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Re-ECMO for congenital diaphragmatic hernia: Is it worth the effort?

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ABSTRACT

Aim: To evaluate the results in CDH patients subjected to a second course of ECMO at a single institution.
Material and methods: Retrospective review of medical charts of patients treated for CDH and ECMO in our center since 1990 to December 2018 was performed. For patients subjected to a second course of ECMO and who survived to hospital discharge charts from follow up visits were also reviewed.
Results and discussion: From Jan 1990 until December 2018, 311 patients with CDH were treated in the department. 267 of these (86%) were discharged alive from the hospital and 81% (237/293) of the Swedish patients were alive by December 2018. 101 patients (32%) were subjected to ECMO treatment of whom 71 survived (70%). 22 patients underwent a second ECMO run and 13 of these survived to hospital discharge. Seven of the Swedish patients [19] were long-term survivors (37%). The vast majority was on V-A ECMO.
Conclusions: It is possible to recannulate the right common carotid artery and internal jugular vein for a second course of venoarterial ECMO in CDH patients, who deteriorate severely after decannulation. Previous research has shown that long-term survivors subjected to ECMO twice reported similar frequencies of pulmonary, gastrointestinal, neurological and musculoskeletal sequelae as the long-term survivors, who needed ECMO support only once, and similar health-related quality of life. Regarding their psychosocial function, they scored within normal range in the behavioral, emotional and social scales domains. A second ECMO run may contribute to a higher survival and that the long-term morbidity among survivors is not more pronounced than among survivors after a single course of ECMO. It is therefore suggested that a second course of ECMO should be offered on the same indications as the first course.
Level of evidence: III Case series.

Congenital diaphragmatic hernia (CDH) occurs in about 1:3000 live births [1]. The major clinical problem is the concomitant pulmonary hypoplasia and pulmonary artery hypertension responsible for mortality and long-term morbidity in some patients. Cornerstones in the treatment today are preoperative stabilization, nonaggressive mechanical ventilation and permissive hypercarbia [2,3]. Attempts to decrease the pulmonary artery hypertension are made by pharmacological pulmonary vasodilatation [4]. In many centers extracorporeal membrane oxygenation (ECMO) is used in selected infants for preoperative stabilization. The rationale behind ECMO treatment in CDH is that the pulmonary hypertension is potentially reversible [5]. Although controversy still exits on the role of ECMO for CDH [6], ECMO seems to increase survival to hospital discharge in the most severely affected children with CDH [7–9]. In experienced centers reporting an overall survival between 69% and 93%, ECMO was used in 11% to 61% of cases [8,10], with survival rates ranging from 50% to 70% [10,11]. If the patients deteriorate after decannulation from ECMO, a second course of ECMO is offered in some centers. Results after second course ECMO in CDH patients have not previously been reported.

The aim of the present investigation was to evaluate the results in CDH patients subjected to a second course of ECMO.

1. Materials and methods

Retrospective review of medical charts of patients treated for CDH and ECMO in our center since 1990 to December 2018 was performed. For patients subjected to a second course of ECMO and who survived to hospital discharge charts from follow up visits were also reviewed.

Since 1990 we have used a strategy of preoperative stabilization and delayed surgery [3,13–15]. Gentle mechanical ventilation was used with the aim not to exceed PIP (peak inspiratory pressure) of 25 cm H_2O. Inhaled nitric oxide was used in patients with moderate and severe pulmonary artery hypertension and in the later period even Sildenafil. The patients were sedated and systemic blood pressure was controlled by inotropic support when needed. If it not was possible to maintain adequate blood gases, the patients were cannulated for ECMO support. Standard criteria for cannulation were used, i.e. if a preductal saturation > 85% is not possible on acceptable ventilator settings (peak inspiratory pressure < 25 cm H_2O), increased lactate levels (≥5 mmol/

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L) or inability to maintain adequate blood pressure in spite of vasoactive and inotropic drugs. In most cases venoarterial (VA) ECMO was preferred. For venoarterial cannulation, single lumen cannulas Bio-Medicus8–14 French (Fr) were used. For venovenous (VV) cannulation, a double lumen OriGen catheter of 12 Fr was used. In the beginning of the period the hernia was repaired on ECMO only if the patient not could be weaned within 7–10 days, but later the patients were generally operated on ECMO within 1–5 days. Standard criteria for decannulation were used [16].

