

## Congestive Heart Failure as the Cause of Early Death in Elderly Patients with an Implantable Cardioverter-Defibrillator

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ON BEHALF OF THE ICD-LABOR INVESTIGATORS

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### Summary

*Thirty-nine medical centers in five countries participated in the non-randomized, retrospective-prospective Latin-American registry ICD-LABOR (ICD Latin-American Biotronik Ongoing Registry). The aim of the registry was to investigate the cardiac causes of mortality. From June 1994 to September 2001, 317 patients with previous, malignant, ventricular tachyarrhythmia or aborted sudden death who had received an implantable cardioverter-defibrillator (ICD) were enrolled in the study. Follow-up could be completed for 279 patients, of which 210 (75%) were male. The primary pathology was coronary artery disease (40.5%), Chagas disease (27.6%), dilated cardiomyopathy (18.6%), and miscellaneous causes (13.3%). Congestive heart failure was the most common cause of death (40%). The Cox proportional hazards regression model established two independent risk factors for death: age and the left ventricular ejection fraction (LVEF). According to the "likelihood of death ratio," the increasing risk was divided into four groups: age  $\leq 65$  years and LVEF  $\geq 31\%$  = 3.7% (Group A), age  $\leq 65$  years and LVEF  $\leq 30\%$  = 10% (Group B), age  $\geq 66$  years and LVEF  $\geq 31\%$  = 13.3% (Group C), age  $\geq 66$  years and LVEF  $\leq 30\%$  = 30.3% (Group D). During the follow-up, 18 deaths related to congestive heart failure occurred. In the Kaplan-Meier analysis of cumulative probability of survival, 50% of those 18 deaths were observed within the first nine months after implantation, all of which corresponded to Group D, the highest risk group. The study showed that the most common cause of death was congestive heart failure. There were nine deaths (50%) during the first nine months after ICD implantation. In all instances, a lethal combination of advanced age (over 65 years) and low LVEF (less than 31%) was present.*

### Key Words

Implantable cardioverter-defibrillator, congestive heart failure, early death

### Introduction

Medical conditions in Latin America are strongly influenced by population, culture, economic resources, and pathologies. The use of implantable cardioverter-defibrillators (ICDs) in the region has dramatically increased in number over the last ten years. The ICD-LABOR (ICD Latin-American Biotronik Ongoing Registry) was developed to analyze the progress of

patients with antecedents of aborted sudden death or drug-refractory, malignant, ventricular arrhythmias treated with an ICD. The ICD-LABOR involved 39 medical centers in five countries: Argentina, Brazil, Chile, Uruguay, and Cuba. In this analysis, the primary investigated outcome was cardiac death related to heart failure.

**Materials and Methods**

From June 1994 to September 2001, 317 patients were enrolled in the study. In each case, the ICD indication was considered a secondary prevention, and the patient was treated according to the "Consensus Statement on Indications, Guidelines for Use, and Recommendations for Follow-up of Implantable Cardioverter Defibrillators" [1]. Within the group, only 279 patients (88%) completed the follow-up, of which 210 (75.2%) were male. Coronary artery disease (CAD) was the most common cardiac condition (40.5%), followed by Chagas disease (27.6%) [2], and primary dilated cardiomyopathy (18.6%). The remaining patients were included in the miscellaneous group: Brugada syndrome, long QT syndrome (LQTS), arrhythmogenic right ventricular dysplasia (ARVD), etc.

Various parameters were considered at the time of implantation:

- age,
- gender,
- pathology,
- pacing threshold,
- true defibrillation threshold, and
- left ventricular ejection fraction (LVEF) immediately before the procedure.

The Cox proportional regression model was used to calculate hazard ratios.

**Results**

During the follow-up period (average  $22.7 \pm 20.2$  months, range 3 – 83 months), 45 deaths were reported, of which 34 (75.5%) were attributed to cardiac causes. The analysis of risk predictors established two independent variables: age ( $p < 0.00073$ ) and LVEF ( $p < 0.008$ ). The likelihood ratio (Cox regression

	Age (years)	LVEF (%)	Annual Mortality (%)
Group A	< 65	> 31	3.7
Group B	≤ 65	≤ 30	10.0
Group C	> 66	> 31	13.3
Group D	≥ 66	≤ 30	30.3

Table 1. Annual likelihood of death ratio from the Cox hazards regression model. LVEF = left ventricular ejection fraction.

