First experience in Spain of cardiac contractility modulation. A new alternative for patients with heart failure

Primera experiencia en España de la modulación de la contractilidad cardiaca. Una nueva alternativa para los pacientes con insuficiencia cardiaca

To the Editor,

Heart failure (HF) is a social and health care challenge, due to its high prevalence and poor prognosis.[1,2] In the case of patients with reduced left ventricular ejection fraction (LVEF), the prognosis may improve with the use of devices, such as an implantable cardioverter-defibrillator (ICDs) or cardiac resynchronization therapy. Cardiac resynchronization therapy also alleviates the symptoms of patients with QRS $>$ 130 ms, but these individuals only account for 30% of this population.[3] Therefore, new treatments are welcome, particularly when the QRS is narrow.

Cardiac contractility modulation (CCM) consists of delivering biphasic high-voltage signals (7.5 V/22 ms) to the interventricular septum during absolute refractory periods. The therapy is administered for several hours a day, using a device which, in its latest model, the Optimizer Smart IPG (Impulse Dynamics, United States), is fitted with 2 conventional pacemaker leads and is recharged wirelessly every week (figure 1). Implantation is similar to pacemaker placement and only requires local anesthesia. In cells, the device optimizes calcium handling by phospholamban phosphorylation and SERCA-2 upregulation, among others, thereby inducing reversal of the fetal myocyte gene program and favorable myocardial remodeling.[4] This effect occurs in the acute stage as well as in the long-term and not only in the area of energy release, but also over the entire myocardium. Several clinical trials support the benefits of this device; in fact, the latest trial, FIX-HF-5C, showed that CCM therapy improves exercise tolerance at 6 months (increase in peak oxygen consumption similar to that seen with cardiac resynchronization therapy, although population differences should be taken into account), quality of life, and a composite endpoint of cardiovascular mortality and HF hospitalizations.[5] Consequently, the European Society of Cardiology considers CCM to be a potential therapy for patients with HF (LVEF 25%-45%) and QRS $<$ 130 ms.[6]

We describe the first 3 cases in Spain of patients with HF and reduced LVEF who were symptomatic despite optimal medical therapy, who had no indication for heart transplant, and who underwent CCM implantation as a result (table 1).

The first patient was a 53-year-old woman with dilated cardiomyopathy, ICD implantation after aborted sudden cardiac death, and considerable limitations in her daily activities despite therapy. Therefore, a CCM device was implanted with no incidents. In the first few weeks, she exhibited a transient increase in the impedance of the CCM leads, probably related to inflammation in the insertion area in the myocardium, but that did not prevent device charging or proper application of the therapy.

The second patient was a 48-year-old man with dilated cardiomyopathy and severe systolic dysfunction. An ICD and a CCM were simultaneously implanted with no complications. At 3 months, the patient experienced an appropriate ICD discharge

