). The main differences were QRS duration (163± 26 ms vs 141±21 ms), ischemic cardiomyopathy (14.6% vs 22.4%), LBBB (63.1% vs 24%), NSVT (34.0% vs 51.2%) and PVC's (51.5% vs 63.2%). CRT-D indicated patients who received any device (CRT-D or ICD) vs those who did not receive an implant (n=366) had differences in QRS (159 ± 26 vs 152 ± 24 ms), LBBB (56.2% vs 48.4%), diabetes (28.6% vs. 34.3%), NSVT (37.1% vs 27.0%), and syncope (7.6% vs 2.7%).Table 2

All-cause Mortality in CRT-D Indicated Patients

Among PP patients indicated for CRT-D, those who received CRT-D had better survival (Figure 2) than those who did not receive a device (CRT-D or ICD). Specifically, patients indicated for CRT-D who received a CRT-D device had a statistically significant 58% risk reduction in mortality compared to those with no implant (adjusted HR 0.42, 95% CI: 0.28-0.61, P<0.0001). There was an observed 41% risk reduction for CRT-D PP indicated patients who received an ICD compared to no implant (adjusted HR 0.59, 95% CI: 0.34-1.01, P=0.05).

When patients received CRT-D according to guideline indications (12, 13), there was a significant reduction in mortality regardless of whether they were Class I or Class II CRT-D indicated (Figure 3). A 63% relative risk reduction in mortality risk was observed in the Class I CRT-D implanted group (adjusted HR 0.37, 95% CI: 0.18-0.78, P = 0.005) and Class II CRT-D-indicated patients had a 53% relative reduction in mortality risk, when treated with a CRT-D device over no implant (adjusted HR 0.47, 95% CI: 0.28-0.77, P=0.003).

A subgroup analysis was conducted to test for the interaction among baseline variables for the impact of CRT-D on mortality. There was an observed benefit to CRT-D implantation across all subgroups including age, gender, QRS duration, QRS morphology, NYHA class, and cardiomyopathy status. When comparing use of a CRT-D or ICD in CRT-D-indicated patients, most of the subgroups observed benefit from CRT-D over ICD. Exceptions were females (where there were only 26 with an ICD implanted) and QRS duration less than 150ms. (Figure 4)

ICD Indicated Patients

Of the 1,545 PP patients who met criteria for an ICD, 37% received an ICD, 6.1% received CRT-D implantation, and the majority 57.3% did not receive any implant.

Among ICD-indicated patients, differences across baseline characteristics were observed between those who received an ICD (n=564) vs. those who received a CRT-D (n=95). The main differences were QRS duration (102±16 ms vs.117± 27 ms), ischemic cardiomyopathy (29.6% vs. 15.8%), LBBB (2.5% vs.13.7%), NSVT (33.9% vs. 47.4%), PVC's (48.4% vs. 61.1%) and hypertension (47.3% vs. 30.5%). Those who received either device had many differences from those who did not have an implant, with the device patients being less healthy than the non-implanted patients in all variables (Table 2).

All-cause Mortality in ICD Indicated Patients

PP patients who met the indications for ICD therapy (Figure 5) had a significant reduction in mortality with either an ICD (43%) or a CRT-D (64%) implant, compared to no implant (CRT-D: adjusted HR 0.36, 95% CI: 0.18-0.75, P=0.006, ICD: adjusted HR 0.57, 95% CI: 0.41-0.81, P=0.002). Mortality was similar between those receiving a CRT-D vs. an ICD (adjusted HR 1.00, 95% CI: 0.48-2.09, P>0.99).

DISCUSSION

After accounting for patient differences, there was still a significant mortality benefit for primary prevention patients who received the device therapy for which guideline indications were met. The major findings in this analysis are, PP Patients who fulfilled the indication for CRT-D therapy and received a CRT-D device had lower risk of mortality compared to those who did not receive CRT-D. And, PP Patients who fulfilled the indication for ICD therapy and received an ICD or CRT-D had lower risk of mortality compared to those who did not receive any device therapy. There is limited data published on the outcome of receiving the device as it is indicated. This information is crucial to improve practice standards in developing geographies. In this

analysis we observed that 34.1% of the CRT-D eligible PP patients did not receive any device. And of the ICD eligible PP patients, 57.3% did not receive any device therapy. Adherence to the guideline indications for CRT-D and ICD therapy is alarmingly discordant in many geographies despite the proven population health benefit.

