


- Greene SJ, Khan MS. Quadruple medical therapy for heart failure: Medications working together to provide the best care. *J Am Coll Cardiol.* 2021;77:1408-1411.
- Shah A, Mentz RJ, Sun JL. Emergency department visits versus hospital readmissions among patients hospitalized for heart failure. *J Card Fail.* 2022;28:916-923.

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2605-1532/

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Sociedad Española de Cardiología.

<https://doi.org/10.1016/j.rcc.2023.03.008>

On-line el 25 de abril de 2023

Initial experience in cardiac contractility modulation combined with subcutaneous cardioverter-defibrillator

Experiencia inicial en modulador de la contractilidad cardiaca combinado con desfibrilador subcutáneo



To the Editor:

Cardiac contractility modulation (CCM) is one of the latest developed therapies aimed for patients with heart failure. Heart failure is a highly prevalent disease with a poor prognosis. Cardiac resynchronization therapy (CRT) has proved to reduce morbidity and mortality¹ in patients with reduced left ventricle ejection fraction (LVEF) and QRS > 150 ms and improve symptoms in patients with QRS > 130 ms. However, there is still a high percentage of patients who do not match these criteria and could benefit from other treatment options. The CCM device implanting procedure is similar to a pacemaker placement. It consists of positioning two bipolar leads at the right ventricular septum (local sense and right ventricle) that deliver non-activating biphasic high voltage impulses (generally 7.5 V at 22 ms) during the absolute refractory period. The use of this device has already been approved for patients with New York Heart Association (NYHA) class III heart failure and LVEF between 25% and 45% who remain symptomatic despite optimized medical treatment and who do not meet criteria for CRT. Four randomized clinical trials have shown benefits in exercise capacity and quality of life though long-term outcome data are still lacking.^{2,3} Many of these patients are also suitable for implantable cardioverter-defibrillator (ICD).⁴ At the moment, a device that combines CCM and ICD has not yet been developed, therefore these patients would need to carry 2 different devices, both on the right and left side, requiring at least 3 transvenous leads. Subcutaneous ICD (S-ICD) is an alternative to transvenous ICD that could be particularly useful in these cases, reducing the risk of lead-related complications and allowing us to keep one of the supe-

rior venous accesses free, so that it is available in case of need. Röger et al. published their long-term results of 20 patients treated with the combination of these two devices, showing successful outcomes with no problematic device interaction.⁵

We present the first 2 cases who underwent combined CCM and S-ICD therapy in our hospital. Patients' written informed consents were obtained.

The first patient is a 76-year-old woman with ischemic cardiomyopathy with LVEF of 31%, a NYHA class III-IV heart failure despite optimal medical treatment and a very limited functional capacity with a respiratory exchange ratio of 1.15 and a peak oxygen consumption (VO₂) of 8 mL/kg/min (Weber: D, Ventilatory Class: IV). The electrocardiogram showed a narrow QRS, so she was not suitable for CRT therapy. Therefore, a CCM Optimizer (Impulse Dynamics, USA) device was implanted. Afterwards, a S-ICD screening was performed both with CCM pacing on and off, with a positive test for the secondary vector in both right and left parasternal positions. Hence, the device was implanted using the 3 incisions technique (Fig. 1). We checked correct S-ICD sensing with CCM pacing activated and performed a successful defibrillation test. At the 6-month-follow-up visit, the patient referred a NYHA II functional class, both devices worked correctly, and she had received no shocks. A new ergospirometry was performed, demonstrating significant functional capacity improvement (Weber: C, Ventilatory class: III). VO₂ increased from 8 to 10 mL/kg/min and respiratory exchange ratio improved from 1.15 to 1.25. There was also an increase in ventilatory equivalent for oxygen (VEVO₂), from 55 to 41, and in the oxygen uptake efficiency slope, which rose from 0.87 to 1.1.



Fig. 1 – Posteroanterior and lateral chest X-ray showing cardiac contractility modulator and subcutaneous implantable cardioverter defibrillator devices in optimal position.

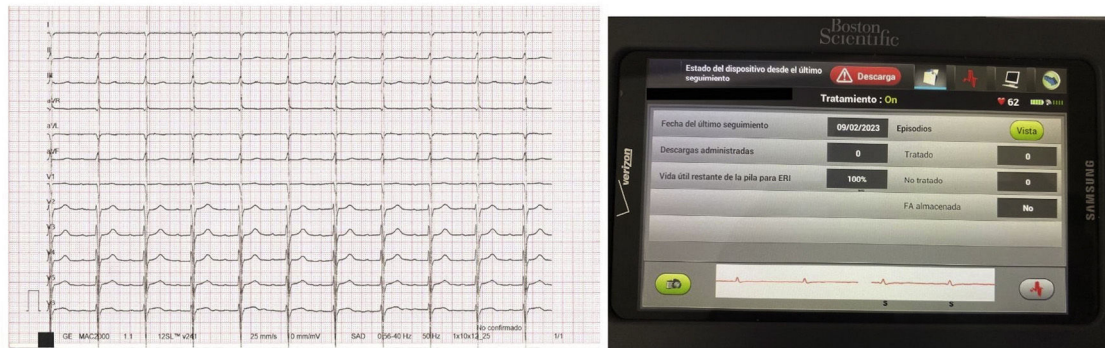


Fig. 2 – Electrocardiogram during cardiac contractility modulator stimulation (left) and subcutaneous implantable cardioverter defibrillator interrogation without noise detection (right).

