



## SCIENTIFIC LETTERS

### Refractory Cardiogenic Shock due to Enterovirus Myocarditis: Experience at one Institution



### Shock cardiogenico refractario secundario a miocarditis por enterovirus: experiencia en una institución

Dear Editor,

Enterovirus (EV) is a common cause of infection in newborns and infants younger than 3 months.<sup>1</sup> Its course can be variable, from a self-limited fever to fulminant hepatitis, sepsis or meningoencephalitis. It may also debut as acute fulminant myocarditis with cardiovascular collapse, secondary to incessant arrhythmias or due to fast hemodynamic deterioration.<sup>2</sup> This cardiogenic shock may be refractory to conventional support (mechanical ventilation and vasoactive drugs), leading to a high risk of mortality<sup>3</sup> and poor prognosis.<sup>4</sup> In recent years, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has become a major life-saving strategy in refractory cardiac failure.<sup>5</sup> However, data regarding ECMO use in newborns affected by EV myocarditis are limited<sup>6</sup> and its use is controversial due to low survival rates and potentially irreversible myocardial damage.

We present two cases with EV myocarditis, all of them males. Main data can be seen in [Table 1](#). Both of them were infected during EV season (summer–autumn) and developed symptoms before 15 days of life during 15 days of life. None of the mothers presented symptoms.

Both patients were admitted to the Intensive Care Unit with the initial suspicions of septic shock but echocardiography and ECG along with cardiac biomarkers guide to myocarditis diagnosis. In the presence of a patient with myocarditis, an infectious extension study is carried out with the collection of samples for multiple viruses and bacteria. The diagnosis of EV infection was made by positive EV RNA with real-time PCR (NucliSENS<sup>®</sup> easyMag<sup>®</sup>, bioMérieux, Marcy l'Etoile, France) in the different isolation sites.

The two patients presented ST depression in the initial ECG. Second case presented ventricular tachycardia and ventricular fibrillation. Both had a severe left ventricular dysfunction with less than 20% of ejection fraction and severe mitral regurgitation.

Initial and worst pH, lactate, troponine, and procalcitonin levels, and renal and hepatic function of the patients are summarized in [Table 1](#).

Due signs of insufficient organ perfusion and repeated runs of tachycardia although conventional inotropic and

respiratory management, veno-Arterial ECMO was initiated.

Approximately 80–100% of the cardiac output was assisted on ECMO being both of them treated with inodilator agents, levosimendan and milrinone, during ECMO therapy.

One patient required balloon atrial septostomy at 2h of ECMO support to decompress the left ventricle. Complications from ECMO included circuit change due to clots and arrhythmias that required medical treatment.

Data about days of mechanical ventilation, ICU and hospital length of stay, and neurological and cardiac outcomes of the all patients are summarized in [Table 2](#). Both received intravenous immunoglobulin (1 g/kg for three consecutive days).

Survival was 100% and they recovered biventricular function after ECMO. None of them has neurological disabilities today.

In our retrospective study, we report a survival rate higher than that previously described in the literature (100%).<sup>7</sup> Therefore although literature survival rates in newborns affected by EV myocarditis are low (33–50%)<sup>3,7</sup> and ECMO support remains controversial, we suggest ECMO support in those patients with high mortality rate expectancy: patient survival and full recovery are possible.

EV may cause inflammatory disease of the myocardium associated with myocyte necrosis, leading to fulminant myocarditis and consequently congestive heart failure, dysrhythmias and cardiogenic shock.<sup>8</sup> This dysfunction might be reversible. The main problem is the situation of refractoriness of the shock that cannot be sustained with the usual ICU measures, so that patients evolve to very precarious conditions, even to irreversible multiorgan dysfunction and/or cardiac arrest.<sup>2</sup> Clinical myocarditis can mimic other clinical patterns. ECMO is a life-saving therapy that is able to restore hemodynamics while allowing for possible recovery. However, patients on ECMO support may develop severe complications including neurologic, bleeding and thrombosis and infection among others.<sup>9</sup> Therefore, the indication of ECMO in these patients can be a challenge, especially their weaning from ECMO support: longer ECMO executions have been associated with poor outcomes.<sup>10</sup>

Arrhythmias may be found in 25–70% of the patients with EV myocarditis.<sup>7–8</sup> The use of high inotropic dosage increases myocardial oxygen consumption and exacerbates these rhythm disturbances. The use of ECMO restores patient hemodynamics, allowing the rapid withdrawal of inotropics and decreasing the incidence of subsequent arrhythmias.<sup>8</sup>

One of the strategies to promote left heart recovery while patients are on VA-ECMO is to decompress the left

