Patients Initially Evaluated During Cardiac Catheterization May Not be Offered an Implantable Cardioverter Defibrillator Despite Meeting Implantation Criteria

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RESUMEN

Introducción: Los criterios para un implante de un Cardiodesfibrilador Implantable (CDI) han sido claramente establecidos por múltiples guías internacionales basadas en ensayos clínicos. Sin embargo algunos pacientes reciben un CDI sin ajustarse a estas recomendaciones y similaramente una proporción importante de pacientes que cumplen con los criterios para recibir un CDI no son referidos para recibir esta terapia que salva vidas. Con el propósito de investigar la posibilidad que algunos pacientes con indicación clara no son referidos para un implante de CDI, revisamos todos los pacientes referidos a nuestra institución que fueron sometidos a evaluación de la función ventricular izquierda (FVI) durante cateterismo cardiaco y determinamos que proporción de los pacientes con disfunción ventricular fueron referidos para un implante de CDI.

Métodos: Revisamos las ventriculografías izquierdas (VI) realizadas de manera consecutiva en nuestra institución durante los dos últimos años. Los pacientes con una FVI \( \leq 35\% \) y posteriormente confirmada mediante ecocardiografía fueron incluidos.

Resultados: Se revisaron 1709 VI, 112 pacientes (6.6%) tuvieron una FVI \( \leq 35\% \) medida por cateterismo cardiaco, que fue confirmada a los 3 meses por ecocardiografía. Doce pacientes fueron excluidos por ser portadores de un CDI y 13 pacientes por falta de seguimiento. La población del estudio consistió de 87 pacientes con una edad promedio (64±13 años), 28% mujeres; 71% con enfermedad coronaria. El seguimiento promedio fue de 374 días (121-611, 25th and 75th percentil). Veinte pacientes (23%) recibieron un CDI. Cuarenta y siete pacientes (54%) no recibieron un CDI debido a una expectativa de vida < 6 meses o por mejoría de la FVI. Veinte pacientes (23%) que cumplían los criterios para implante de un CDI no lo recibieron; 6 pacientes rehusaron la recomendación y 14 pacientes (16%) no fueron referidos para un CDI. Cuatro pacientes murieron portando un CDI otros 4 pacientes que cumplían con los criterios para un CDI murieron durante el seguimiento, 3 (21%) por muerte súbita.

Conclusiones: 16% de los pacientes con una FVI \( \leq 35\% \) inicialmente calculada durante cateterismo cardiaco y que cumplían con los criterios recomendados por las guías para implante de CDI para prevención primaria de muerte súbita no recibieron esta terapia. Tres muertes durante un promedio de un año de seguimiento podrían haber sido evitadas por un CDI. El tamizaje y adherencia a las guías clínicas para prevención primaria de muerte súbita deben ser implementadas para identificar a los pacientes en alto riesgo que se pueden beneficiar con un CDI.
Abstract

**Introduction:** Some patients receive an ICD not based on established guidelines and others who meet those criteria may not receive the life-saving device. To investigate this possibility, we reviewed all patients at our institution that underwent initial evaluation of left ventricular function during cardiac catheterization to determine whether an ICD was recommended in those with a depressed left ventricular function.

**Methods:** We reviewed consecutive left ventricular angiograms (LVG) performed at our institution during the last two years. Patients with left ventricular ejection fraction (LVEF) $\leq 35\%$ during left ventricular angiography which was later confirmed by echocardiography were included.

**Results:** After reviewing 1709 LVG, 112 patients (6.6%) were found to have LVEF $\leq 35\%$ during cardiac catheterization, confirmed within 3 months by echocardiography. Twelve patients were excluded because they already had an ICD and 13 patients because inadequate follow-up. The study population consisted of 87 patients (mean age=64±13 years; 28% women; 71% coronary artery disease). Median follow-up was 374 days (121-611, 25th and 75th percentile). Twenty patients (23%) received an ICD. Forty-seven patients (54%) did not receive an ICD due to short life expectancy or improvement in LVEF. Twenty patients (23%) who met criteria for ICD, did not receive this therapy due to patient refusal (n=6) or because the ICD was not offered to the patient (14 patients, 16%). Four patients died having an ICD, and four who met criteria for ICD died during follow-up (3 sudden deaths).