If the patients deteriorated after decannulation and for a second time fulfilled ECMO entry criteria [3], a second course was offered. Same criteria as described above for recannulation were used. The same vessels were used for the recannulation. There was generally no flow from the right common carotid artery, when the central ligature was removed. After introduction and withdrawal of a thin Fogarthy catheter down (at this point a short manual compression of the left carotid artery was performed) to the aortic arch a flow was achieved and it was possible to recannulate the artery in all cases. In some cases a new arteriotomy was performed slightly more central. The right internal jugular vein was also possible to recannulate in all patients. In some cases it was dilated with a Fogarthy catheter. As large cannulas as possible were introduced both in the artery and in the vein. Decannulation from the second course of ECMO was performed on standard criteria.

Data are presented as median, mean, range, interquartile range (IQR), absolute values (n) and percentages (%). For categorical data, Fisher's test was performed to investigate differences in survival between groups ECMO once or more than once.

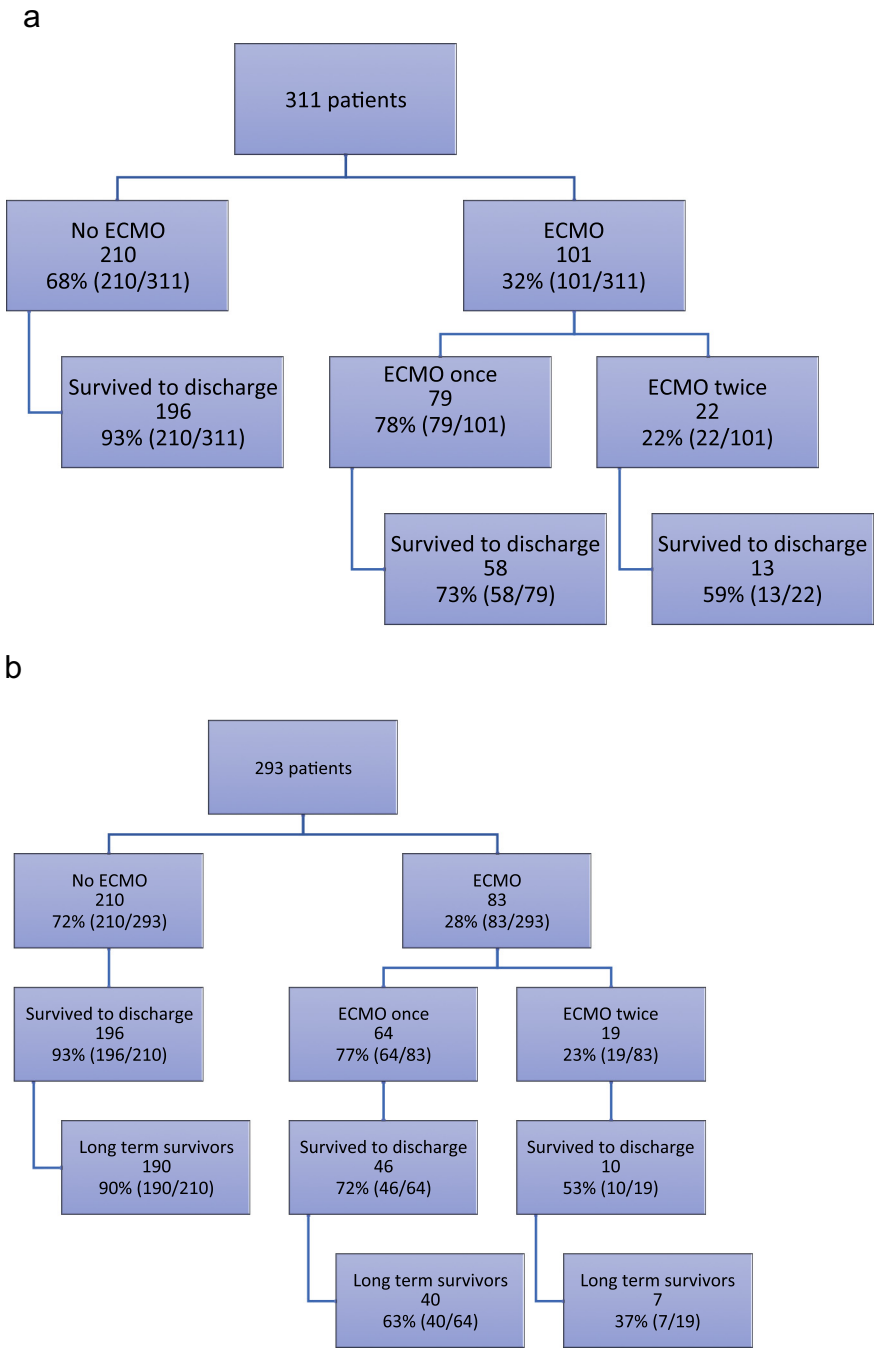

Fig. 1. (a) Number of patients and survival to discharge given for the whole CDH group. (b) Number of patients, survival to discharge and long term survival given for the Swedish CDH patients.