**Table 1** Demographic data and clinical parameters before ECMO.

Parameter before ECMO	Case 1	Case 2
Sex	Male	Male
Delivery mode	Vaginal	Vaginal
GA (weeks)	38 + 4	35 + 6
Birth weight (g)	2400	2520
Mother symptoms	No	No
Admission ICU (days of life)	10	9
ECMO entry (days of life)	10	9
EV isolation	Blood, CSF	Blood, NPA, CSF
Associated disease	Meningo/encephalitis	Meningo/encephalitis
Worst SOFA score (points)	19	17
PIP (cmH <sub>2</sub> O)	28	30
PEEP (cmH <sub>2</sub> O)	10	9
Initial/Worst pH	7.21/7.1	7.24/7.2
Initial/Worst lactate (mmol/L)	4.1/7.3	3.3/5.2
Initial/Worst troponine (μg/L)	7.5/7.7	14.5/14.5
Initial/Worst PCT (ng/mL)	0.2/1.2	0.06/0.7
Initial/Worst DB (mg/dl)	0.7/0.9	0.5/1.1
Initial/Worst ALT (UI/L)	44/85	30/125
Initial/Worst creatinine (mg/dl)	0.4/1.1	0.6/1.3
Cardiac arrest	No	No
iNO (yes)	No	No
Median VIS Inotrope	26	28
Initial ECG	ST depression in lateral leads	ST depression in anteroseptal leads
Dhysrhythmia	No	VT, VF
LV dysfunction/EF	Severely decreased/10%	Severely decreased/20%
MR	Severe	Moderate
TR	No	No

CSF: cerebrospinal fluid. DB: direct bilirubin. ECMO: extracorporeal membrane oxygenation implantation. EF: ejection fraction. GA: gestational age. ICU: intensive care unit. EV: enterovirus. iNO: inhaled nitric oxide. LV: Left ventricular. MR: mitral regurgitation. NPA: nasopharyngeal aspirate. PCT: procalcitonin. PEEP: positive end-expiratory pressure. PIP: positive inspiratory pressure. SOFA: Sepsis Organ Failure Assessment score. SVT: supraventricular tachycardia. TR: tricuspid regurgitation. VIS: vasoactive-inotropic score. VF: ventricular fibrillation. VT: ventricular tachycardia.

**Table 2** Summary of parameter during ECMO and outcomes.

Parameter during ECMO	Case 1	Case 2
V/A cannula size	12/10	12/8
Procedures in ECMO	BAS/levosimendan	Milrinone
CVVHDF (yes)	No	No
CVVHDF (days)	0	0
Assistance (% CO)	75%	85%
Complications	Chylothorax	No
Evolution		
ECMO (days)	10	9
MV (days)	15	16
ICU (days)	20	25
Hospital LOS (days)	30	35
Neurological disability (Yes)	No	No
Last echocardiography	Mild biventricular dysfunction, EF 48%	Normal biventricular function, EF 55%
Outcome	6 months of life	12 months of life
Survival	Yes	Yes

BAS: balloon atrial septostomy. CO: cardiac output. CVVHDF: continuous veno-venous hemodiafiltration. ECMO: extracorporeal membrane oxygenation. EF: ejection fraction. ICU: intensive care unit. LOS: hospital length of stay. LV: left ventricular. MV: mechanical ventilation. V/A: veno/arterial.

ventricle through balloon atrial septostomy or left ventricular venting. This strategy avoids the myocardial ischemia due to left-ventricular high end-diastolic pressures and also ameliorates the pulmonary edema secondary to left-atrial hypertension. In our sample, one patient did not require septostomy due to a patent foramen ovale. Left-to-right shunt might have helped to decrease end-diastolic pressure, favouring recovery and minimizing the pulmonary edema. Also appropriate afterload reduction with the use of inodilators such as milrinone and levosimendan is key to improving left ventricular stroke volume and promoting effective decompression.

In previous studies<sup>8</sup> in which ECMO was used in neonatal EV myocarditis patients, the average duration was 7 days; in our experience it was 9 and 10 days, with a complete recovery in both and 100% survival. If ECMO support had not been initiated in the situation of hemodynamic refractoriness to conventional treatment, we expected a higher mortality rate. Inwald et al. in 2004<sup>3</sup> reported 7 patients with EV myocarditis: three did not receive support with ECMO, and all survived; the 4 who required ECMO, the mortality rate was 75%. However, the small sample of both studies precludes us from being emphatic in our conclusions.

We believe that more studies about ECMO in EV myocarditis are required to draw stronger conclusions about ECMO viability. However, we believe that our data are encouraging, since the reported mortality of these patients without ECMO. Our results reveal that survival can be achieved without neurological damage. As ECMO support is improving, complications, although they may be severe, are becoming less frequent.

