the vessel treated at the index PCI was needed in 2 patients due to disease progression.

Although our experience is based on a small, heterogeneous population (with similar characteristics to other series),[3–5] we believe that PCI is both feasible and safe for pediatric patients and is a useful option for long-term transplant recipients with GVD and for the treatment of early and late complications of surgical procedures involving coronary manipulation. In such cases, it is important to act as quickly as possible as delays are associated with rapid hemodynamic deterioration, cardiogenic shock, and high mortality risk. All pediatric interventional hospitals must thus be familiar with PCI techniques.

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Levosimendan as bridge to transplant in patients with advanced heart failure

Levosimendán como terapia puente a trasplante cardiaco en pacientes con insuficiencia cardiaca avanzada

To the Editor,

Heart transplant is the most effective treatment for advanced heart failure (aHF). Due to the shortage of donors, there is growing interest in bridge-to-transplant therapies, such as medication with inotropic drugs.

Levosimendan is an inodilator drug whose active metabolite, OR-1896, has a prolonged action extending beyond the time of administration. Cycles of intermittent levosimendan (CIL) infusion have been shown to have clinical and hemodynamic benefits and to improve neurohormonal markers.[1,2] However, CIL therapy has been linked to a worrying risk of ventricular arrhythmia during infusion.[2] The main goal of the current study was to analyze the safety of outpatient CIL as a bridge to transplant.

We performed a prospective observational analysis of aHF patients[3] included in a CIL program while on the heart transplant waiting list (HTWL) between January 2016 and May 2018. The initial 24-hour cycle was administered with electrocardiographic monitoring during a hospital admission. Infusion was begun at 0.1 μg/kg/min, and the infusion rate was increased to 0.2 μg/kg/min after 1 hour if systolic blood pressure remained ≥ 80 mmHg. Subsequent outpatient cycles were scheduled every 2 months with a standard 6-hour protocol including hourly blood pressure readings, preceded by an electrocardiogram and blood analysis. At the time of inclusion on the HTWL, patients underwent right heart catheterization (RHC), with subsequent hemodynamic evaluations every 6-12 months.[4] All patients were carriers of an implantable cardioverter-defibrillator (ICD). Follow-up continued from the first infusion cycle until heart transplant, implantation of a left-ventricular assist device, death, or end of study. Major adverse events were symptomatic hypotension or systolic blood pressure < 80 mmHg, ventricular tachycardia during follow-up

Table 1
Baseline characteristics

	N = 11
Age, y	53.0 [41-63]
Male sex	7 (63.6)
Hypertension	4 (36.4)
Dyslipidemia	3 (27.3)
Diabetes mellitus	2 (18.2)
Exsmoker	5 (45.5)
COPD	2 (9.1)
Sleep apnea	3 (27.3)
Atrial fibrillation	2 (18.2)
Etiology	
Ischemic heart disease	5 (45.5)
Hypertrophic cardiomyopathy	1 (9.1)
Dilated cardiomyopathy	5 (45.5)
Idiopathic cardiomyopathy	1 (9.1)
Valve disease	1 (9.1)
Familial cardiomyopathy	1 (9.1)
Noncompacted cardiomyopathy	1 (9.1)
Danon disease	1 (9.1)
LVEF	28 [19-30]
ICD	11 (100)
CRT	3 (27.3)
INTERMACS Class 3	11 (100)
Systolic blood pressure, mmHg	98.0 [86-103]
Diastolic blood pressure, mmHg	71.0 [60-75]
Heart rate, bpm	70.0 [61-84]
Weight, kg	80.0 [77-91]
BMI	30.11 [24.7-31.7]
Creatinine, mg/dL	1.5 [1.3-1.9]
Glomerular filtration rate (mL/min/1.73 m²)	45.9 [36.9-59.7]
< 90 mL/min/1.73m²	11 (100)

