

## Prognostic impact of defibrillator shocks in a Colombian cohort

*Impacto pronóstico de las descargas del desfibrilador en una cohorte colombiana*

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### Key words:

Sudden cardiac death, defibrillators, appropriate therapy, inappropriate therapy.

### Palabras clave:

Muerte cardíaca repentina, desfibriladores, terapia apropiada, terapia inapropiada.

### Abbreviations:

ICD = Implantable cardioverter defibrillator.  
SCD = Sudden cardiac death.  
ICM = Ischemic cardiomyopathy.  
NICM = Non ischemic cardiomyopathy.  
PP = Primary prevention.  
SP = Secondary prevention.

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### ABSTRACT

**Introduction:** The implantable cardioverter defibrillator (ICD) has become the first-line treatment option for SCD prevention. In Colombia, while ICD therapy has been available for several years, extensive registries or studies documenting the impact of ICD therapy are lacking. **Objective:** To evaluate the association between appropriate and inappropriate ICD therapies and mortality in Colombian patients. **Methods:** Prospective observational cohort study including 530 patients with cardiomyopathy of varied etiology, from eight clinics in Medellín, Colombia, from 2013 to 2016. Adjusted and survival analyses were performed. **Results:** Of all participating patients, 72.1% were men, and median age was 64 years. Mean follow-up time was  $1.5 \pm 0.92$  years, with a follow-up rate of 353.3 patients/year. The most common indication for ICD implantation was ischemic heart disease (48.7%), and indication of primary prevention (63.4%). Mortality was 12.8%, and patients with ischemic etiology had 1.8-times greater risk of death compared to non-ischemic patients. 14% of the patients received appropriate therapies, while 13.6% were inappropriate. There was a 65% greater risk of appropriate therapies in patients with ischemic heart disease. High blood pressure, being over 61 years of age, and having left ventricular ejection fraction  $< 35\%$ , were risk factors for death, while use of beta-blockers was associated with a reduced risk of death. **Conclusions:** The main indication for ICD was ischemic etiology and primary prevention. Mortality is higher in patients with ischemic etiology, who in addition have increased risk of presenting appropriate therapies. The frequency of device therapies was decreased compared to previous reports.

### RESUMEN

**Introducción:** El desfibrilador cardioversor implantable (DCI) se ha convertido en la opción de primera línea de tratamiento para la prevención de la MCS. En Colombia, aunque la terapia DCI ha estado disponible durante varios años, faltan extensos registros o estudios que documenten el impacto de la terapia DCI. **Objetivo:** Evaluar la asociación entre las terapias apropiadas e inapropiadas de DCI y la mortalidad en pacientes colombianos. **Métodos:** Estudio prospectivo observacional de cohorte que incluye 530 pacientes con cardiopatía de etiología variada, de ocho clínicas en Medellín, Colombia, de 2013 a 2016. Se realizaron análisis ajustados y de supervivencia. **Resultados:** De todos los pacientes participantes, el 72.1% fueron hombres y la edad mediana fue de 64 años. El tiempo medio de seguimiento fue de  $1.5 \pm 0.92$  años, con una tasa de seguimiento de 353.3 pacientes/año. La indicación más común para la implantación del DCI fue la cardiopatía isquémica (48.7%) y la indicación de prevención primaria (63.4%). La mortalidad fue del 12.8% y los pacientes con etiología isquémica tuvieron un riesgo de muerte 1.8 veces mayor en comparación con los pacientes no isquémicos. Catorce por ciento de los pacientes recibieron terapias apropiadas, mientras que el 13.6% fueron inapropiadas. Hubo un riesgo 65% mayor de terapias apropiadas en pacientes con cardiopatía isquémica. La hipertensión arterial, el tener más de 61 años de edad y haber dejado la fracción de eyección ventricular  $< 35\%$ , fueron factores de riesgo de muerte, mientras que el uso de betabloqueantes se asoció con un menor riesgo de muerte. **Conclusiones:** La principal indicación para la DCI fue etiología isquémica y prevención primaria. La mortalidad es mayor en pacientes con etiología isquémica, que además tienen mayor riesgo de presentar terapias apropiadas. La frecuencia de las terapias con dispositivos se redujo en comparación con los informes anteriores.

