Lack of current implantable cardioverter defibrillator guidelines application for primary prevention of sudden cardiac death in Latin American patients with heart failure: a cross-sectional study

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Aims
This cross-sectional study evaluated the application of accepted international implantable cardioverter defibrillator (ICD) guidelines for primary prevention of sudden cardiac death in patients with heart failure.

Methods and results
The PLASMA (Probabilidad de Sufrir Muerte Arritmica) study was designed to characterize management of cardiac patients in Latin America. Twelve centres included 1958 consecutively admitted patients in cardiology units in 2008 and 2009. Discharged patients were evaluated for primary prevention, ICD indication and prescription by general cardiologists. Of 1711 discharged patients, 1525 (89%) had data available for evaluating indication status. Class I indications for ICD therapy were met for 153 (10%) patients based on collected data. Only 20 (13%, 95% confidence interval: 7.7–18.4%) patients with indication were prescribed an ICD. Patients prescribed an ICD were younger than patients who were not prescribed an ICD (62 vs. 68 years, P = 0.01). The reasons given by cardiologists for not prescribing an ICD for 133 patients with an indication were: indication criteria not met (75%), life expectancy <1 year (9.7%), rejection by the patient (5.2%), no medical coverage paying for the device (3.7%), psychiatric patient (2.2%), and other reasons (4.2%).

Conclusions
In Latin America, international guidelines for primary prevention ICD implantation are not well followed. The main reason is that cardiologists believe that patients do not meet indication criteria, even though study data confirm that criteria are met. This poses a significant challenge and underlines the importance of continuous and improved medical education.

Keywords
Implantable cardiac defibrillators • Sudden cardiac death • Heart failure • Guidelines

Introduction
Ventricular tachyarrhythmias are the leading cause of sudden cardiac death (SCD) in developed countries. Randomized clinical trials have shown that implantable cardioverter defibrillators (ICDs) reduce mortality from any cause in high-risk populations.1,2 Current international guidelines consider ICDs to be the best therapy choice for patients with ischaemic and non-ischaemic heart disease, heart failure, and ejection fraction (EF) ≤ 35%.3
The annual incidence of SCD in Latin America is not known. In the general Argentinian population it is similar to what is seen in developed countries. However, the annual rate of ICD implants varies considerably between Latin American countries and is typically much lower than in developed countries. The lower rate of ICD implants in Latin America may be influenced by several factors including the degree of guideline knowledge, physicians’ acceptance of this therapy option, and the availability of resources that allow access to this intervention.

Limited published data exist reporting the number of primary prevention patients in Latin America who meet guidelines and are prescribed an ICD. The PLASMA (Spanish acronym for Probabilidad de Sufrir Muerte Arritmica) study investigated the clinical features and therapy choice for patients in cardiac care centres who met ICD guideline indications. The specific objectives of this study were to (i) estimate how many hospitalized patients meet primary prevention ICD indications in Latin America, (ii) estimate how many indicated patients were prescribed an ICD, (iii) compare the ICD prescription proportion between three well-defined indication groups (based on patient profiles), and (iv) report reasons for not prescribing devices to patients meeting criteria for indication.

Methods

PLASMA was a cross-sectional study carried out in 12 Latin American medical centres (Argentina, Chile, Colombia, Mexico and Dominican Republic) between August, 2008 and December, 2009. Electrophysiologists served as the principal investigator at each centre. The study protocol was approved by the ethics committees at each participating centre and all patient participants provided informed consent. This study complies with the Declaration of Helsinki. The Appendix shows a list of all participating centres and researchers.

Participants

All patients hospitalized for any cause at a coronary care unit or cardiology service were eligible to participate. To avoid possible selection bias, all hospitalized patients were included except for those who died during hospitalization because they would have no chance to have an ICD prescribed. The number of participants was solely based on how many patients were hospitalized during the study timeframe.

Statistical methods

For reporting patient characteristics, proportions were used for categorical variables and means with standard deviations were used for continuous variables. Comparisons between patients with ICDs prescribed and not prescribed were performed using the Wilcoxon–Mann–Whitney test for numerical or ordinal variables and the \( \chi^2 \) test or Fisher’s exact test for categorical variables. The \( \chi^2 \) test was used to compare indication groups. Two-tailed \( P \) values were reported. Statistical significance was claimed for values of \( P < 0.05 \). Confidence intervals (CIs) for proportions were constructed using the normal approximation method.