In our analysis, the mortality benefit was not only significant in Class I indicated patients but also in Class II CRT-D-indicated PP patients when compared to those patients who did not receive a device implant. This benefit was observed across all subgroups examined including QRS morphology, QRS duration, NYHA class, and cardiomyopathy etiology. The benefit of CRT-D vs. ICD is questionable in non-LBBB patients regardless of NYHA class, especially in patients with a QRS 120-149ms. These findings are consistent with the MADIT-CRT study (15) which showed the hazard ratio of the primary endpoint was 1.24 in non-LBBB patients. Further study on CRT therapy in this patient population may be warranted.

It is important to note in this non-randomized study that among the non-implanted patients, there were some characteristics suggesting better health than those who received a device including; age, NYHA class, congestive heart failure status, PVCs, LBBB, and QRS (as shown in the baseline characteristics Table 2). While the reported hazard ratios are adjusted for many of these factors, the visible curves in the figures are not, therefore the baseline health status of non-implanted vs implanted patients may have an even more significant benefit than what is reflected in the unadjusted graph.

Adherence to the CRT-D Therapy Effect on Mortality

The COMPANION trial randomized 1,520 ambulatory patients with NYHA class III or IV to optimal medical therapy, CRT, or CRT-D.(16) Both CRT and CRT-D significantly reduced the

combined primary end points of time to death (P=0.014) or hospitalization for any cause (P=0.01). The CARE-HF trial (n=813 patients) showed that CRT improves the symptoms and reduces the risk of death in patients with heart failure and cardiac desynchrony.(17) The RAFT trial (n=1798 patients) studied NYHA class II and III HF patients with a wide QRS and left ventricular systolic dysfunction, and found that CRT-D therapy (on optimal medical therapy) reduced mortality and HF hospitalizations over ICD alone (P<0.001).(18) These trials all led to the consensus that CRT has been well-established as an important therapy to reduce all-cause mortality, relieve the symptoms of HF, and to improve left ventricular function in patients with advanced HF.(19)

In this analysis we observed that implantation of a CRT-D reduced the mortality risk by 63% (p=0.005) in patients with class I indication for CRT-D therapy, and the reduction was 53% (p=0.003) for Class II CRT-D indicated patients, compared to those who did not receive a device.

Adherence to ICD Therapy Effect on Mortality

ICD is the standard therapy for prevention of sudden cardiac death (SCD) in high-risk patients. (13) Current practice guidelines therefore recommend an ICD implantation for high-risk patients to prevent SCD regardless of ischemic or non-ischemic cardiomyopathy.(13) However, there is more data on the effect of ICD therapy in patients with ischemic heart disease than there is on patients with non-ischemic heart diseases.(20, 21) Hauga et al. recently reported that only 40% of medical centers in Europe routinely implanted an ICD for primary prevention in patients with non-ischemic heart disease. They suggest that clinical practice was influenced by the DANISH trial(22), which did not support device implantation in NICM patients. Huaga et al. called for further investigation in the NICM patient population ICD benefit.(23)

In this study a large proportion of the implanted patients had NICM (56%). We observed that in PP patients who were indicated for an ICD, and received implantation of either an ICD or CRT-D had a significantly reduced mortality risk compared to those without a device implanted (ICD adjusted HR: 0.57, p=0.002, CRT-D HR: 0.36, P=0.006). Using subgroup analysis, our data estimates that, when indicated for CRT-D implant, ischemic (46% reduction) and non-ischemic (30% reduction) showed benefit with CRT-D over ICD.

Past studies have shown that although indicated, patients do not consistently receive the appropriate device.(7, 24-26) This is a barrier to optimizing patient outcomes, quality of life and long-term cost-effectiveness.(27-30) The consistent reasons for underutilization cited throughout the literature are, financial, the question of cost-effectiveness, and belief in the therapy benefit regarding risk benefit ratio.(31) The Improve SCA study found the main reasons to be financial, reimbursement issues, and not believing in the benefits of the therapy.(32) A recent study in Turkey found that only one-third of eligible chronic HF patients receive a CRT-D and one-fifth receive an ICD. The main reason was cited that physicians do not evaluate patients for or offer the option of device therapy due to financial and cost-effectiveness concerns.(8) A Swedish study found only 10% of eligible HF patients received ICD therapy despite a demonstrated one year and five-year reduction in all-cause mortality (HR, 0.73 and 0.88, respectively).(33) The main reason cited for underutilization was due to a clinical questioning of the risk-benefit ratio of PP ICD therapy in SCD prevention. The Schrage et al. study findings support guideline recommendations of PP ICD therapy in HF with low EF and call for better clinical practice.(33)