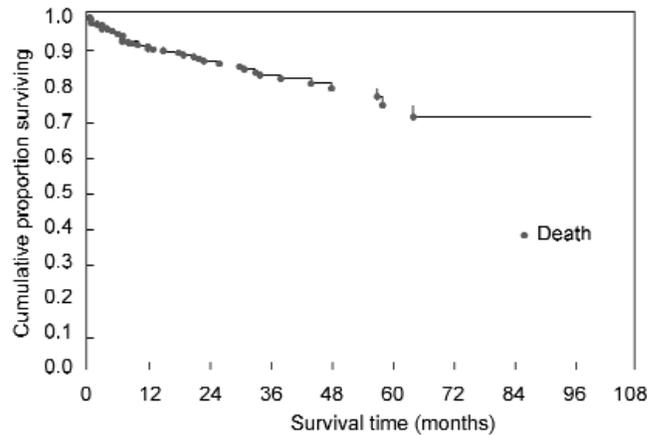


Figure 1. Kaplan-Meier analysis of the probability of survival for cardiac causes. Non-cardiac deaths were not considered for the present graphic.

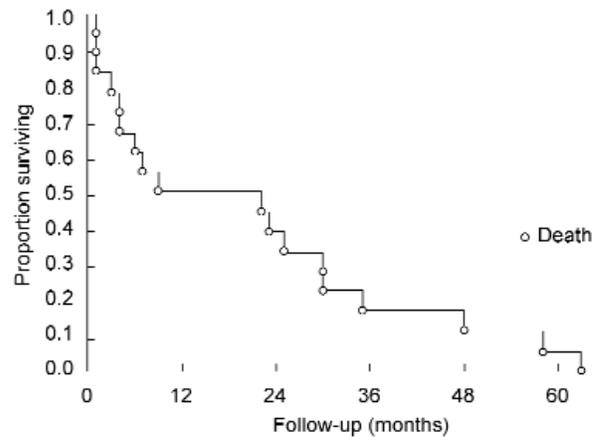


Figure 2. Deaths related to congestive heart failure (CHF). During the first 9 months after implantation, all patients who died due to CHF belonged to the highest risk group: over 65 years of age and ejection fraction less than 31% ( $p$ -value < 0.01).

model) demonstrated four different prognoses according to the different combinations of age and LVEF (Table 1). Among the 34 deaths due to cardiac causes (Figure 1), 18 were related to heart failure; 9 (50%) of these 18 deaths occurred during the nine months immediately following the ICD implantation (Figure 2), and they belonged to the highest risk group, Group D (over 65 years of age, LVEF less than 31%).

**Discussion**

Survivors of cardiac arrest caused by ventricular tachycardia or ventricular fibrillation have a high risk

of death within the two years immediately following the indexed event. Several large randomized trials [3-5] have confirmed a reduction in mortality following the implantation of an ICD as compared with antiarrhythmic drug therapy in patients with antecedents of fatal ventricular arrhythmias. However, given the high cost and invasiveness of the procedure, it is especially important to establish which patients are likely to benefit most from ICD treatment. Consequently, different randomized trials have demonstrated that patients who are most likely to benefit from receiving an ICD are also those at the highest risk of death [6,7]. In those trials, predictors of total mortality were related to age, LVEF, and high NYHA class. Although there is general agreement that ICDs markedly reduce the risk of sudden death, there are wide variations in overall mortality benefit among different populations [8]. In the absence of a randomized study, any consideration of evidence for prolonging survival must take into account two types of conditions:

- a comparison of the actuarial survival curves of the non-randomized registry and a randomized trial [9]; and
- a careful analysis of all causes of death in the non-randomized group undergoing ICD treatment.

Age and LVEF were the only variables that exhibited significant differences. According to a multivariate analysis, the increasing likelihood of death ratio was divided into four groups, formed on the basis of age and LVEF combinations. The overall annual cardiac death rate was  $5.3\% \pm 1.72\%$  for the entire group, but for those in the worst condition (age  $\geq 66$  years and LVEF  $\leq 30\%$ ) the annual cardiac death rate was 30.3%. There were 18 deaths attributed to congestive heart failure (CHF) [10], of which nine were observed during the first nine months after ICD implantation; all nine patients belonged to Group D, the highest risk group. Although the extent of the benefits associated with ICD therapy remains unknown, various randomized trials have demonstrated that patients who are most likely to benefit from an ICD are also those who have the highest overall risk of death [7]. However, the final outcome observed in our registry of patients who were of advanced age, had a poor LVEF, and died due to CHF, suggests that those patients should remain under close supervision during the course of their CHF therapy. Moreover, the possibility for the indication of an ICD with resynchronization capabilities should be taken into account.

## Study Limitation

The present study was observational and non-randomized. The LVEF was determined by various methods at different medical centers.

## Conclusion

- In the ICD-LABOR registry, CHF was the most common cause of death.
- In the entire group of patients who died due to CHF, 50% of deaths occurred early, during the first nine months after implantation. All of the patients belonged to the highest risk group: advanced age (over 65 years) and low LVEF (less than 31%).
- An ICD with resynchronization capabilities should be considered for this patient group.

## ICD-LABOR Investigators

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