Table 1 *(Continued)*
Baseline characteristics

	N = 11
< 60 mL/min/1.73m^2	8 (72.7)
< 30 mL/min/1.73m^2	1 (9.1)
NT-proBNP, pg/mL	4858.0 [3047.0-5801.0]
Treatment	
ACEI	6 (54.5)
ARB	1 (9.1)
Beta-blockers	10 (90.9)
Aldosterone antagonists	11 (100)
Ivabradine	4 (36.4)
Hydralazine + nitrates	2 (18.2)
Sacubitril-valsartan	0 (0%)
Furosemide	11 (100)
Baseline RHC	
RAP, mmHg	15.0 [8-20]
SPAP, mmHg	51.0 [48-65]
MPAP, mmHg	35.0 [32-42]
PCP, mmHg	23.0 [20-25]
CI, L/min/m^2	1.7 [1.4-2.0]
PVR, WU	3.9 [2.6-4.5]

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CI, cardiac index; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter-defibrillator; LVEF, left-ventricular ejection fraction; MPAP, mean pulmonary arterial pressure; NT-proBNP, N-terminal pro-brain natriuretic peptide; PCP, pulmonary capillary pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RHC, right heart catheterization; SPAP, systolic pulmonary arterial pressure.
Data are expressed as No (%)or median [interquartile range].

(defined as symptomatic or hemodynamically unstable sustained ventricular tachycardia [>30 s]), and death.

A total of 11 patients were included on the HTWL; all were in INTERMACS Class 3, 63.6% (7) were men, and the median age was 53 years [interquartile range, 41-63 years] (table 1). The median follow-up was 6 months [4-12 months], and the median number of infusion cycles during follow-up was 12 [8-25]. Only 1 patient had symptomatic hypotension during the treatment (systolic blood pressure, 70 mmHg), which was resolved by reducing the infusion rate to 0.1 μg/kg/min. None of the patients had ventricular arrhythmias during drug infusion, and there were no episodes of ventricular tachycardia during ICD interrogation. None of the patients died during the study period.

During the CIL infusion program, 6 patients (54.5%) had at least 1 admission for decompensated heart failure, and 2 patients (18.2%) were admitted twice during this period. These figures are significantly lower than for the same length of time before initiation of levosimendan therapy, when 10 patients (90.9%) had at least 1 admission and the maximum number of single-patient admissions was 6. The median number of admissions in the CIL and pre-CIL periods were 1.0 [0-1] vs 2.0 [1-4] (P = .02).

Of the cohort, 8 patients (72.7%) underwent RHC during follow-up, a median 8 months [7.1-9.9 months] after the baseline RHC. Parameters were stable between baseline and follow-up RHC, with only pulmonary vascular resistance showing a downward trend (table 2).

At the time of the last levosimendan infusion, 7 patients (63.6%) were in INTERMACS Class 3 and 4 (36.4%) were in INTERMACS Class 2. All patients had subjective clinical improvement, and treatment was suspended in 1 patient. Of the patients, 9 (81.8%) underwent heart transplant, 2 of them (22.2%) in an emergency situation.

There were no statistically significant differences between baseline and end of follow-up concentrations of N-terminal

Table 2
Comparison of hemodynamic parameters at baseline and during follow-up

n = 8	RAP, mmHg	SPAP, mmHg	DPAP, mmHg	MPAP, mmHg	PCP, mmHg	TPP, mmHg	CO, L/min	CI, L/min/m^2	PVR, WU
Baseline RHC	13.0 [8-18]	52.5 [47.5-63.5]	24.0 [21.25-27.25]	35.5 [31.5-41.0]	23 [20-25]	11 [8.5-18.0]	3.6 [3.0-4.1]	1.8 [1.5-2.1]	3.5 [2.3-4.5]
Follow-up RHC	12.5 [9.3-19.8]	59.0 [41.0-66.0]	25.0 [20.8-32.3]	40.0 [29.3-45.8]	27.5 [21.8-29.8]	10 [6-15]	3.8 [2.7-5.0]	2.1 [1.4-2.3]	2.2 [2.1-3.3]
P	.6	.2	.6	.4	.2	.4	.5	.5	.06