Raatikainen et al. examined the use of device therapy in the European Society of Cardiology countries over the course of a decade. They found significant differences in training and

certification requirements for physicians and well as economic reasons contributing to the limited use of ICD therapy for PP SCD prevention.(6)

Clinical Implication

This contemporary study supports previous clinical evidence that PP CRT-D therapy, where indicated, significantly improves survival, specifically in the regions of the world where device therapy is underutilized. Patients who did not meet CRT-D indication but were ICD-indicated only, also achieved a significant mortality benefit vs no implant (43% mortality benefit). There is a clear mortality benefit in receiving defibrillator therapy, and PP patients who met CRT-D indication realized an even greater benefit when they received the guideline indicated device. This point is supported by data in several other studies, such as RAFT and MADIT CRT (3, 15, 18).

There is an apparent need for the dissemination of clinical and economic data to facilitate the progression of evidence-based medical practice to reinforce reimbursement initiatives for the improvement of population health in underserved geographies. This analysis supports continued work to advance the efficacy of patient care through evidence-based decisions. Enhancing adherence to clinical guidelines will improve clinical outcomes as observed in this study.

LIMITATIONS

We acknowledge that this sub analysis has limitations. Patients were not randomized to capture the real-world clinical experience in these regions. However, hazard ratio adjustments were made to account for baseline medical differences. In addition, the choice to implant a device was left to the discretion of the physician and patient. To account for these population differences, baseline

medical factors were corrected for in the mortality analyses, however other unmeasured variables such as financial status could not be accounted for.

Another possible limitation is that the Improve SCA study(4) implant rates were higher than historical rates for these regions. Reasons for this higher implant rate are not known but are likely associated with the involvement of the physicians and patients in a clinical trial.

CONCLUSION

Receiving a defibrillation device significantly improves survival for primary prevention patients who meet the indicated guidelines.(14) There is an even greater effect on survival when CRT-D indicated patients receive CRT-D therapy. This analysis verifies that in many regions, many eligible patients do not receive ICD therapy according to the established guidelines. Our data further validates the importance of following evidence-based guidelines when choosing the appropriate cardiac therapy for primary prevention patients.

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452 **Table 1. Class I, Class II CRT-D Indications.**

Variable	CRT-D Class I	CRT-D Class II		
LVEF	≤ 35%	≤ 35%	≤ 35%	≤ 35%
LBBB	LBBB	LBBB	Non-LBBB	Non-LBBB
QRS Duration	≥ 150 ms	120-149	≥ 150 ms	120-149
NYHA Class	II, III, or IV	II, III, or IV	II, III or IV	III, IV

453 Indications from the 2015 ESC guidelines. CRT-D cardiac resynchronization therapy-defibrillator, LVEF-left ventricular ejection fraction,
454 LBBB-left bundle branch block, ms- milliseconds, NYHA-New York Heart Association

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Table 2. Baseline Characteristics