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## INTRODUCTION

Sudden cardiac death (SCD) accounts for the majority of deaths from cardiovascular disease and mortality around the world.<sup>1</sup> Multiple pharmacologic and interventional therapies have led to increased survival of patients presenting aborted SCD (secondary prevention-SP), as well as of patients at risk of presenting, but that have not yet presented, SCD event (primary prevention-PP).

The implantable cardioverter defibrillator (ICD) has become the first-line treatment option for primary and secondary SCD prevention, since it significantly reduces mortality, it has the capability of detecting ventricular arrhythmias, and can quickly apply high-voltage electrical discharge that correct such arrhythmias. However, several studies have shown that use of ICD for both appropriate and inappropriate therapy (generated by conditions other than malignant ventricular arrhythmia) is associated to increased risk of mortality or morbidity.<sup>2-4</sup>

In Colombia, even though ICD therapy has been available for several years, extensive registries or studies documenting the impact of ICD therapy in patients at risk of SCD are not currently available. Therefore, in this study, we have evaluated the association and prognostic impact of appropriate and inappropriate ICD therapies during follow-up visits in a cohort of Colombian patients in several Colombian hospitals.

## METHODS

This was a prospective observational cohort study including 530 patients with cardiopathy of any etiology, or with primary electrical disease with high risk of SCD with ICD or cardiac resynchronization device, that attended clinical electrophysiology consultation provided by CES Cardiology at eight different clinics in Medellín, Colombia, from June 2013 to December 2016, and had a follow-up of at least six months and two controls. Patients whom arrhythmic events were not registered were excluded from this study.

The clinical visit at the hospital or medical office includes device reprogramming and election of therapeutic approach. Upon completion of clinical visit, the attending

physician accessed the patient's register stored on Google Drive® online database, where findings were added.

Medical and hospital records were reviewed, and missing information was obtained by telephone and an additional appointment for revision. Mortality of patients missing reprogramming appointments was established by telephone, and online consultation of the Colombian National Registry Department database by providing the patients ID number.

The assessed outcomes were incidence of appropriate or inappropriate ICD therapy and its association with mortality. Stratified analyses according to etiology (ischemic cardiomyopathy-ICM, non-ischemic cardiomyopathy-NICM), and according to indication, were performed. In addition, the association between electrical storm and mortality was evaluated, as well as the relationship between programmed therapy zones and ICD shocks.

## Statistical analysis

Categorical variables are presented as absolute numbers and percentages, and continuous variables as average and standard deviation (SD) or median and interquartile range-according to normal distribution. Differences between groups were assessed by t-test for continuous variables, and by  $\chi^2$  test for categorical variables. Kaplan-Meier survival curves and log-rank tests were used to compare mortality according to etiology, as well as to compare the incidence of appropriate or inappropriate therapy and its association to mortality according to etiology and indication.

Multivariate analysis, and Cox proportional hazards analysis were performed for mortality, appropriate ICD therapy, and inappropriate ICD therapy. According to their significance in bivariate analysis and clinical relevance, the following variables were analyzed in these models: etiology, high blood pressure, diabetes mellitus, chronic kidney disease, dyslipidemia, use of beta-blockers, use of amiodarone, left ventricular ejection fraction > 35%, left ventricular ejection fraction < 35%, age > 61 years, and age < 61 years. P value < 0.05 was considered statistically significant. Analyses were conducted with SPSS software (version 21), licensed to CES University.

Table I. Characteristics of study population.