**Conclusions:** Sixteen percent of patients with LVEF $< 35\%$ initially determined during cardiac catheterization who met criteria for primary prevention were not offered an ICD. Three deaths may have been prevented. Screening methods need to be implemented to identify all high risk patients who can benefit from ICD therapy.

**Introduction**

Ventricular arrhythmias are common in patients with heart failure (HF). Ventricular tachycardia (VT) and ventricular fibrillation (VF), can lead to syncope or sudden cardiac death. It is estimated that SCD accounts for about one-third of the mortality in HF patients$^1$. The implantable cardioverter-defibrillator (ICD) has become standard of care in the treatment of patients with reduced left ventricular systolic function as several randomized trials have found that this therapy reduces sudden death in survivors of VT/VF and among patients in whom the ICD is implanted for primary prevention.$^2,^9$ The survival benefit has been shown in patients with both ischemic and non-ischemic cardiomyopathy, adding to the benefit of optimal pharmacological therapy and superior to antiarrhythmic drug therapy.$^9$ Current practice guidelines from the American College of Cardiology and the American Heart Association confer a class I indication to the use of ICDs for primary prevention of sudden cardiac death in patients with persistent left ventricular ejection fraction (LVEF) $\leq 35\%$ despite optimal pharmacological therapy and after reversible causes have been excluded.$^{10}$ A recent study indicates that some patients receive an ICD even though they do not meet established guidelines.$^{11}$ In contrast, some patients who have clear indication for an ICD, may not be offered the device.$^{12,13}$ Waiting to evaluate the systolic function after an intervention or for potential recovery after an acute event may prevent the primary providers from addressing this therapy. In the present study, we investigated whether all patients who underwent initial evaluation of left ventricular function during cardiac catheterization at our institution and met established ICD implantation criteria, had this therapy recommended.
Methods

Study population and Methods
We reviewed consecutive left ventricular angiograms from July 1st 2008 to June 30, 2010 at our institution. Patients with LVEF ≤ 35 % confirmed by subsequent echocardiography within 3 months of the initial evaluation were included. Patients with an existing ICD and those not followed at our institution where excluded. Medical records and cardiac imaging data were reviewed to evaluate follow-up and management decisions regarding ICD therapy. Follow up data was obtained by direct communication with the physician taking care of the patient.

Determination of Left Ventricular Ejection Fraction by Angiography
Let ventricular angiography was acquired by the single-plane method (30 degrees right anterior oblique projection and) with a cineangiographic system (Siemens). A 5 or 6 French pigtail catheter was introduced into the LV via the femoral or brachial artery. A right anterior oblique projections during power injection of nonionic contrast was injected into the LV at suspended shallow inspiration, using a power injector. The endocardial borders of the left ventricle during end-diastole and end-systole were outlined manually by tracing the ventricular silhouettes at the outermost margins of visible radiographic contrast, including trabeculations and papillary muscles within the perimeter. Once the borders were outlined, they were converted to areas. End-diastolic and end-systolic projections were obtained by selecting images with the largest and smallest contours, respectively. The LVEF was calculated using the formula: \[(\text{end-diastolic area} - \text{end-systolic area}) ÷ \text{end-diastolic area}] \times 100\%.

Determination of Left Ventricular Ejection Fraction by Echocardiography
Quantitative echocardiographic studies were performed with the patient in the left lateral recumbent position. LVEF images were acquired from the apical two- and four-chamber views. LVEF was calculated based on volume as: LVEF = \[(\text{end-diastolic volume} - \text{end-systolic volume}) ÷ \text{end-diastolic volume}] \times 100\%.