	CRT-D Indicated						ICD Indicated					
Variable	**CRT-D (n = 582)**	**ICD (n= 125)**	**P-Value**	**Any Device (n=707)**	**No Implant (n= 366)**	**P-Value**	**CRT-D (n = 95)**	**ICD (n = 564)**	**P-Value**	**Any Device (n=659)**	**No Implant (n= 886)**	**P-Value**
Age (years)	62.4 ± 10.7	62.5 ± 10.6	0.96	62.4 ± 10.7	61.8 ± 13.1	0.43	61.3 ± 11.9	59.6 ± 12.4	0.23	59.9 ± 12.3	57.2 ± 13.4	<0.0001
QRS Duration (ms)	163 ± 26	141 ± 21	<0.0001	159 ± 26	152 ± 24	<0.0001	117 ± 27	102 ± 16	<0.0001	104 ± 19	101 ± 17	<0.0001
LVEF (%)	26.4 ± 5.4	26.7 ± 5.2	0.58	26.5 ± 5.3	26.6 ± 5.8	0.80	26.5 ± 7.0	26.0 ± 5.7	0.49	26.1 ± 5.9	26.9 ± 5.9	0.01
Gender male	71.3%	79.2%	0.07	72.7%	74.3%	0.57	73.7%	78.5%	0.29	77.8%	80.4%	0.23
Ischemic CM	14.6%	22.4%	0.03	16.0%	18.6%	0.28	15.8%	29.6%	0.005	27.6%	22.1%	0.01
LBBB	63.1%	24.0%	<0.0001	56.2%	48.4%	0.02	13.7%	2.5%	<0.0001	4.1%	5.0%	0.42
NYHA III/IV	72.5%	76.8%	0.33	73.3%	69.7%	0.21	48.4%	40.8%	0.16	41.9%	34.9%	0.005
Diabetes	28.7%	28.2%	0.92	28.6%	34.3%	0.05	29.5%	32.9%	0.52	32.4%	28.6%	0.11
NSVT	34.0%	51.2%	0.0003	37.1%	27.0%	0.001	47.4%	33.9%	0.01	35.8%	21.2%	<0.0001
PVCs	51.5%	63.2%	0.02	53.6%	53.6%	0.99	61.1%	48.4%	0.02	50.2%	37.8%	<0.0001
Syncope	7.4%	8.8%	0.59	7.6%	2.7%	0.001	7.4%	9.2%	0.56	9.0%	4.2%	0.0001
Congestive Heart Failure	46.2%	46.4%	0.97	46.3%	42.1%	0.19	34.7%	39.7%	0.36	39.0%	36.5%	0.31
Hypertension	33.7%	34.4%	0.88	33.8%	38.3%	0.15	30.5%	47.3%	0.002	44.9%	38.1%	0.008
Antiarrhythmics excluding beta blockers	44.5%	52.8%	0.09	46.0%	43.4%	0.43	43.2%	39.9%	0.55	40.4%	32.7%	0.002
Beta blockers	75.9%	69.6%	0.14	74.8%	76.2%	0.61	63.2%	71.3%	0.11	70.1%	81.6%	<0.0001
ACE Inhibitors - Angiotensin II Receptor Blockers-Inhibitors	73.9%	71.2%	0.54	73.4%	70.8%	0.3583	65.3%	71.3%	0.24	70.4%	70.8%	0.88
Diuretics	87.3%	88.0%	0.83	87.4%	89.1%	0.4286	80.0%	83.2%	0.45	82.7%	80.8%	0.34

ACE= angiotensin converting enzyme, CM=cardiomyopathy, CRT-D cardiac resynchronization therapy-defibrillator, ICD= implantable cardioverter defibrillator, ms=milliseconds, LBBB= left bundle branch block, LVEF=left ventricular ejection fraction, NSVT=non-sustained ventricular tachycardia, NYHA=New York Heart Association, PVCs= premature ventricular contractions.

Figure Legends

Figure 1 – Implant status **s**ummary of PP patients included in the analysis.

Figure 2 – Mortality of CRT-D Indicated Primary Prevention Patients. All patients indicated for CRT-D are included, along with paired mortality comparisons of patients implanted with CRT-D or ICD, and patients not implanted. Hazard ratios and p-values are adjusted for differences in baseline characteristics.

Figure 3 – Mortality of CRT-D Class I and Class II indicated PP patients, CRT-D vs no implant, ICD vs no implant, and CRT-D vs ICD implant. A comparison of mortality between implanted and non-implanted patients with Class I (3A) and Class II (3B) indications for CRT-D. Hazard ratios and p-values are adjusted for differences in baseline characteristics.

Figure 4 – Subgroup analysis PP CRT-D indicated patients**.** Subgroup analysis of the effectiveness of CRT-D in reducing mortality vs. no implant (left panel), and vs. ICD (right panel) in patients indicated for CRT-D. Hazard ratios and p-values are adjusted for differences in baseline characteristics.

Figure 5 – Mortality of ICD Indicated PP patients. Includes all patients with a primary prevention indication for ICD but without a CRT-D indication comparing mortality rates between those implanted with CRT-D or ICD, and those not implanted. Hazard ratios and p-values are adjusted for differences in baseline characteristics.