| Characteristics                                    | Value (%)  |
|--|------------|
| Gender   |            |
| Male (n = 382)                                     | 72.1       |
| Comorbidities                                      |            |
| High blood pressure                                | 73.8       |
| Diabetes mellitus                                  | 24         |
| Chronic kidney disease                             | 12.1       |
| Hypothyroidism                                     | 22.1       |
| Dyslipidemia                                       | 43.4       |
| Ischemic cardiopathy                               | 48.7       |
| COPD   | 12.1       |
| Left ventricular ejection fraction                 |            |
| Median   | 35 (20-35) |
| < 35%  | 74         |
| Medication   |            |
| Beta blockers                                      | 91.3       |
| ACEIs  | 37.4       |
| ARBs   | 37.9       |
| Spironolactone                                     | 55.7       |
| Amiodarone   | 25.1       |
| Furosemide   | 55.3       |
| Statins  | 65.3       |
| Digoxin  | 10.4       |
| ASA  | 63.4       |
| Clopidogrel  | 10         |
| Rhythm   |            |
| Sinus  | 83.4       |
| Non-sinus  | 16.6       |
| Previous Holter-documented ventricular tachycardia |            |
| Yes  | 39.7       |
| No   | 60.3       |
| ICD indication                                     |            |
| Primary prevention (PP)                            | 63.4       |
| Secondary prevention (SP)                          | 36.6       |
| Type of device                                     |            |
| Single chamber ICD                                 | 13.6       |
| Dual chamber ICD                                   | 55.9       |
| Resynchronization therapy ICD                      | 30.5       |
| Complications related to device                    | 14.9       |
| Device therapy                                     |            |
| Appropriate ICD therapy                            | 14         |
| Inappropriate ICD therapy                          | 13.6       |
| Therapy zones                                      |            |
| One zone   | 21.5       |
| Two zones  | 73.8       |
| Three zones  | 4.7        |
| Electrical storm                                   | 3.8        |
| Death  | 12.8       |

COPD = chronic obstructive pulmonary disease; ACEI = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II receptor blockers; ASA = acetyl salicylic acid.

This study was approved by the Institutional Committee for Ethics in Human Research at the CES University and does not need additional requirements since it is an observational study in which an intervention is not performed.

## RESULTS

This study included 530 patients. Median age was 64 years (i.q.r. 56-72), with the youngest patient being 16 years old at time of implantation (18 years old at time of study initiation), and the oldest patient was 90 years old. Population characteristics are shown in *table I*.

Average follow-up time was  $546.96 \pm 336$  days, ( $1.5 \pm 0.92$  years), with a follow-up rate of 353.3 patients/year. Follow-up times of at least six months were not achieved for 31 patients (5.8% of total), which were excluded from the study: 7 patients (1.3%) in the ICM group (5 patients in PP, 2 patients in SP), and 24 patients (4.5%) in the NICM/primary electrical disease group (14 patients in PP, 10 patients in SP).

Incidence of appropriate therapy was 14%, while incidence of inappropriate therapy was 13.6%. Electrical storm, defined by three or more episodes of ventricular arrhythmias within 24 hours with or without therapy, was detected in 3.8% of the study population, and total mortality was 12.8% (*Table II*). Bivariate analysis of the total population did not show an association between appropriate ICD therapy and mortality ( $p = 0.18$ ), or between inappropriate ICD therapy and mortality ( $p = 0.19$ ). Compared to NICM, patients with ICM exhibited higher risk of mortality (RR 2.12 [1.25; 3.60]), higher risk of appropriate ICD therapy (RR 1.65 [1.00; 2.73]), higher risk of electrical storm (RR 3.29 [1.18; 9.20]), and lower risk of inappropriate ICD therapy (RR 0.51 [0.30; 0.86]).

### Impact of device programming on risk of shock

We observed an association between zones of therapy and appropriate ICD therapy, since compared to patients with three programmed zones, patients with 1 or 2 programmed zones

showed a 61% lower risk of appropriate therapy (RR 0.39 CI 95% [0.15; 0.97]).

#### Prognostic value of Holter-documented ventricular tachycardia

We did not find an association between previous Holter-documented ventricular tachycardia and mortality ( $p = 0.79$ ), appropriate therapy ( $p = 0.30$ ), or inappropriate therapy ( $p = 0.054$ ).

#### Multivariate analysis

High blood pressure (RR 3.31 CI 95% [1.22; 8.95]) and age  $\geq 61$  years (RR 2.38 CI 95%

[1.15; 4.93]) were associated with increased mortality. On the other hand, use of beta-blockers was associated to lower risk of death ( $p = 0.02$ ) (RR 0.32 CI 95% [0.12; 0.84]).

Use of amiodarone was associated with appropriate ICD therapy ( $p = 0.000$ ) (RR 3.01 CI 95% [1.79; 5.06]) as well as with inappropriate ICD therapy ( $p = 0.007$ ) (RR 2.21 CI 95% [1.24; 3.95]) (Table III).

Diabetes mellitus ( $p = 0.013$ ) (RR 2.88 CI 95% [1.24; 6.68]), and age  $\geq 61$  years ( $p = 0.01$ ) (RR 1.97 CI 95% [1.11; 3.48]) were associated with inappropriate ICD therapy (Table IV).