CI, cardiac index; CO, cardiac output; DPAP, diastolic pulmonary arterial pressure; MPAP, mean pulmonary arterial pressure; PCP, pulmonary capillary pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RHC, right heart catheterization; SPAP, systolic pulmonary arterial pressure; TPP, transpulmonary pressure.
Data are expressed as median [interquartile range].

pro-brain natriuretic peptide (NT-proBNP) (4858.0 [3047-5801] pg/mL vs 3407.0 [2188-4853] pg/mL; $P = .3$). Similarly, there were no differences between baseline and end of follow-up glomerular filtration rate (45.9 [36.9-59.7] mL/min/1-73m^2 vs 47.0 [43.6-105.0] mL/min/1-73m^2; $P = .3$).

This study examined a cohort of patients with aHF who received CIL as a bridge to heart transplant. Follow-up was longer than in previous reports,[1,2] and ICDs were interrogated periodically, allowing analysis of levosimendan safety in patients included on a HTWL. Only 22% of the patients required an emergency heart transplant, contrasting with emergency transplant rates of 64% and 44% for HTWL patients in European and Spanish registries, respectively, in 2017.[5,6] These data indicate that CIL is a practical bridge-to-transplant option.

Levosimendan infusion was safe in all patients, with no incidents of ventricular arrhythmia recorded during treatment or follow-up; however, the sample size is too small to allow definitive conclusions. Nevertheless, our results are important, since the prolonged action of the drug means that beneficial and adverse effects will not be limited to the infusion, but will also manifest in the days afterwards. The most concerning adverse effects are ventricular arrhythmias, but to our knowledge, no previous study has analyzed the occurrence of arrhythmias in the postinfusion period. Moreover, the heart failure admission rate in our cohort was lower than that reported in previous studies.[1,2]

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CONFLICTS OF INTEREST

Juan F. Delgado has delivered presentations at Orion Pharma conferences and has participated in clinical trials funded by Orion Pharma. Javier de Juan and Inés Ponz have delivered presentations at Orion Pharma conferences.

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Arrhythmogenic right ventricular cardiomyopathy presenting as myocarditis in young patients: a concealed relationship

Miocardiopatía arritmogénica del ventrículo derecho en pacientes jóvenes con miocarditis: una asociación oculta

To the Editor,

Diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) can be challenging. Recent evidence indicates that the natural history of this disease includes a first concealed phase, characterized by acute exacerbations of myocardial inflammation and life-threatening ventricular arrhythmias, occurring prior to the onset of classical characteristics and contributing to its pathogenesis and progression.[1] This has been demonstrated by reports of ARVC presenting as recurrent myocarditis-like episodes in young patients with evidence of myocardial inflammation on cardiac magnetic resonance.[2] Instead of the classical replacement in this disease of myocytes by fibrous or fibroadipose tissue in the right ventricular (RV) myocardium,[3] inflammatory infiltrates can often be seen in affected areas.[4] This article intends to illustrate this association, making a compelling argument for a thorough investigation of the RV in young patients presenting with ventricular arrhythmias and signs of active or past myocarditis.

Patient 1, a previously healthy girl, presented at the age of 15 years with aborted sudden cardiac death during competitive sports. Rhythm was pulseless ventricular tachycardia. The baseline electrocardiogram (ECG) showed low voltage and T wave inversion in the right leads (figure 1), thought to be normal for her age. Her father had the same T wave pattern, but family history was otherwise not relevant. One week before the current event, she was diagnosed with tracheobronchitis, with 1 day of fever. During the current admission, she progressed well. Twenty-four hour Holter monitoring showed isolated, polymorphic ventricular ectopic beats (28 beats/h). Cardiac magnetic resonance revealed indirect signs of active inflammation with enhanced spontaneous left ventricular (LV) myocardial SSFP signal, and multiple locations of subepicardial late gadolinium enhancement (LGE), which were more evident at the inferior LV wall (figure 1). LV ejection fraction (EF) was 58%, and end-diastolic volume was normal (85 mL/m^2). RV ejection fraction was 48%, and end-diastolic volume was at the upper