Cardiac resynchronization therapy pacemakers versus defibrillators in older non-ischemic cardiomyopathy patients

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ABSTRACT

Introduction: With the recent publication of the negative DANISH trial, the mortality benefit of the implantable cardioverter-defibrillator (ICD) has been put in question in patients with non-ischemic cardiomyopathy (NICM). Because a majority of patients in DANISH receive cardiac resynchronization therapy (CRT) devices, we investigated in the present study the survival of recipients of CRT pacemakers (CRT-P) versus CRT ICDs (CRT-D) in a cohort of older (≥75 years) NICM patients at our institution.

Methods: A total of 135 NICM patients with CRT device were identified (42 with CRT-P and 93 with CRT-D) and were followed to the endpoint of all-cause mortality. Overall survival was compared between the CRT-P and CRT-D groups with adjustment for differences in baseline characteristics.

Results: Over a median follow-up of 46 months from the time of CRT device implantation, there were 54 total deaths (40%): 14 in the CRT-P (33%) and 40 in the CRT-D (43%) groups. Overall, CRT-P recipients had similar unadjusted mortality compared to CRT-D recipients (hazard ratio [HR] 1.04, 95% confidence interval [CI] 0.56–1.93), and this remained unchanged after adjusting for unbalanced covariates (HR 0.95, 95% CI 0.47–1.89) including left ventricular ejection fraction, used of angiotensin converting enzyme inhibitors/angiotensin receptor blockers, and the Charlson comorbidity index.

Conclusion: Our data support that in older NICM patients with CRT devices, the addition of ICD therapy does not improve survival.

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1. Introduction

With the recent publication of the negative DANISH trial [1], the mortality benefit of the implantable cardioverter-defibrillator (ICD) has been put in question in patients with non-ischemic dilated cardiomyopathy (NICM) patients, despite it being recommended as a class I indication in this population according to the 2017 ACC/AHA/HRS guideline publication on management of patients with ventricular arrhythmias and prevention of sudden cardiac death [2]. Of note, 58% of all patients in the DANISH trial received cardiac resynchronization therapy (CRT) both in the ICD (CRT-D) and control (CRT-P) arms. Although subgroup analysis did not find a difference in the relative benefit of ICD therapy by CRT status [1], DANISH raises the question as to how much additional survival benefit the ICD provides over CRT in patients with NICM. In addition, subgroup analyses of DANISH [1] suggested that, in older patients in particular, ICD therapy has no incremental survival. Based on these data, the goal of our present study was to examine whether older NICM patients implanted with a CRT-D have decreased all-cause mortality compared to those implanted with a CRT-P device.

2. Methods

To study the effect of adding defibrillator to CRT in NICM patients, we analyzed patients who had undergone CRT device implantation between March 2002 and May 2013 at the University of Pittsburgh Medical Center hospitals. Patients were followed until death or last clinical encounter before December 21, 2015. The institutional review board of the University of Pittsburgh approved the study and the need for informed consent was waived. Patients with history of myocardial infarction, prior surgical or intervention- nal revascularization, and significant coronary artery disease classified by >75% obstructive lesion in 1 main coronary artery, or 2 or more epicardial vessel were excluded. In addition, patients with any prior history of sustained ventricular arrhythmias were...
3. Results

A total of 135 NICM patients with CRT device were identified (42 with CRT-P and 93 with CRT-D). Table 1 details the baseline characteristics of the overall population stratified by type of CRT device implanted. There were no significant differences in age, pre-implant serum creatinine level, QRS duration on the surface electrocardiogram, prevalence of diabetes mellitus, hypertension, or in the calculated Charleston Comorbidity index. Compared to CRT-P recipients, CRT-D patients had however lower baseline LVEF (24.1 ± 6.42 vs. 28.0 ± 5.50, p = 0.002) and higher usage of angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACE/ARB) and the Charleston comorbidity index.