#### Survival analysis

Compared to NICM, an increased risk of death was found for ICM patients (log rank  $\chi^2$  6.38;  $p = 0.01$ ). Furthermore, ICM was associated to a 1,8-fold increased risk of death after  $1.5 \pm 0.9$  years of follow-up, compared to NIMC (HR 1.87 [1.14-3.09]) (Figure 1). However, the association between etiology and mortality was not observed in the adjusted analysis ( $p = 0.35$ ). Patients with ICM had a 65% greater risk of presenting appropriate ICD therapy than patients with NICM ( $p = 0.045$  con RR 1.65

Table II. Outcomes according to etiology.

| Outcomes in total events     | ICM (%)  | NICM (%) | p value |
|------------------------------|----------|----------|---------|
| Appropriate device therapy   | 44 (8.3) | 30 (5.7) | 0.04    |
| Inappropriate device therapy | 25 (4.7) | 47 (8.9) | 0.01    |
| Electrical storm             | 15 (2.8) | 5 (0.9)  | 0.01    |
| Death                        | 44 (8.3) | 24 (4.5) | 0.00    |

ICM = ischemic cardiomyopathy; NICM = non-ischemic cardiomyopathy.

Table III. Variables related to presence of appropriate therapies. Bivariate and multivariate analysis.

| Variable analyzed                                  | BV<br>p value | RR   | CI 95%     | MV<br>p value | RR   | CI 95%     |
|--|---------------|------|------------|---------------|------|------------|
| Etiology   | 0.045         | 1.65 | 1.00; 2.73 | 0.76          | -    | -          |
| High blood pressure                                | 0.90          | -    | -          | 0.73          | -    | -          |
| Diabetes mellitus                                  | 0.83          | -    | -          | 0.76          | -    | -          |
| Chronic kidney disease                             | 0.98          | -    | -          | 0.74          | -    | -          |
| COPD   | 0.42          | -    | -          | NE            | -    | -          |
| Dyslipidemia                                       | 0.13          | -    | -          | 0.89          | -    | -          |
| Gender   | 0.99          | -    | -          | NE            | -    | -          |
| Use of beta-blockers                               | 0.79          | -    | -          | 0.34          | -    | -          |
| Use of amiodarone                                  | 0.000         | 3.06 | 1.84; 5.09 | 0.00          | 3.01 | 1.79; 5.06 |
| Previous Holter-documented ventricular tachycardia | 0.30          | -    | -          | NE            | -    | -          |
| Base rhythm  | 0.22          | -    | -          | NE            | -    | -          |
| Left ventricular ejection fraction $\leq 35\%$     | 0.20          | -    | -          | 0.24          | -    | -          |
| Age $\geq 61$ years                                | 0.69          | -    | -          | 0.44          | -    | -          |

COPD = chronic obstructive pulmonary disease; BV = bivariate analysis; MV = multivariate analysis; NE = not evaluated.

CI 95% [1.00-2.73]. Patients with ICM had a 49% lower risk of inappropriate therapy ( $p = 0.011$  y RR 0.51 CI 95% [0.30-0.86] (Figure 2).

### DISCUSSION

ICD therapy has consistently been shown to reduce SCD-related mortality.<sup>5</sup> However, the response is heterogeneous among the broad spectrum of patients requiring this therapy. While several studies, including our own, have shown that ICD therapy is beneficial for patients with ICM, other studies suggest a similar benefit for patients with NICM.<sup>6-8</sup> In our study, outcome analysis based on indications for ICD implantation (PP compared to SP), did not show any significant differences. However, a long-term follow-up study by van Welses and colleagues reported a lower risk of appropriate therapy in PP and comparable all-cause mortality between PP and SP groups.<sup>9</sup> However, the difference in their observations and our own may be explained by the fact that a relevant factor in reduction of risk of appropriate therapy is the number of programmed zones and adherence to medication such as beta-blockers, and in our registry over 90% of patients were receiving medication, and around 95% had one or two programmed therapy zones.

