Evaluation of Cardiac $^{123}$I-MIBG Imaging in Patients With Severe Left Ventricular Dysfunction and Indication for Implantable Cardioverter Defibrillator

**Estudio de la inervación simpática cardíaca con $^{123}$I-MIBG en pacientes con disfunción ventricular izquierda grave e indicación de desfibrilador**

To the Editor,

Identification of noninvasive prognostic markers in patients with left ventricular dysfunction (LVD) is a challenge for the clinician. Although LVD is in itself an important predictor of adverse cardiac events, other markers are needed to refine risk stratification, as a poor correlation between the degree of LVD and adverse cardiac events is often observed in clinical practice.

The presence of myocardial fibrosis in cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement$^{1,2}$ and the deterioration of sympathetic cardiac innervation quantified by $^{123}$I-metaiodobenzylguanidine ($^{123}$I-MIBG) scintigraphy$^{3-6}$ have been introduced as new risk markers in recent years. We designed a prospective observational study with the aim of assessing whether the combination of information from these 2 techniques can improve risk stratification when an implantable cardioverter defibrillator is indicated for primary prevention.

We studied 47 consecutive patients with cardiac failure in New York Heart Association functional class II or III at baseline, left ventricular ejection fraction ≤35%, optimum pharmacological treatment, and class I indication for implantable cardioverter defibrillators, who had undergone prior cardiac MRI and $^{123}$I-MIBG scintigraphy. Events were recorded during follow-up. The study was approved by the ethics committee of our hospital and patients provided their informed consent in writing. Here, we present the findings of cardiac innervation and its association with cardiac events during follow-up.

Scintigraphy of cardiac innervation was performed by intravenous injection of 10 mCi of $^{123}$I-MIBG and subsequent image acquisition in the anterior region of the chest at 15 min and 4 h after injection of the tracer. Myocardial uptake of $^{123}$I-MIBG was quantified by the early and late heart-to-mediastinum ratio (HMR) and the washout rate.

Categorical variables are expressed as percentages and quantitative ones as mean (SD). Variables were compared using the $\chi^2$ test (categorical) or the Fisher and Student t test (quantitative). Predictors of events were established by univariate analysis and variables with $P < .1$ were included in the Cox multivariate analysis and expressed as hazard ratio (HR). The cumulative incidence of events was estimated by the Kaplan-Meier method, and compared using the log-rank test. The SPSS Statistics 17 program was used. Statistical significance was set at $P < .05$.

Baseline characteristics and findings of the cardiac innervation study are shown in the Table. There was a predominance of male patients, who were relatively young and had limited comorbidities. The etiology of LVD was ischemic, as is usually the case in primary prevention of sudden death. Eighteen events were recorded during a mean follow-up of 12.9 (8.6) months: 2 deaths (1 sudden death and 1 death due to heart failure), 7 hospitalizations due to heart failure, 7 appropriate implantable cardioverter defibrillator shocks, and 1 acute myocardial infarction.

The sample was divided into 2 groups according to the incidence of events. The groups had comparable pharmacological treatment, LVD etiology, presence of late gadolinium enhancement, and left ventricular ejection fraction quantified by cardiac MRI. However, the QRS interval was significantly greater in patients with events. With regard to the findings of cardiac innervation, markedly pathologic HMR values were observed (<1.20, 15 patients; 1.20-1.40, 13 patients; 1.40-1.60, 15 patients; >1.60, 4 patients) and only 1 patient had a normal (>1.80) value. The patients with events had a significantly lower late HMR (1.27 [0.13] vs 1.37 [0.23]; $P = .049$). The multivariate analysis included QRS interval, creatinine levels, treatment with angiotensin converting enzyme inhibitors/angiotensin II receptor antagonists, and early and late HMR <1.38 (median). An association was observed between late HMR <1.38 (HR = 5.19; 95% confidence interval [95%CI], 1.4-19.6; $P = .015$) and creatinine levels (HR = 3.84; 95%CI, 1.8-8.4; $P = .001$) and an increased risk of experiencing an event. When only arrhythmic events were analyzed, no significant differences were observed in any of the variables. The Figure shows the survival curves for cardiac events and arrhythmic events, stratified using the median value of late HMR (log-rank test, $P = .001$ and $P = .128$, respectively).

The results of our study show a marked deterioration in cardiac innervation, as assessed by $^{123}$I-MIBG scintigraphy, in patients with severe LVD and indication for implantable cardioverter defibrillator. Moreover, this deterioration was more marked than

**REFERENCES**


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that reported in previous studies.\textsuperscript{3–6} In fact, only 5 of the 47 patients had late HMR $>$ 1.6 (cut-off point for poor prognosis found in the ADMIRE study\textsuperscript{5}). Even in this setting, this technique manages to identify high-risk patients and could improve noninvasive prognostic stratification, thereby assisting in decision-making.

We recognize the limitations inherent in this design; the study was observational with a limited sample size and a short follow-up period. The study forms part of a larger project in which the combined information provided by \textsuperscript{123}I-MIBG scintigraphy and cardiac MRI will be assessed. The results presented here should therefore be considered as preliminary.