Results

Participants

One thousand, nine hundred and fifty-eight patients were enrolled (1125 men and 833 women) with a mean age of 64 ± 14.6 years (range 7–99). Patients who died during hospitalization were not included (n = 247), leaving 1711 patients with collected data. Patient diagnosis at admission was acute coronary syndrome without ST-segment elevation in 36% (n = 611), heart failure in 15% (n = 247), cardiac arrhythmia in 26% (n = 453), AMI in 14%
Information for determining indication group was documented for 1525 (89%) of the 1711 discharged patients. Patients classified as ‘unknown if indicated’ differed by diagnosis at admission (9% for acute coronary syndrome, 17% for heart failure, 16% for cardiac arrhythmia, 0% for AMI; and 11% for other, \( P < 0.001 \)). After excluding patients with MI \( n = 246 \), cardiac intervention \( n = 245 \), no heart failure \( n = 547 \), NYHA class IV \( n = 18 \), EF > 35% \( n = 316 \), and those ‘unknown if indicated’ \( n = 186 \), 153 patients with an ICD indication remained for further analyses. Figure 1 depicts the complete patient flow. Of all 1525 discharged patients with a known indication status, 153 (10%) met a primary prevention indication according to ICD therapy guidelines.

**One hundred and fifty-three patients with implantable cardioverter defibrillator indications**

Clinical characteristics of the patients who met ICD indications are shown in Table 1. The patients were predominantly male (75.8%) with a mean age of 67.1 ± 13 years (range 32–94). Heart failure aetiologies were reported as ischaemic (61.3%), idiopathic (8.1%), valvular (10.5%), hypertensive (5.7%), Chagasic (5.7%), alcoholic (4%), and chronic obstructive pulmonary disease (1.6%). The pharmacological treatments were angiotensin enzyme inhibitors or angiotensin II receptor blockers (78%), beta-adrenergic blockers (75%), aldosterone antagonists (46%), and amiodarone (25%). Ninety-eight patients were in Group 1 (64%), 38 in Group 2 (25%), and 17 in Group 3 (11%). Fifty-one patients (33%) met MADIT II criteria for primary prevention of sudden death, 102 (67%) met SCD-HeFT criteria, and no patients met MADIT I criteria.

**Implantable cardioverter defibrillator prescription**

Of the 153 patients with a class I ICD indication according to the guidelines, 20 (13.1%, 95% CI: 7.7–18.4%) had an ICD prescribed [includes cardiac resynchronization therapy-defibrillator (CRT-D) prescriptions]: 17 during hospitalization and 3 prior to hospitalization. Four patients were prescribed a CRT-D and 16 an ICD. Table 1 shows the clinical characteristics for patients who were prescribed an ICD and those who were not. Patients prescribed an ICD were younger than patients who were not (62 vs. 68 years, \( P < 0.01 \)), had more Chagas’ disease, were more often obese and were more likely to use spironolactone and amiodarone. An ICD was prescribed in 13.2% of Group 1 patients (13/98), 18.4% of Group 2 patients (7/38), and 0% of Group 3 patients (0/17; Figure 2). The proportion of ICD prescriptions did not differ significantly between the three groups (\( P = 0.17 \)). None of the 186 patients who were ‘unknown if indicated’ had an ICD prescribed.

The main reasons general cardiologists gave for not prescribing an ICD for 133 patients with indication (according to study data) were ‘indication criteria not met’ (75%), life expectancy < 1 year (9.7%), rejection by the patient (5.2%), no medical coverage paying for the device (3.7%), psychiatric patient (2.2%), and other reasons (4.2%). When considering the 34 patients for whom general cardiologists believed indication criteria were met, the distribution of reasons became life expectancy < 1 year (38.2%), rejection by the patient (20.5%), no
medical coverage paying for the device (14.7%), psychiatric patient (8.8%), and other reasons (17.6%; Figure 3). ‘Indication criteria not met’ was the most frequent reason cited by the physician in all three indication groups, with reported frequencies of 68 (80%), 16 (52%), and 15 (88%) in Groups 1, 2, and 3, respectively. General cardiologists were more likely to report this reason for patients in Groups 1 and 3 compared with Group 2 (P = 0.009).