| # Patients | TOTAL | CRT-P | CRT-D | P-value |
|------------|-------|-------|-------|---------|
| Age at Implant (years) | 81.0 ± 4.11 | 81.6 ± 5.26 | 80.7 ± 3.47 | 0.25 |
| Congestive Heart Failure | 107 (79.3%) | 36 (85.7%) | 71 (76.3%) | 0.25 |
| Hypertension | 95 (70.4%) | 30 (71.4%) | 69 (74.2%) | 0.33 |
| Diabetes mellitus | 33 (24.4%) | 8 (19.0%) | 25 (26.9%) | 0.42 |
| Peripheral Vascular Disease | 14 (10.4%) | 6 (14.3%) | 8 (8.6%) | 0.26 |
| Cerebrovascular Event | 15 (11.1%) | 4 (9.5%) | 11 (11.8%) | 0.78 |
| Dementia | 5 (3.7%) | 3 (7.1%) | 2 (2.2%) | 0.13 |
| Chronic Obstructive Pulmonary Disease | 25 (18.5%) | 10 (23.8%) | 15 (16.1%) | 0.21 |
| Connective Tissue Disease | 2 (1.5%) | 0 (0.0%) | 2 (2.2%) | 0.35 |
| Chronic Kidney Disease | 4 (3.0%) | 2 (4.8%) | 2 (2.2%) | 0.37 |
| Leukemia | 1 (0.7%) | 1 (2.4%) | 0 (0.0%) | 0.12 |
| Lymphoma | 7 (5.2%) | 4 (9.5%) | 3 (3.2%) | 0.10 |
| Solid Tumor | 35 (25.9%) | 9 (21.4%) | 26 (28.0%) | 0.54 |
| Charlson Comorbidity Index | 3.82 ± 1.75 | 4.28 ± 2.15 | 3.63 ± 1.52 | 0.051 |
| Left Ventricular Ejection Fraction (%) | 25.2 ± 6.40 | 28.9 ± 5.50 | 24.1 ± 6.42 | 0.002 |
| Left Ventricular End-Diastolic Volume (mm) | 45.0 ± 10.1 | 41.3 ± 10.1 | 46.4 ± 9.76 | 0.023 |
| Mitral Regurgitation | 54.9 ± 9.03 | 51.2 ± 7.61 | 56.2 ± 9.18 | 0.013 |
| Mild | 62 (45.9%) | 18 (42.9%) | 44 (47.3%) | 0.78 |
| Moderate | 38 (28.1%) | 11 (26.2%) | 27 (29.0%) | |
| Severe | 19 (14.1%) | 4 (9.5%) | 15 (16.1%) | |
| Serum Creatinine (mg/dL) | 1.33 ± 0.53 | 1.30 ± 0.43 | 1.34 ± 0.57 | 0.68 |
| QRS Width (ms) | 157 ± 28.3 | 152 ± 34.4 | 159 ± 24.9 | 0.21 |
| Beta-Blocker | 104 (77.0%) | 31 (73.8%) | 73 (78.5%) | 0.71 |
| ACE-I/ARB | 103 (76.3%) | 22 (52.4%) | 81 (87.1%) | <0.001 |
| Aldosterone Agonist | 15 (11.1%) | 2 (4.8%) | 13 (14.0%) | 0.12 |
| Amiodarone | 23 (17.0%) | 6 (14.3%) | 17 (18.3%) | 0.55 |

ACE-I/ARB – Angiotensin Converting Enzyme inhibitor/Angiotensin Receptor Blocker.
managing these patients.

The present analysis has limitations. First, its small sample size and its single center, retrospective, observational design may introduce inherent biases. We corrected for these potential biases using multivariate statistical adjustments and the results were consistent for both the unadjusted and adjusted models. In addition, the cause of death could not be ascertained in most patients in this dataset.

Our results support the main findings of the DANISH trial, which suggest that in the presence of a CRT device, ICD therapy may not portend further survival benefits, in older NICM patients. This highlights the need for a pivotal, non-inferiority, randomized control trial of CRT-P versus CRT-D in this population. Additionally, careful consideration of patients’ goals, comorbidities, and frailty measures are essential when prescribing CRT-D or CRT-P in this population.

Disclosures

Drs. Wang, Sharbaugh, Althouse and Mulukutla have no disclosures to make; Dr. Saba discloses research support from NHLBI, Boston Scientific and Medtronic.

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