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\textbf{Table}

Baseline Characteristics of the Overall Sample and According to Whether Major Cardiac Events Occurred

<table>
<thead>
<tr>
<th></th>
<th>Total number of patients (n=47)</th>
<th>Patients with events (n=18)</th>
<th>Patients without events (n=29)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>34 (72.3)</td>
<td>12 (66.7)</td>
<td>22 (75.4)</td>
<td>.493</td>
</tr>
<tr>
<td>Age, years</td>
<td>63.4±9.8</td>
<td>65.2±9.8</td>
<td>62.2±9.8</td>
<td>.319</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>28 (61)</td>
<td>12 (66)</td>
<td>18 (62)</td>
<td>.518</td>
</tr>
<tr>
<td>QRS, ms</td>
<td>119.8±38.9</td>
<td>134.4±43.1</td>
<td>105.7±33.0</td>
<td>.037</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>31 (62)</td>
<td>12 (67)</td>
<td>19 (65)</td>
<td>.869</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>1.16±0.6</td>
<td>1.41±0.8</td>
<td>0.99±0.3</td>
<td>.052</td>
</tr>
<tr>
<td>Hemoglobin, mg/dl</td>
<td>12.9±2.0</td>
<td>12.6±2.0</td>
<td>13.1±1.0</td>
<td>.382</td>
</tr>
<tr>
<td>BNP, pg/mL</td>
<td>1087.4±776.6</td>
<td>1134.4±823.8</td>
<td>1040.4±773.3</td>
<td>.806</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors or ARB</td>
<td>44 (94)</td>
<td>15 (83)</td>
<td>29 (100)</td>
<td>.051</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>47 (100)</td>
<td>18 (100)</td>
<td>29 (100)</td>
<td>1</td>
</tr>
<tr>
<td>Diuretics</td>
<td>41 (87)</td>
<td>18 (100)</td>
<td>23 (82)</td>
<td>.243</td>
</tr>
<tr>
<td>Antialdosterones</td>
<td>31 (66)</td>
<td>13 (72)</td>
<td>18 (62)</td>
<td>.475</td>
</tr>
<tr>
<td>Cardiac magnetic resonance imaging</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF, %</td>
<td>24.9±9.0</td>
<td>26.0±10.8</td>
<td>24.4±8.4</td>
<td>.650</td>
</tr>
<tr>
<td>LVEDV, mL/m$^3$</td>
<td>136.9±43.7</td>
<td>137.5±28.4</td>
<td>136.7±49.0</td>
<td>.961</td>
</tr>
<tr>
<td>LVESV, mL/m$^3$</td>
<td>104.7±42.5</td>
<td>102.9±30.6</td>
<td>105.5±47.0</td>
<td>.874</td>
</tr>
<tr>
<td>LGU present</td>
<td>40 (85.1)</td>
<td>17 (94)</td>
<td>23 (79)</td>
<td>.161</td>
</tr>
</tbody>
</table>

\textsuperscript{123}I-MIBG: \textsuperscript{123}I-metaiodobenzylguanidine; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; HMR, heart-to-mediastinum ratio; LGU, late gadolinium uptake; LVEDV, left ventricular end diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end systolic volume. Data expressed as percentage, No. (%), or mean ± SD.

**Figure.** Kaplan-Meier major cardiac event-free survival curve (A) and arrhythmic event-free survival curve (B) stratified by the median value (1.38) of the late heart-to-mediastinum ratio (HMR). HMR, heart-to-mediastinum ratio.
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Subcutaneous Infusion of Furosemide Administered by Elastomeric Pumps for Decompensated Heart Failure Treatment: Initial Experience

Tratamiento de la insuficiencia cardíaca descompensada con furosemida subcutánea mediante bombas elastoméricas: experiencia inicial

To the Editor,

In Spain, the prevalence of heart failure (HF) exceeds 15% among the elderly.1 Managing HF consumes 1% to 2% of the healthcare budget and hospitalizations consume two-thirds of this expenditure.2 Diuretics are the main treatment and furosemide is the most commonly used drug. Its action may be decreased by multiple factors, leading to the need for intravenous infusion2 and often involving hospitalization. Experience in the use of subcutaneous (s.c.) furosemide is scarce and the systems most frequently used are dependent on health care personnel.3 Elastomeric infusion pumps are non-electric, disposable, continuous-flow pumps that are widely used in antimicrobial therapy, analgesia, and cancer treatment.5 They are little used in HF, but could be an alternative diuretic treatment for patients with decompensated HF. We describe the response to treatment of a series of ambulatory HF patients with indications for parenteral diuretic therapy treated with s.c. furosemide using elastomeric pumps.

Between December 2010 and December 2011, s.c. furosemide was administered in the Heart Failure Unit (University Hospital, Valladolid, Spain) to resolve 41 episodes in 24 patients with decompensated Heart Failure. We included 65 clinical and laboratory variables. Patients who did not meet the criteria for parenteral administration were excluded.

Continuous s.c. furosemide was administered by elastomeric pump in an outpatient setting. Treatment was given for 4 or 5 days (96 mL at 1 mL/h or 240 mL at 2 mL/h) depending on pump volume and preset flow rate. The pumps were connected to a catheter (Abbocath 20–22G™) implanted subcutaneously in chest or abdominal tissue (Figure A). The catheter was maintained indefinitely in the absence of complications. The daily dose was calculated at the discretion of the prescribing physician and administered in dextrose 5% Patients were monitored in the HF Unit every 5 to 7 days. Blood was collected at baseline and at the end of treatment. The

Figure. A, infusion pump, components, and subcutaneous implantation technique (1, infusion pump; 2, elastometric reservoir with furosemide in dextrose 5%; 3, flow controller; 4, extension; 5, plastic catheter implanted subcutaneously in chest tissue; 6, transparent patch). B, variations (Δ) in weight and serum creatinine, potassium, and sodium at the beginning and end of treatment with a confidence interval of 95% (95% CI). Significant weight loss was observed.

REFERENCES

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