**Discussion**

**Patients with an indication and implantable cardioverter defibrillator prescriptions**

PLASMA provides insights into real-world practices for primary prevention of SCD in Latin America. This cross-sectional sample showed that 10% of patients hospitalized for any reason at cardiology services met guideline indications for ICD therapy. Thirteen percent of patients meeting indication criteria were prescribed an ICD. The ICD prescription proportion did not differ between three defined indication groups based on patient measurements of EF, NYHA class, ischaemic aetiology, and history of MI. The observed ICD prescription rate in PLASMA is lower than reported in the GWTG-HF registry in which only one of every five potentially eligible patients either arrived at implant or were told about ICD therapy at discharge. The IMPROVE HF study reported that 51% of

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**Table 1 Clinical characteristics for patients meeting implantable cardioverter defibrillator indications**

<table>
<thead>
<tr>
<th>Variable</th>
<th>ALL (n = 153)</th>
<th>ICD (n = 20)</th>
<th>No ICD (n = 133)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean, SD)</td>
<td>67.1 ± 13.0</td>
<td>61.5 ± 9.6</td>
<td>68.0 ± 13.3</td>
<td>0.012</td>
</tr>
<tr>
<td>Male</td>
<td>116 (76%)</td>
<td>17 (85%)</td>
<td>99 (74%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Diabetes</td>
<td>48 (31%)</td>
<td>6 (30%)</td>
<td>42 (32%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>53 (35%)</td>
<td>6 (30%)</td>
<td>47 (35%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Obesity</td>
<td>30 (20%)</td>
<td>8 (40%)</td>
<td>22 (17%)</td>
<td>0.029</td>
</tr>
<tr>
<td>Smoking</td>
<td>35 (23%)</td>
<td>8 (40%)</td>
<td>27 (20%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>109 (71%)</td>
<td>15 (75%)</td>
<td>94 (71%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>10 (67%)</td>
<td>1 (5%)</td>
<td>9 (7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>61 (40%)</td>
<td>10 (50%)</td>
<td>51 (38%)</td>
<td>0.32</td>
</tr>
<tr>
<td>NYHA III</td>
<td>38 (25%)</td>
<td>8 (40%)</td>
<td>30 (23%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>51 (34%)</td>
<td>4 (20%)</td>
<td>47 (35%)</td>
<td>0.17</td>
</tr>
<tr>
<td>LVEF (mean, SD)</td>
<td>26.3 ± 5.9</td>
<td>25.3 ± 5.6</td>
<td>26.5 ± 6.3</td>
<td>0.42</td>
</tr>
<tr>
<td>QRS duration (ms) (mean, SD)</td>
<td>112 ± 29</td>
<td>129 ± 31</td>
<td>109 ± 28</td>
<td>0.012</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>10 (7%)</td>
<td>2 (10%)</td>
<td>8 (6%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Ischaemic</td>
<td>75 (49%)</td>
<td>11 (55%)</td>
<td>64 (48%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Chagas</td>
<td>7 (5%)</td>
<td>3 (15%)</td>
<td>4 (3%)</td>
<td>0.048</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>119 (78%)</td>
<td>15 (75%)</td>
<td>104 (78%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>115 (75%)</td>
<td>13 (65%)</td>
<td>102 (77%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>71 (46%)</td>
<td>14 (70%)</td>
<td>57 (43%)</td>
<td>0.023</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>38 (25%)</td>
<td>9 (45%)</td>
<td>29 (22%)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

ARB, angiotensin receptor blockers; ACEI, angiotensin-converting enzyme inhibitors; CM, cardiomyopathy; ICD, implantable cardioverter defibrillator; LVEF, left ventricle ejection fraction; NYHA, New York Heart Association.
eligible US patients received ICD or CRT-D therapy. Other studies have found a low adherence to guidelines for ICD implantation, although this appears to be even lower in Latin America.

Reasons for not prescribing an implantable cardioverter defibrillator for patients with criteria for indication

The most cited reason (75% overall) for not prescribing an ICD during hospitalization was 'indication criteria not met' in all three patient groups, even though these patients met indications according to collected study data. The most likely explanation is that general cardiologists in Latin America, often not well versed in device therapy, were not aware of or meticulously applying the guidelines criteria. A previous study showed that the lack of electrophysiologists or limitations in hospital facilities were significant causes for low implant rates. In PLASMA, participating centres had state-of-the-art technology and personnel specializing in ICD implants and management, including electrophysiologists. However, when general cardiologists care for patients in Latin American coronary care units, typical practice does not usually include consulting an electrophysiologist.