Figure 1. Summary of PP Patients Included in the Analysis

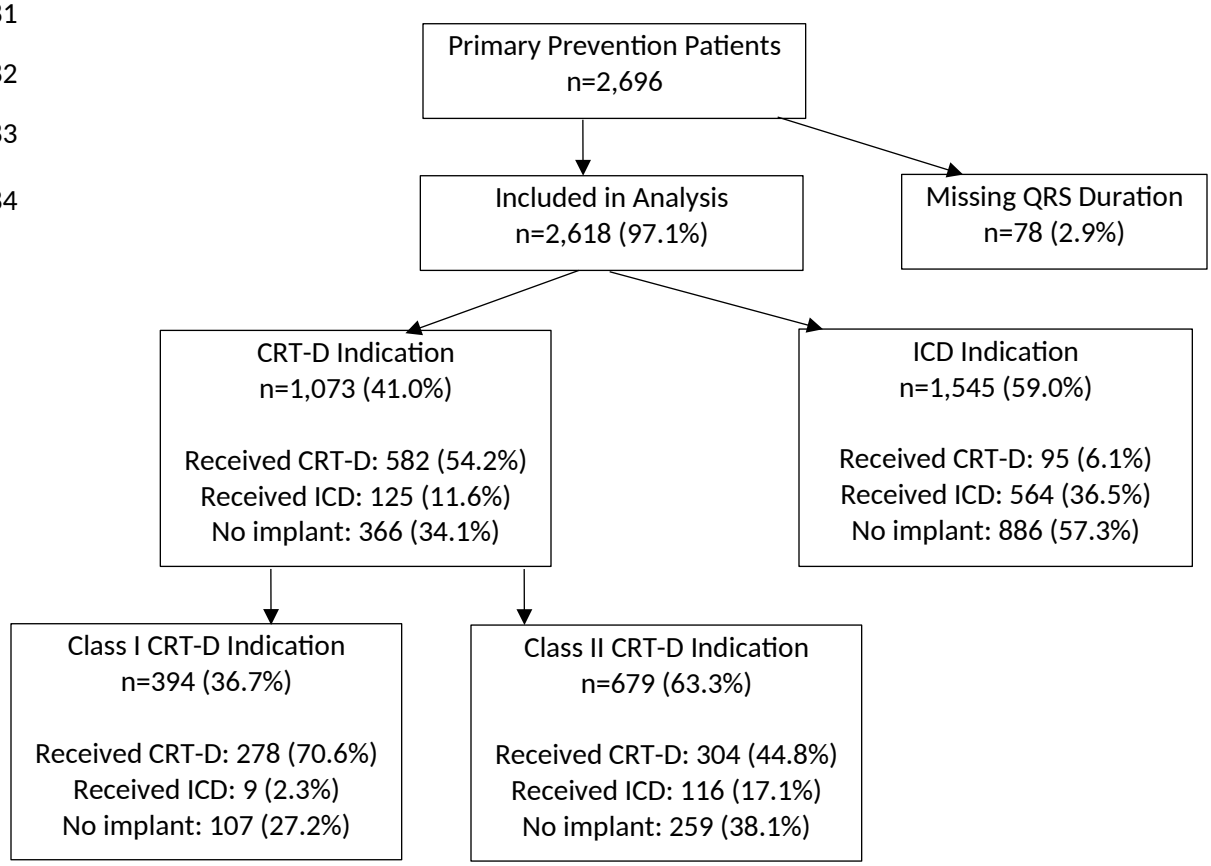
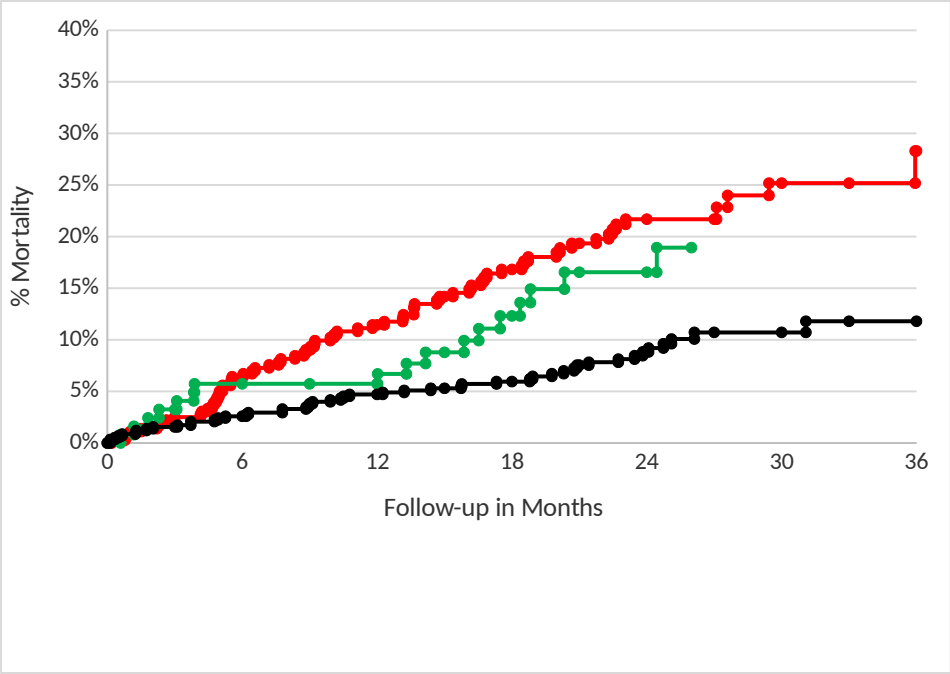