On the other hand, outcome analysis according to etiology (ICM vs. NICM) showed significant differences in frequency of appropriate therapy, electrical shock, and mortality, being all of them more frequent in patients with ICM. Appropriate therapy is frequently observed

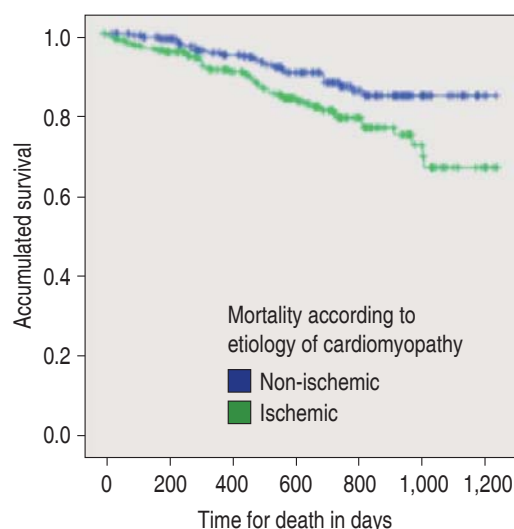


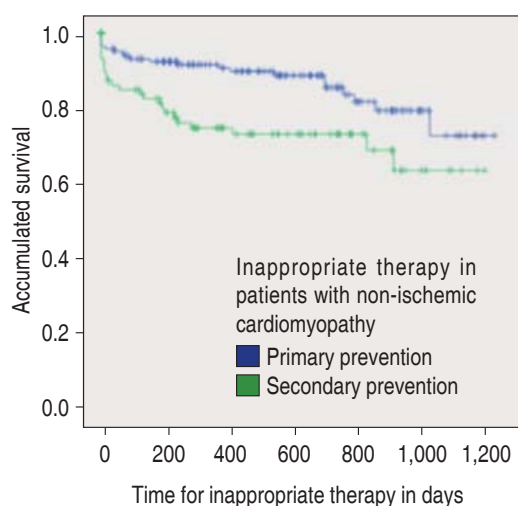
Figure 1. Kaplan-Meier survival curve: mortality according to etiology of cardiomyopathy. Follow-up time in days. ICM = ischemic cardiomyopathy, NICM = non-ischemic cardiomyopathy.

Table IV. Variables related to presence of inappropriate therapies. Bivariate and multivariate analysis.

| Variable analyzed                                  | BV         |      |            | MV         |      |            |
|--|------------|------|------------|------------|------|------------|
|  | Valor de p | RR   | CI 95%     | Valor de p | RR   | CI 95%     |
| Etiology   | 0.011      | 0.51 | 0.30; 0.86 | 0.09       | -    | -          |
| High blood pressure                                | 0.019      | 0.53 | 0.32; 0.91 | 0.20       | -    | -          |
| Diabetes Mellitus                                  | 0.002      | 0.30 | 0.13; 0.68 | 0.02       | 2.88 | 1.24; 6.68 |
| Chronic kidney disease                             | 0.29       | -    | -          | NE         | -    | -          |
| Dyslipidemia                                       | 0.56       | -    | -          | 0.89       | -    | -          |
| Gender   | 0.24       | -    | -          | NE         | -    | -          |
| Use of beta-blockers                               | 0.09       | -    | -          | 0.13       | -    | -          |
| Use of amiodarone                                  | 0.009      | 1.99 | 1.18; 3.36 | 0.007      | 2.21 | 1.24; 3.95 |
| Previous Holter-documented ventricular tachycardia | 0.054      | -    | -          | 0.22       | -    | -          |
| Appropriate therapies                              | 0.054      | -    | -          | NE         | -    | -          |
| Left ventricular ejection fraction $\leq 35\%$     | 0.003      | 1.99 | 1.18; 3.36 | 0.08       | -    | -          |
| age $\geq 61$ years                                | 0.27       | -    | -          | 0.01       | 1.97 | 1.11; 3.48 |

BV = bivariate analysis; MV = multivariate analysis; NE = not evaluated.





**Figure 2.** Kaplan-Meier survival curve: inappropriate therapy in patients with non-ischemic cardiomyopathy stratified by implant indication for primary or secondary prevention. Follow-up time in days. ICM = ischemic cardiomyopathy; NICM = non-ischemic cardiomyopathy; PP = primary prevention; SP = secondary prevention.

in patients with ICM. Recently, a systematic review reported even higher numbers (17 and 31%) than those observed in our study (14%).<sup>10</sup> The negative impact on mortality is consistently reported throughout the literature, as shown by two recent metaanalyses.<sup>11,12</sup> Furthermore, other data show that regardless of the type of therapy (shock or over-stimulation), appropriate therapy is associated with increased risk of mortality.<sup>13</sup> This may be explained by the possibility that the underlying arrhythmia –triggered by the intervention– is a damaging event for an already diseased heart, or by being a marker of severity of the underlying disease.