Statistical analysis
Continuous variables are expressed as mean ± standard deviation and comparisons are made with unpaired t-test for normally distributed data. The data that were not normally distributed expressed as the medians with 25th and 75th percentiles and comparisons are made with Mann–Whitney rank sum test. Chi-square analysis or the Fisher exact test, where appropriate, was used for categorical parameters. Survival curves were generated using the Kaplan-Meier method and compared by the log-rank test. A p-value < 0.05 was considered as significant. Statistical analysis was done with SIGMASTAT, version 2, statistical software (SPSS Science Marketing Development, SPSS, Chicago, Illinois).

Results
During the study period, 1709 LVG were performed and 87 were found to have LVEF ≤ 35 % by left ventricular angiography subsequently confirmed by echocardiography within the next 3 months had no ICD and were followed in our institution. Twelve patients already had an ICD and 13 were followed elsewhere. The study population therefore consisted of 87 patients. The mean age of these patients was 64±13 years (Table 1). The etiology of the depressed left ventricular function was coronary artery disease in 71% and non-ischemic cardiomyopathy in 29%. The mean LVEF was 27.4±6.5%. There were 61 patients (70.5%) with NYHA class II – III, and 16 (14.3%) with NYHA class IV (Table 1). Median with 25th-75th percentile for follow up duration was 374 days (121-611).
| Age, years | 63.6 ± 12.7 |
| Female (%) | 31 (27.7) |
| Diabetes (%) | 35 (31.3) |
| Hypertension (%) | 92 (82.1) |
| Dyslipidemia (%) | 82 (73.2) |
| Tobacco abuse (%) | 40 (35.7) |
| Chronic renal insufficiency (%) | 15 (13.4) |
| Prior MI (%) | 50 (44.6) |
| Prior revascularization (%) | 55 (49.1) |

**Indication for Left Heart Catheterization**
- Acute MI (%) 24 (21.4)
- Cardiogenic shock (%) 6 (5.4)
- Congestive Heart Failure (%) 32 (28.6)

**CHF**
- NYHA Class IV (%) 16 (14.3)
- NYHA Class II/III (%) 79 (70.5%)

**Medications**
- Diuretics 88 (78.3)
- ACE /ARB (%) 106 (94.6)
- Beta blockers (%) 107 (95.5)
- Hydralazine/nitrates (%) 12 (10.7)
- Digoxin (%) 27 (24.1)
- Aldosterone antagonists (%) 44 (39.3)
- LVEF (%) 27.4 ± 6.5
- LV end diastolic dimension, mm 60.1 ± 0.77
- QRS duration, milliseconds 144 ± 37.2

**Table 1.** Baseline characteristics of all patients.
MI, myocardial infarction; CHF, congestive heart failure; NYHA, Newyork heart association; LVEF, left ventricular ejection fraction; ACE, angiotensin converting enzyme; ARB, angiotension receptor blockers

**Recommendation for Implantable Cardiverter Defibrillator Implantation**

Among 32 patients in whom the ICD was considered indicated, 20 (62.5%) received an ICD based on the depressed left ventricular function. Three patients also had a secondary prevention indication. (Table 2). There were 15 (75%) patients with NYHA class II-III symptoms. Two patients (10%) were in NYHA class IV and were awaiting cardiac transplantation and 3 patients were in NYHA class I. The median time for ICD implantation from initial assessment of left ventricular ejection fraction was 119.5 (25th and 75 percentiles = 39.5-366) days (Figure 1)
Forty-seven patients (54%) did not receive an ICD due to short life expectancy or improvement in LVEF to more than 35% during follow-up. Twenty patients (23%) who met criteria for ICD, did not receive this therapy due to patient refusal (n=6) or because the ICD was not offered to the patient (n=14, 16%). Four patients died having an ICD, and four who met criteria for ICD died during follow-up (3 sudden deaths).

In the remaining 20 patients who met criteria for ICD, 6 refused and in 14 patients an ICD was never offered. The follow-up LVEF among these 14 patients was 28.9 ± 7.4%.