It is also possible that other patient characteristics were considered in addition to guidelines criteria. In this population, patients prescribed an ICD were younger and more likely to use spironolactone and amiodarone compared with those not prescribed an ICD. Voller et al. also reported that younger patients were more likely to receive an ICD. PLASMA patients meeting primary prevention indications were 67 years old on average, which is higher than SCD-HeFT (60 years) and MADIT II (64 years). However, advanced age is not a contraindication for ICD therapy. Another explanation is that physicians were content to use medications first even though ICDs have proven survival benefit compared with conventional medical therapy.

Several randomized trials have shown that angiotensin-converting enzyme inhibitors, beta blockers, and aldosterone antagonists improve survival in patients with heart failure. The percentage of patients receiving these drugs at discharge was 78, 75, and 46%, respectively, which is comparable to reports from developed countries. Amiodarone was prescribed for 25% of patients which is typical practice in Latin America for treating atrial and ventricular arrhythmias. In our study, 34% of patients had atrial fibrillation for which the first drug treatment is amiodarone.

Economic considerations

The cost of treatment is another decision-making point in ICD prescription. Cost-effectiveness studies conducted in the USA and Europe showed an acceptable result for ICD therapy. Alcaraz et al. studied an Argentinian population, concluding that devices are clearly cost-effective in the MADIT I population and are moderately cost-effective for patients with MADIT II characteristics or in secondary prevention. Mark et al. found ICDs to be economically efficient at improving health benefits in SCD-HeFT patients. In PLASMA, 33% of patients met MADIT II criteria and 67% met SCD-HeFT criteria for primary prevention of SCD. Ribeiro et al. showed that the costs associated with ICD treatment are proportionately higher in Brazil compared with developed countries, but the cost-benefit ratio still favours the ICD. Given that 14.9% of patients meeting criteria for indication in the PLASMA study did not receive an ICD due to a financial reason, cost played a modest role in not prescribing ICD therapy.

Patient refusal

Current medicine is faced with a paradigm change in which patients have become active participants in the decision-making process regarding their health. In PLASMA, when physicians...
believed ICD indications were met and discussed that therapy option, 20.9% of patients refused. Voller et al. reported 29.2% of patients denied ICD therapy; a sizeable impact on ICD therapy application. The ‘availability heuristic’ of Tversky and Kahneman shows that behaviour is influenced by how easily an event is remembered. Thus, the decision to use a therapy is affected by physician and patient knowledge of the risk-benefit ratio, the way in which the information is presented and past experiences.

Limitations
The guidelines recommend ICD therapy without distinction between outpatients or inpatients. All patients included in this study were hospital inpatients at state-of-the-art medical institutions. Thus the indication and ICD prescription rates reported may not represent the broader Latin American population. One hundred eighty-six patients (10.8%) were classified as ‘unknown if indicated’ thereby excluding them from analysis. The ‘unknown’ classification differed by admission reason, most notably being 0% for AMI admissions because they were automatically classified as not meeting indication criteria (MI < 40 days). No patients with an ‘unknown’ classification were prescribed an ICD. However, how many of those patients would have met indications if pertinent information was available remains unknown.

Conclusion
The PLASMA study investigated patients hospitalized in Latin American cardiac care centres and found that only 13% who met the ACC/AHA/HRS guidelines class I criteria for primary prevention ICD indication had a device prescribed. The main reason cited by general cardiologists for not prescribing an ICD was ‘indication criteria not met’ (75% of patients), even though study data confirmed indication. This reveals a lack of adherence to internationally accepted guidelines and emphasizes the need for increased awareness and committed application of guidelines in Latin American medical practice. This may be achieved through increased collaboration with electro-physiologists and more effective and continuous medical education by universities, medical institutions, and scientific societies.

Faced with the dual epidemic of SCD and heart failure, increasing application of cost-effective ICD therapy could save thousands of lives.

Conflict of interest: C.A.M. and B.J.P. are employed by Medtronic.

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Appendix

PLASMA investigators

References


Images in Electrophysiology

Pseudo T-wave variations on internal loop recorder: predictor or confounder?

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An internal loop recorder (ILR) was implanted in a 37-year old man with a history of palpitations and syncope. A subsequent asymptomatic automated recording showed ‘pseudo’ T-wave alternans (TWA) with parallel variation of T-wave and QRS complexes (emphasized in the upper panel) that was quickly followed by monomorphic non-sustained ventricular tachycardia (NSVT). Previous reports of pseudo TWA have emphasized the non-arrhythmic nature of this phenomenon. Indeed, in this patient pseudo TWA were frequently recorded but this was the only episode of NSVT and subsequent invasive ventricular programmed stimulation failed to produce any arrhythmia.

Conflict of interest: none declared.

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