Consistent with previous studies,<sup>14,15</sup> while inappropriate therapy was more frequently observed in patients with NICM, no significant association was found between them and mortality.

### Characteristics of the study population

#### *Number of patients*

The number of patients included in our study is –to our knowledge– the highest reported

in Colombia, and is comparable to other series reported in Latin American countries. Alvarez et al<sup>16</sup> reported 72 patients in Bogotá, Colombia, with a one year follow-up; Dubner et al,<sup>17</sup> and Ramos et al<sup>18</sup> reported registries with similar number of patients involving several Latin American countries. Our results provide a close and current view of the state of therapy with cardioverter defibrillators in our country. Even though our study was performed in one city in Colombia, it included patients from all socioeconomic status, social security affiliations, eight hospitals, and device implantations performed by 10 different medical doctors, representing around 15% of electrophysiologists in the country. Furthermore, follow-up included patients that have had the implant for more than five years. In addition to information related to complications, this longer-term follow-up provides relevant information regarding the variation in time of the frequency of appropriate or inappropriate therapy.

#### *ICD in primary prevention:*

*Are there differences between Colombia and the rest of the world?*

While in the ICD Registry<sup>18</sup> only 37.3% of patients had indication of PP, in our study around two thirds (63.4%) of our patients received an ICD as indication for primary prevention. However, the trend observed in the registry is similar to that observed in other countries; a greater number of implants indicated for PP of SCD, as reported by an Israeli study,<sup>19</sup> as well as by a Spanish registry<sup>20</sup> in which similar rates were observed. Additionally, a recently published meta-analysis,<sup>12</sup> representative of the current scenario, indicated that around 75% of implants are performed as PP strategy. This trend is supported by early diagnosis of disease, efficacy of pharmacological and ICD interventions, and a stable percentage of complications. The cost-effectiveness of this intervention may be considered a limitation in itself, as it is clearly established in developed countries,<sup>21,22</sup> while in Latin America the cost-effectiveness is conditioned by multiple factors in countries such as Argentina,<sup>23</sup> Brazil,<sup>24</sup> and Colombia.<sup>25</sup>

### *Etiology:*

#### *Is ischemic heart disease still prevalent?*

Ischemic cardiomyopathy is the most frequent indication for ICD implantation, since ICM has been associated to a greater risk of mortality compared to non-ischemic cardiomyopathy. Consistent with this, in our study, patients with ICM had 2.1-fold greater risk of death than those with NICM. Close to 50% of participating patients had ICM, while the remaining half included patients with NICM and primary electrical disease. In the ICD LABOR study, 39.7% of patients had ICM,<sup>17</sup> in the ICD Registry Latin America 43.6% of patients had ICM,<sup>18</sup> and in the 2014 Spanish registry 53.6% of patients had ICM.<sup>20</sup> In this regard, several points must be addressed, starting with the increase of indication of ICD for non-ischemic disease. Early diagnosis of structural cardiopathies such as arrhythmogenic right ventricular cardiomyopathy (ARVC), left ventricular non-compaction (LVNC), and primary electrical alterations such as long QT syndrome (LQTS), broaden the number of patients potentially benefiting from ICD therapy. Furthermore, in a patient suffering a coronary event, efficacy and proper timing of revascularization is pivotal to avoid the worsening of left ventricular ejection fraction, and to subsequently lead to lower risk of arrhythmias and SCD.

#### *Appropriate therapy and mortality*

Altogether, 14% of the assessed patients presented appropriate ICD therapy. In recent studies, a trend towards a decrease of appropriate therapies has been identified, going from 60% in earlier studies, to rates of 10% in more recent studies.<sup>26-28</sup> Compared to NICM, patients with ICM had a 65% greater risk of presenting appropriate therapy, which is consistent with our multivariate and survival analyses. Stratifying by indication and comparing PP to SP, no significant differences were observed. An association between appropriate therapy and mortality was not identified. While the variable of age was a predictive factor of risk of appropriate therapy in the bivariate analysis, in the adjusted analysis the only predictor of risk was the use of amiodarone.