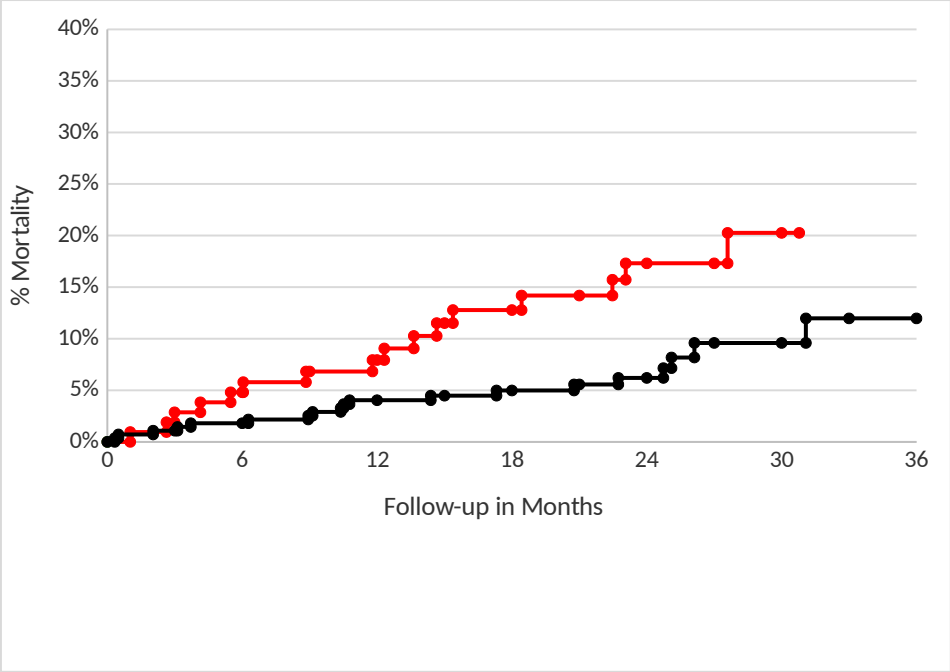
Figure 2. CRT-D Indicated Primary Prevention Patients



2. – Mortality of CRT-D Indicated Primary Prevention Patients. All patients indicated for CRT-D are included, along with paired mortality comparisons of patients implanted with CRT-D or ICD, and patients not implanted. Hazard ratios and p-values are adjusted for differences in baseline characteristics.