The second patient is a 75-year-old male who also suffers from ischemic cardiomyopathy with a NYHA III functional class and a LVEF of 29%, severe pulmonary hypertension, persistent atrial fibrillation and a narrow QRS complex. In December 2022 an Impulse Dynamics Optimizer CCM was implanted. One month later, after a positive screening for the 3 vectors, a S-ICD was also implanted. During the second procedure a crosstalk test was performed. At the beginning, the S-ICD detected as noise some of the QRS complexes during CCM pacing at 7.5 V in all the different vector configurations. We recognized that the CCM was programmed with a very short delay between local sense and right ventricle stimulation. After reprogramming the device with a 45 ms delay the problem was solved and no further noise was detected (Fig. 2).

Our initial experience suggests that the combination of CCM and S-ICD is a safe strategy provided that a crosstalk test is performed during the implant procedure to rule out device interference and adjust the configuration if necessary.

This manuscript was conducted in accordance with the Declaration of Helsinki and meets the requirements for manuscripts submitted to biomedical journals of the ICMJE.

Funding

None.

Authors' contributions

L. Valverde Soria, L. Jordán-Martínez and F. Bermúdez, collected and analyzed the data. L. Valverde Soria wrote the manuscript with the help of the other authors. E. Cabrera Borrego, M. Molina-Lerma and M. Álvarez performed and supervised the technical procedures. M. Álvarez and M. Molina-Lerma conceived the idea and supervised the overall process. All authors discussed the results and contributed to the final manuscript.

Conflicts of interest

M. Álvarez has participated on a Boston Scientific (Abbott) Advisory Board. The rest of the authors have no conflicts of interest.

BIBLIOGRAFÍA

1. Cleland JG, Abraham WT, Linde C, et al. An individual patient meta-analysis of five randomized trials assessing the effects of cardiac resynchronization therapy on morbidity and mortality in patients with symptomatic heart failure. *Eur Heart J*. 2013;34:3547-3556.
2. Abraham WT, Kuck KH, Goldsmith RL, et al. A randomized controlled trial to evaluate the safety and efficacy of cardiac contractility modulation. *JACC Heart Fail*. 2018;6:874-883.
3. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:e895-e1032, <http://dx.doi.org/10.1161/CIR.0000000000001063>.
4. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J*. 2022;43:3997-4126.
5. Röger S, Rudic B, Akin I, et al. Long-term results of combined cardiac contractility modulation and subcutaneous defibrillator therapy in patients with heart failure and

reduced ejection fraction. *Clin Cardiol*. 2018;41:518-524.

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2605-1532/

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<https://doi.org/10.1016/j.rccl.2023.05.002>

Available online 27 May 2023

Serie de casos: síndrome de Kounis, una entidad infradiagnosticada

Case series: Kounis syndrome, an underdiagnosed entity



Sr. Editor:

El síndrome de Kounis se define como aquel síndrome coronario agudo desencadenado por una reacción de hipersensibilidad. Se describen tres variantes: tipo I (mayoritaria; 72%) en la que se produce vasoespasmo con arterias coronarias sin lesiones. Tipo II, donde sobre una base de enfermedad aterosclerótica aparece vasoespasmo, erosión o ruptura de placa. Y tipo III, en el que se produce trombosis de stent previamente implantado¹. Existe una gran variedad de factores desencadenantes (tabla 1), y es un cuadro de creciente incidencia en los últimos años.

Fisiopatológicamente, la exposición a alérgenos desencadena una respuesta inmunitaria principalmente a expensas de mastocitos (células muy presentes a nivel coronario) con mayor densidad en zonas de lesión endotelial y placa ateromatosa. La activación plaquetaria, su agregación y la liberación de citoquinas (histamina, serotonina, heparina, interleucina-6...) acaban desencadenando trombosis, rotura de placa o vasoespasmo coronario. En la actualidad destaca la creciente relación de este fenómeno con los eventos de trombosis tardía de stent, donde encontramos principalmente infiltrado de eosinófilos y mastocitos³.

Se da principalmente en pacientes de mediana edad con antecedentes alérgicos, asmáticos y con factores de riesgo

cardiovascular⁴. Entre los desencadenantes destacan las picaduras de insectos y el uso de antibióticos, y dentro de estos últimos, los betalactámicos.

Presentamos cuatro casos que hemos recogido en nuestro centro entre 2018 y 2022.

1. **Kounis tipo I.** Mujer de 69 años, quien sufrió parada cardiorrespiratoria tras administración de contraste intravenoso durante tomografía computarizada ambulatoria. Alternaba ritmos de fibrilación ventricular y asistolia, durante reanimación. Presentaba inestabilidad hemodinámica y precisó de noradrenalina y dobutamina a su ingreso en la Unidad de Cuidados Intensivos (UCI). Tenía trazados electrocardiográficos con bradicardia y ascenso de ST inferior, y la ecocardiografía en fase aguda mostró segmentariedad en territorio inferior, compatible con afectación de arteria coronaria derecha. Tras un pico de troponina T ultrasensible de 29.700 ng/L, la coronariografía emergente no reveló lesiones. Tuvo una rápida recuperación con retirada del soporte vasoactivo y hemodinámico en el segundo día de estancia en UCI, con normalización eléctrica y ecocardiográfica.
2. **Kounis tipo I.** Mujer de 33 años alérgica a ceftriaxona que presentaba, tras uso de ciprofloxacino, un cuadro de enro-