The clinical characteristics of the patients who received an ICD and those who qualified but in whom this therapy was not offered is shown in Table 2. There were no differences between these two groups except history of prior revascularization which was more frequent among patients not offered an ICD.
Table 2. Comparison between patients with and without an ICD

MI, myocardial infarction; CHF, congestive heart failure; NYHA, Newyork heart association; LVEF, left ventricular ejection fraction; ACE, angiotensin converting enzyme; ARB, angiotension receptor blockers

Mortality during Follow-Up
A total of 18 patients (20%) died during follow-up; 7 during their index admission for Left ventricular angiography (5 due to heart failure and 2 related to other medical comorbidities). Three patients died within a month due to complications of a subsequent prolonged hospitalization for pneumonia or sepsis (Figure 2). Among the remaining 8 patients who died during follow up, 4 died with an ICD and 4 who met criteria but an ICD was not offered; one of them died from complications of cancer and three suffered sudden death. One patient had an out of hospital cardiac arrest with documented VF, and two died suddenly.
at home with no rhythm documentation. Out of the 14 patients with no an ICD ever been offered despite clear indication, 3 had sudden death that could have been potentially prevented by an ICD. All were males (age 58-74) with coronary artery disease and NYHA class II/III failure.

Discussion

Large randomized clinical trials have demonstrated that prophylactic implantation of an ICD reduces total mortality in high risk patients with ischemic and non ischemic cardiomyopathy. Current guidelines for the management of heart failure and prevention of sudden cardiac death in patients with left ventricular systolic dysfunction are based on two pivotal trials: MADIT II and SCD-HeFT. MADIT II included patients aged <80 with prior myocardial infarction and persistent LVEF <30% despite optimal medical treatment and revascularization. The SCD-HeFT trial included patients with LVEF ≤35% regardless of the etiology and NYHA class II or III also on optimal pharmacological treatment. A meta-analysis of five trials before SCD-HeFT also confirmed the benefit of the ICD for primary prevention of sudden cardiac death in patients with nonischemic cardiomyopathy. Despite the evidence supporting the role of the ICD in prevention of sudden death and efforts of the heart failure and electrophysiology communities in educating physicians and patients, the ICD may not be always offered to those who could benefit from this therapy. On the contrary, a recent report indicates that suggests that 22.5% of patients who receive ICD don't meet the strict criteria outlined in published practice guidelines. Barriers to the adoption of new therapeutic interventions are common in medicine.
have systolic dysfunction during a LVG performed in the setting of a diagnostic coronary angiogram or percutaneous coronary revascularization procedure which is common setting for screening candidates for ICD. A LVEF ≤ 35 % was later confirmed by echocardiography and patients returned to the care of their regular physicians which included cardiologists, internists and primary care physicians. When subtracting those patients who refused the ICD or had contraindications documented, 16 % of patients with confirmed LVSF <35% did qualify for an ICD but this therapy was not offered despite having medical follow up. Three of them died suddenly and an ICD may have prevented it. The fact that 10 of the 14 patients not offered an ICD where not followed by a cardiologist demonstrates the limitations of care system in which a patient may have contact with an specialized service through a procedure but not during follow up. Significant differences in outcomes for the treatment of heart failure between specialists and primary care providers have been well documented.

Even in the hand of a cardiologist, the management of heart failure patients is quite complex, often requiring consultation with heart failure and electrophysiology specialists. A structured follow up system is necessary to assure that patients in whom a depressed left ventricular function is identified, an adequate and specialized process of diagnosis, education, and treatment should be activated.

**Limitations**

Review of medical records and telephone interviews with the patient's physician may not reflect all conversations that occur between patients and physicians offering ICD therapy. Nevertheless, the fact that 3 out of 14 patients who had no ICD implanted died suddenly stressed the point that this therapy needs to be discussed with all patients with depressed left ventricular function to reduce sudden cardiac death.

**Conclusions:**

ICD therapy has proven to be life-saving for many patients, and few other therapy modalities have such compelling documentation of its effectiveness. Out of 14 patients (16% of total population) who qualified and were not offered an ICD, 3 had sudden death that could have been prevented. A follow-up and referral system is required to identify all high risk patients who can benefit from ICD therapy.

**References**


6. Desai, AS, Fang, JC, Maisel, WH, Baughman, KL. Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-