## References

1. Esteva C, Esteban E, Noguera A, García JJ, Muñoz-Almagro C. Severe enterovirus disease in febrile neonates. *Enferm Infecc Microbiol Clin*. 2009;27:399–402.
2. Madden K, Thiagarajan RR, Rycus PT, Rajagopal SK. Survival of neonates with enteroviral myocarditis requiring extracorporeal membrane oxygenation. *Pediatr Crit Care Med*. 2011;12:314–8.
3. Inwald D, Franklin O, Cubitt D, Peters M, Goldman A, Burch M. Enterovirus myocarditis as a cause of neonatal collapse. *Arch Dis Child Fetal Neonatal Ed*. 2004;89:461–2.
4. Freund MW, Kleinvelde G, Krediet TG, Van Loon AM, Verboon-Macielek MA. Prognosis for neonates with enterovirus myocarditis. *Arch Dis Child Fetal Neonatal Ed*. 2010;95:206–12.

5. Conrad S, Bridges B, Kalra Y, Pietsch JB, Smith AH. Extracorporeal cardiopulmonary resuscitation among patients with structurally normal hearts. *ASIAO*. 2017;63:781–6.
6. Schlapbach LJ, Ersch J, Balmer C, Prete R, Tomaske M, Caduff R, et al. Enteroviral myocarditis in neonates. *J Paediatr Child Health*. 2013;49:451–4.
7. Cortina G, Best D, Deisenberg M, Chiletto R, Butt W. Extracorporeal membrane oxygenation for neonatal collapse caused by enterovirus myocarditis. *Arch Dis Child – Fetal Neonatal Ed*. 2018;103:370–6.
8. Casadonte JR, Mazwi ML, Gambetta KE, Palac HL, McBride ME, Eltayeb OM, et al. Risk factors for cardiac arrest or mechanical circulatory support in children with fulminant myocarditis. *Pediatr Cardiol*. 2017;38:128–34.
9. Pinto VL, Pruthi S, Westrick AC, Shannon CN, Bridges BC, Le TM. Brain MRI findings in pediatric patients post ECMO. *ASAIO*. 2017;63:810–4.
10. Distelmaier K, Wiedemann D, Binder C, Haberl T, Zimpfer D, Heinz G, et al. Duration of extracorporeal membrane oxygenation support and survival in cardiovascular surgery patients. *J Thoracic Cardiovasc Surg*. 2018;155:2471–6.

S. Bobillo-Perez<sup>a</sup>, J. Sanchez-de-Toledo<sup>b,c</sup>, S.S. Matute<sup>d</sup>, M. Balaguer<sup>d</sup>, I. Jordan<sup>e,\*</sup>, J. Rodriguez-Fanjul<sup>f</sup>

<sup>a</sup> Pediatric Intensive Care Unit Service, Critical patient Research Group, Institut Recerca Hospital Sant Joan de Déu, Hospital Sant Joan de Déu, Barcelona, Spain

<sup>b</sup> Pediatric Cardiology Service, Hospital Sant Joan de Déu and University of Barcelona, Barcelona, Spain

<sup>c</sup> Critical Care Medicine Department, University of Pittsburgh, Pittsburgh, PA, United States

<sup>d</sup> Pediatric Intensive Care Unit Service, Hospital Sant Joan de Déu and University of Barcelona, Barcelona, Spain

<sup>e</sup> Pediatric Intensive Care Unit, Paediatric Infectious Diseases Research Group, Institut Recerca Hospital Sant Joan de Déu, Hospital Sant Joan de Déu, CIBERESP, Barcelona, Spain

<sup>f</sup> Pediatric Intensive Care Unit, Pediatric Service, Hospital Joan XXIII, Tarragona, Spain

\* Corresponding author.

E-mail address: [ijordan@sjdhospitalbarcelona.org](mailto:ijordan@sjdhospitalbarcelona.org) (I. Jordan).

<https://doi.org/10.1016/j.medin.2019.03.006>  
0210-5691/ © 2019 Elsevier España, S.L.U. y SEMICYUC. All rights reserved.

## ECMO in severe trauma patient with intracranial bleeding requiring surgery



### ECMO en trauma grave con sangrado intracraneal amenazante que requiere cirugía

Dear Editor:

Brain Trauma incidence is about 235/100 000 inhabitants/year in Europe, frequently co-existing with thoracic trauma (35%).<sup>1</sup> Avoiding hypoxic brain damage is crucial but difficult to achieve in case of respiratory failure, given

the potential harmful effect of ventilatory strategies (prone positioning, alveolar recruitment) on intracranial hypertension (ICH).

ECMO is a lifesaving technique, assisting the failing heart or lungs, but circuit anticoagulation is required, which could increase the risk of bleeding. Consequently, trauma bleeding, and especially brain trauma are still formal contraindications for ECMO.<sup>2</sup>

We present the case of a severe BTI with intracranial bleeding requiring surgical drainage and VV ECMO for severe respiratory failure.

26 years old male suffered a motorbike crash accident. Initially presenting with GCS 4 on the scene, bilateral non-reactive pupils; BP 110/60 mmHg. Injury severity score (ISS)