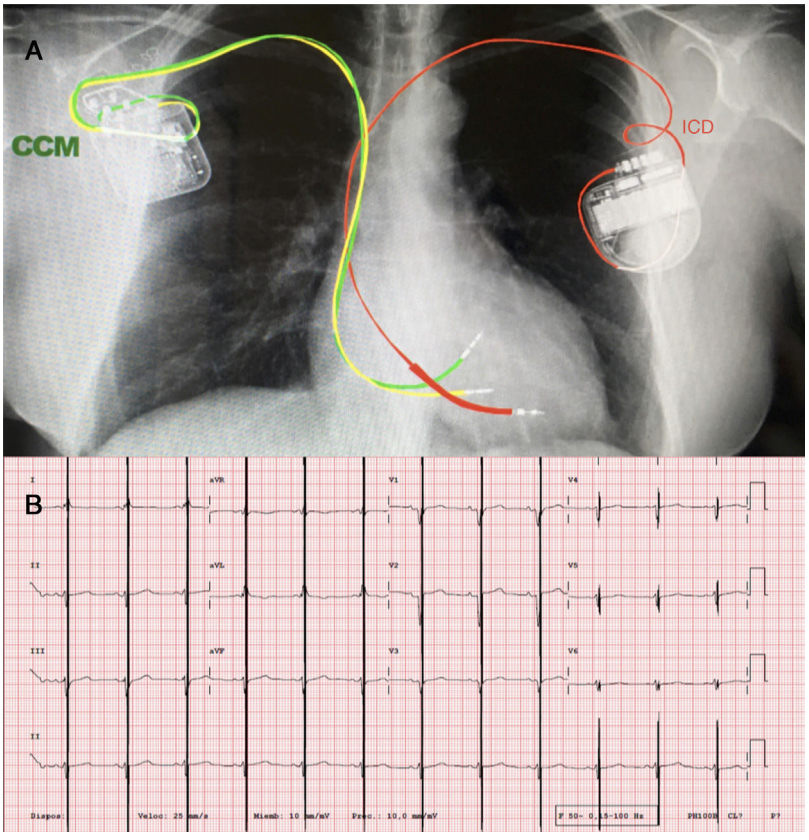

Figure 1. A: posteroanterior thoracic radiograph, showing the ICD generator at the top left, with its leads in the right ventricular apex, and the CCM generator at the top right, with its leads inserted in the interventricular septum. B: electrocardiogram showing the CCM therapy artifact in the middle of the QRS (intermittent treatment not seen in some electrocardiograms).

Table 1
Baseline characteristics and clinical progress of the 3 patients who received CCM therapy

	Patient 1		Patient 2		Patient 3	
Sex	Female		Male		Female	
Age, y	53		48		57	
Cause of LV dysfunction	DCM due to desmoplakin truncation		Idiopathic DCM		Ischemic (anterior infarction)	
Medical therapy						
ACEIs/ARB-IIs/ARNIs	SV 200 mg/12 h		SV 200 mg/12 h		SV 50 mg/12 h	
Beta-blockers	Bisoprolol 5 mg/d		Carvedilol 50 mg/12 h		No	
MRAs	Eplerenone 50 mg/d		Spironolactone 25 mg/d		Spironolactone 150 mg/d	
Ivabradine	No		7.5 mg/12 h		5 mg/12 h	
Diuretics	Furosemide 40 mg/d		Furosemide 40 mg/d		Furosemide 120 mg/d	
SGLT2I	No		Empaglifozin 25 mg/d		Empaglifozin 10 mg/d	
Rhythm	Sinus, QRS 109 ms		Sinus, QRS 100 ms		Sinus, QRS 95 ms	
ICD	Yes, secondary prevention		Yes, primary prevention		Yes, primary prevention	
	Baseline	6 mo	Baseline	6 mo	Baseline	6 mo
NYHA functional class	III	II	II	II	IV	II
LVEF by biplane Simpson, %	34	41	25	30	34	39
Indexed LVEDV, mL/m²	88	89	103	122	53	64
Indexed LVESV, mL/m²	57	53	78	86	35	39
TAPSE, mm	23	21	22	22	13	21
Peak VO_2, *mL/kg/min*	12	14	14	12.1	9	10.3
RER	1.01	1.15	1.09	1.1	1.28	0.94
VO_2, *mL/kg/min, at anaerobic threshold*	5.7	11.3	9	10.1	6	7.1
NT-proBNP, pg/mL	889	716	205	147	1228	1178

ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor antagonists; ARNIs, angiotensin receptor-neprilysin inhibitors; CCM, cardiac contractility modulator; DCM, dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; LV, left ventricle; LVEDD, left ventricular end-diastolic volume; LVESD, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; MRAs, mineralocorticoid-receptor antagonists; NYHA, New York Heart Association; RER, respiratory exchange ratio; SGLT2i, sodium-glucose co-transporter-2 inhibitors; SV, sacubitril-valsartan; TAPSE, tricuspid annular plane systolic excursion; VO_2, oxygen consumption.

due to ventricular fibrillation, which did not affect CCM functioning. This patient and the first one both had Medtronic ICDs with lead integrity alert algorithms, and during follow-up had occasional high-impedance measurements at the tip-coil dipole and detection of short V-V intervals which, after technical analysis by the 2 companies, were interpreted as episodic interference between the CCM and the ICD, with no repercussions on the functioning of either device.

The third patient was a 57-year-old woman with ischemic heart disease and severely reduced LVEF who had an ICD and a mechanical mitral valve. She progressed to dyspnea on minimal exertion. The CCM device was implanted with no incidents but, as in the first patient, it initially displayed a CCM device alarm due to increased impedance in the leads.

At 6 months (table 1), 2 patients had improved clinically, all 3 showed slight LVEF improvement, and peak oxygen consumption had improved in 2 but had worsened in the other. Additionally, oxygen consumption at the anaerobic threshold (considered the parameter least modifiable by motivation and training) had increased in all 3 patients, and although there were a slight decrease in the N-terminal fraction of probrain natriuretic peptide (NT-proBNP), it did not appear to be clinically significant. There were no changes in neurohormonal or diuretic medical treatments.