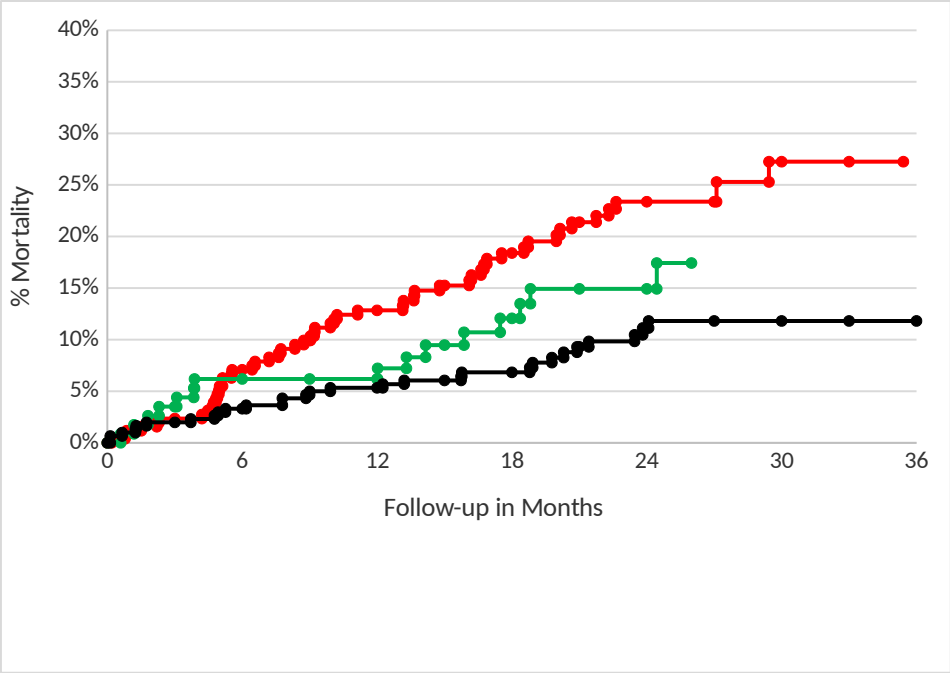
Figure 3. CRT-D Indicated Primary Prevention Patients by Indication Class

Figure 3A. Class I Indication



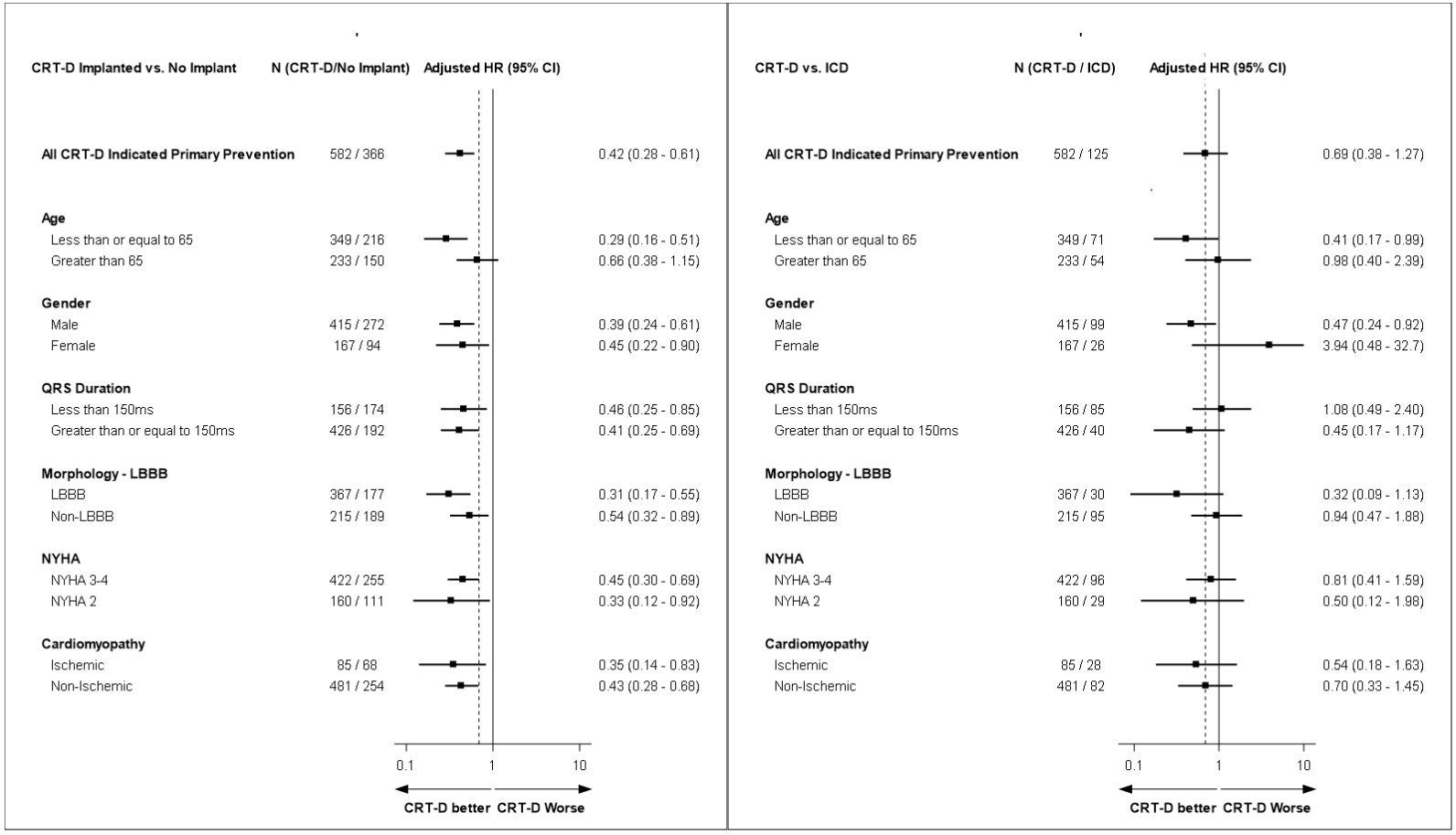
3A. Mortality of CRT-D Class I and Class II indicated PP patients, CRT-D vs no implant, ICD vs no implant, and CRT-D vs ICD implant. A comparison of mortality between implanted and non-implanted patients with Class I.