Multiple analyses have evaluated possible predictors of appropriate therapies including advanced age, renal insufficiency, left ventricular dysfunction, ischemic etiology, previously documented non sustained ventricular tachycardia, high blood pressure, non-use of beta-blockers, among others.<sup>10,29</sup> Amiodarone has been the standard of care for ventricular arrhythmias, and continues to be an alternative for patients with appropriate or inappropriate ICD therapy in order to reduce arrhythmic load and interventions. Use of this medication is more frequent in patients that are more ill, with previous arrhythmia, with appropriate or inappropriate ICD therapy. Therefore, instead of a predisposing factor, it may actually be a marker that can identify patients with increased risk of death.

#### *Inappropriate therapy and mortality*

Incidence of inappropriate therapy was 13.6%, being lower than that reported in previous Latin American studies. Compared to patients with NICM, patients with ICM had a 49% lower risk of inappropriate therapy. Patients with NICM receiving ICD therapy and presenting inappropriate therapy had an 11% greater risk of mortality compared to patients with ICM. Inappropriate therapies are not harmless, as they reflect the presence of concomitant arrhythmias and may lead to myocardial injury. Several studies have reported an association between inappropriate therapies, loss of quality of life, and mortality.<sup>30,31</sup> However, in the recent studies by Dichtl et al, and Deyell et al, an association between inappropriate therapy and mortality was not identified.<sup>15,32</sup> The discrepancy among results may be explained by several factors such as evolution of optimal therapy, shock reduction, increased use of overstimulation therapy, and earlier implantation of ICD in relatively less ill patients. Nonetheless, while there is no significant association with mortality, all efforts geared towards reducing inappropriate therapies consistently improve patients' quality of life.

#### **Study limitations**

This study has limitations that must be taken into account in order to interpret the data. First, our

sample size may be insufficient to determine all-cause mortality and cardiovascular mortality outcomes. A census was performed, and the power of the group of participating patients was determined. The power was calculated for all-cause mortality as an outcome, however, by performing subgroup analysis the power and subgroup size are limited, as is the frequency of events, which may affect the statistical significance of our results. Nonetheless, our sample size is the largest reported for Colombia, and is comparable to other multinational registries in Latin America, and thus our conclusions are valuable for clinical practice. Secondly, registering patients in a single geographical region of the country may imply a selection bias and may limit the generalization of our findings to the rest of the Colombian territory, particularly for areas with patients with Chagas heart disease. However, the diversity of the participating patients in regards to etiology, socioeconomic status, attending physician, and extent of treatment, may support that the information gained in our study provides an overall picture of patients with ICD in our environment. Finally, we were not able to determine cause of patients' death, and therefore we could not establish whether it was of cardiovascular origin. Thus, having all-cause mortality as an outcome in our study constitutes a limitation, despite it being commonly used as outcome in many other studies.

### CONCLUSIONS

This study reports the largest number of patients with ICD, and the longest follow-up time in Colombian. In our patients, ischemic cardiomyopathy is the main etiology for which ICD are implanted, and primary prevention the main indication. The demographic profile of patients receiving ICD implantation and prescription of appropriate medication for heart failure is comparable to those reported in previous international studies. Rates of appropriate and inappropriate therapy are lower than those reported in recent series, favoring reduction of costs due to unnecessary hospital admissions and improving patients' quality of life. Our survival analysis suggests that ischemic etiology is associated with a greater

rate of appropriate therapy and a higher risk of mortality, whereas non-ischemic etiology was associated to greater rates of inappropriate therapy compared to ICM. Optimized device programming is associated to lower risk of appropriate therapy. Based on our results, therapeutic protocols for patients with ICD in Colombia may be modified in order to reduce the rate of inappropriate therapy by proper device programming, following parameters proposed by international guidelines.

### Key points

What is known about appropriate and inappropriate therapies?

- Appropriate and inappropriate ICD therapies have been associated to increased mortality in several North American and European studies.
- In Latin American countries, information regarding prognostic impact of ICD therapies are scarce.

What is the contribution of this study?

- The profile of comorbidities and indications of patients with cardioverter defibrillator are similar to that of developed countries. Incidence of inappropriate therapy has decreased.
- In our cohort, ischemic etiology is more frequently associated with appropriate therapies.
- We did not identify an association between appropriate or inappropriate ICD therapy and mortality at short-term follow-up.

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