Therefore, our initial experience with CCM has been positive. The treatment has been demonstrated to be effective, as well as safe until this point in follow-up. In HF, these devices are known to have a placebo effect. However, the improvement observed in peak oxygen consumption at the anaerobic threshold suggests a beneficial therapeutic effect. Our patients experienced no device complications or relevant interferences with the ICD, other than the lead integrity alerts described.

CONFLICTS OF INTEREST

J. de Juan Bagudá, J.F. Delgado Jiménez, and F. Arribas Ynsaurriaga have participated as speakers at lectures sponsored by Impulse Dynamics. The Cardiology Department of the *Hospital Universitario 12 de Octubre* is participating in a clinical trial funded by Impulse Dynamics.

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Available online 6 May 2020

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https://doi.org/10.1016/j.rec.2020.04.003
1885-5857/

Surgery in patients with stents. New challenges in congenital heart disease

Cirugía sobre stents. *Nuevos retos en cardiopatías congénitas*

To the Editor,

Percutaneous interventions for the treatment of congenital heart disease are constantly improving.[1] As surgeons we must be familiar with the advances in this technology for 2 reasons:

- The approach to certain heart diseases has changed, particularly complex defects, which require staged percutaneous intervention and surgery.
- We will come across stents in the operating room; we must therefore learn how to deal with them and establish patterns or protocols to follow.

We present a series of 105 patients enrolled over 7 consecutive years (2013-2019) in whom previously implanted stents were manipulated during surgery. A previous study[2] reviewed the few publications on stents in tetralogy of Fallot,[3] patent ductus arteriosis,[4] and pulmonary arteries.[5]

In total, 131 stents were manipulated (table 1) in the following positions: 18 in ductus arteriosus, 34 in the right ventricular outflow tract, 11 in atrial septal defect, 14 in the right pulmonary artery (RPA), 36 in the left pulmonary artery, 7 in the superior vena cava, 7 in the inferior vena cava, 2 in the ascending aorta, and 2 in the left atrium (figure 1). The surgical procedures performed in the 105 patients (table 1) were as follows: 25 transplants, 13 Fontan procedures, 7 Glenn procedures, 2 comprehensive repairs (Norwood + Glenn), 2 Glenn take-downs, 23 conduit replacements (between the right ventricle and the pulmonary arteries), 11 Fallot repairs, 6 Rastelli procedures, 1 Ross-Konno procedure, 1 Yasui procedure (Norwood + Rastelli) and 14 others. Forty-seven of the patients had univentricular physiology.

Depending on the anatomical location, the stents were ligated externally (ductal clip) and partially removed (longitudinal opening and/or trimming the edge) or completely removed (after blunt dissection of the underlying structures). The criteria for partial or complete removal was based on the fragility/consistency of the stented vessel (pulmonary branches, right ventricle) and the surgeon's judgement (according to their experience). In addition, any additional unplanned procedures were also recorded, such as the use of deep hypothermic circulatory arrest (which increases surgical time and morbidity).

The most common anatomical locations stented were the left pulmonary artery and the right ventricular outflow tract. Together these represented two thirds (66%) of all stents. Transplants, conduit replacements and univentricular surgery together made up 80% of the main diagnoses. Unsurprisingly, these were all reinterventions (in some cases, multiple interventions were performed) and in children undergoing staged surgery and percutaneous procedures. Transplant surgery was where most double (or triple) stents were encountered (usually in the left pulmonary artery and superior or inferior vena cava).

The position of the device was not necessarily related to whether it was completely or partially removed. Paradoxically, a left pulmonary artery stent from a Glenn procedure can be cut to accommodate the suture in an extracardiac Fontan procedure (partial removal, easy), while the same patient would require complete removal of a stent in an identical position (plus pericardial patch enlargement of the pulmonary arteries) to allow a transplant to be performed (complete removal, difficult).

In the case of ductal stents, we should differentiate 2 groups: the 10 patients who ultimately would undergo Fallot or Rastelli procedure (external clip, simple procedure) and the other 8 with a hybrid procedure[6] and subsequent complex surgery (Norwood-Glenn, Ross-Konno, Yasui, transplant).

Table 1
Stent locations and surgical procedures

Stent locations	n = 131
Left pulmonary artery	36
Right ventricular outflow tract	34
Ductus	18
Right pulmonary artery	14
Atrial septum	11
Superior vena cava	7
Inferior vena cava	7
Ascending aorta	2
Left atrium	2
Interventions performed	n = 105
Transplant	25
Conduit replacement	23
Fontan	13
Fallot	11
Bidirectional Glenn	7
Rastelli	6
Glenn take-down	2
Norwood-Glenn (comprehensive)	2
Ross-Konno	1
Norwood-Rastelli (Yasui)	1
Other	14