Figure 3B. Class II Indication



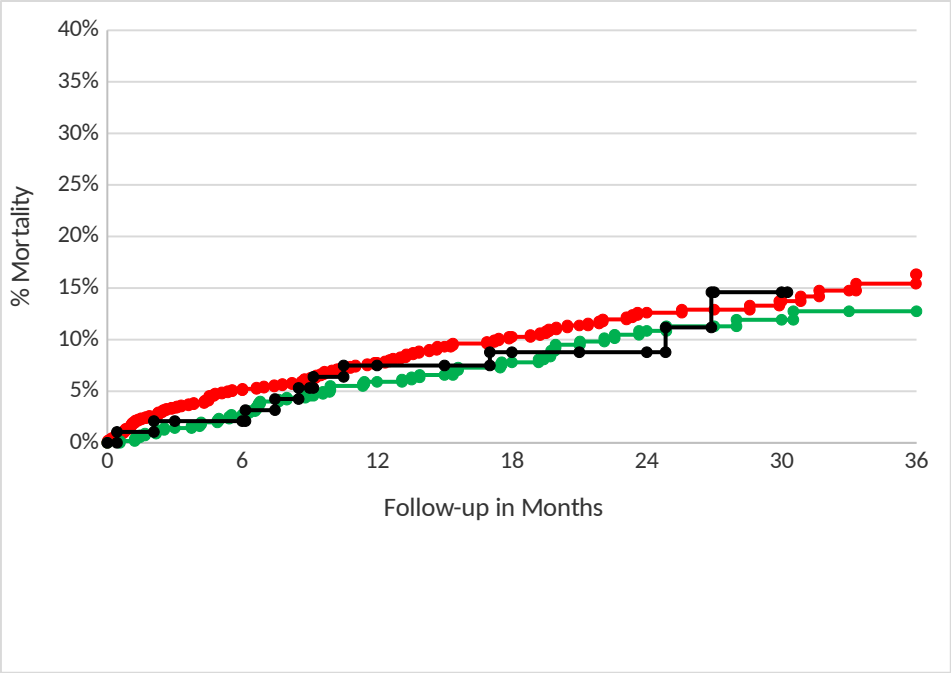
3B. Mortality of CRT-D Class I and Class II indicated PP patients, CRT-D vs no implant, ICD vs no implant, and CRT-D vs ICD implant. Class II indications for CRT-D. Hazard ratios and p-values are adjusted for differences in baseline characteristics.

Figure 4. Subgroup analysis of mortality in PP CRT-D indicated patients.



4. Subgroup analysis PP CRT-D indicated patients. Subgroup analysis of the effectiveness of CRT-D in reducing mortality vs. no implant (left panel), and vs. ICD (right panel) in patients indicated for CRT-D. Hazard ratios and p-values are adjusted for differences in baseline characteristics.

Figure 5. ICD Indicated PP patients



5. Mortality of ICD Indicated PP patients. Includes all patients with a primary prevention indication for ICD but without a CRT-D indication comparing mortality rates between those implanted with CRT-D or ICD, and those not implanted. Hazard ratios and p-values are adjusted for differences in baseline characteristics.