Significance was defined as $P \leq 0.05$. Analyses were performed using PRISM 6 (Graphpad Software Inc., La Jolla, CA).

2. Results

From January 1990 until December 2018, 311 patients with CDH were treated in the department. 267 of these (86%) were discharged alive from the hospital. Eighteen of these were patients from abroad and thus lost to follow up. Of the remaining 293 Swedish patients, 237 (81%) were alive by December 2018. 101 patients (32%) were subjected to ECMO treatment of whom 71 survived to discharge (70%).

22 patients (19 of them Swedish) underwent a second ECMO run, 11 patients between 1990 and 2007 and 11 patients between 2008 and 2018, and 13 (59%) of these (10 Swedish) survived to hospital discharge (Fig.1) and 7 were long-term survivors (37%). Patients who underwent ECMO only once had better survival rates to discharge (72% vs 53%, $p = 0.1$) and better long-term survival (63 vs 37%, $p = 0.1$) than those who needed ECMO support more than once, but the difference was not statistically significant owing to the limited numbers.

Seven of the patients subjected to two ECMO runs were retrieved from other hospitals by our mobile ECMO team [17].

In three of the 22 patients the hernia was repaired before the first ECMO course: one at 8 days of life (DOL) and in the other two on the second DOL, all at other hospitals and subsequently referred to us after deterioration. 16 patients had the hernia repaired during the first ECMO run and three during the second run.

Of the patients subjected to second course ECMO, 3 were V-V in the first run and the remaining 19 were venoarterial initially. Initially, 2 patients were started on V-VECMO on the second run, but were finally converted to V-A. Thus, all 22 were V-A during the second run. It was possible to recannulate the vein in all patients, but the size of the cannula had to be reduced by one or two steps in 11/22 patients (vein cannula 12 Fr in average at first run, 10 Fr in average at second run, range 8–14 Fr). The artery could be recannulated in all 19 cases subjected to venoarterial ECMO during the first run (arterial cannula 8 Fr in average at both first and second run, range 6–10 Fr).

At decannulation from the first ECMO run FiO_2 was in average 0.40 (range 0.30–0.55), PIP 21 (range 18–23) and PEEP (post end expiratory pressure) 3.9 (range 1–5).

The median age of the 22 patients at initiation of ECMO was 19.2 h (Table1). The median length of the first run was 11.6 days (IQR 6.7–17.5) and that of the second run was 10.3 days (IQR 7.4–13.7). The interval between the two runs was on average 3.8 days (IQR 2.4–5.3). The median length of hospital stay (LOS) was 54 days (IQR 33.7–86) (Table1).

One patient died from an ECMO complication soon after recannulation. The others were decannulated, but eight died before hospital discharge. Thus, 13 out of 22 patients subjected to a second course ECMO were discharged alive. Of these, 10 were Swedish citizens and could be followed up. Three out of these 10 died after discharge from complications related to their severe pulmonary hypoplasia and/or pulmonary hypertension.

The 7 long-term survivors (37%) were aged 4 months–28 years (median 10.1 years) at last follow-up. None was on supplemental oxygen or tube feeding. There was one with a known neurological handicap (cerebral infarction), but was well functioning and admitted to normal school classes. Four patients had reached school age and had been admitted to normal school classes. One of them had graduated from high school.

Table1
Characteristics for the patients who underwent a second ECMO run.

Re-ECMO	$n = 22$
Gender: female	50%
Prenatal diagnosis	73%
GA birth (median)	37 weeks
Bw (median)	2.8 kg
Age at intubation <6 h	100%
Age at surgery (median) (IQR)	5.1 (2.7–7.5) days
Patch repair	100%
Defect size	
Unknown	10
B	3
C	7
D	2
Side: Left	86%
Age at first ECMO (median) (IQR)	19 (7.2–52.3) h
Time first ECMO run (median) (IQR)	11.6 (6.7–17.5) days
Time between first and second ECMO run (median) (IQR)	3.8 (2.4–5.3) days
Time second ECMO run (median) (IQR)	10.3 (7.4–13.7) days
ECMO mode	
1st run	3 VV/19 VA
2nd run	22 VA
LOS (median)	54.5 (33.7–86) days
Survival to discharge	59%
Long-term survival[a]	37%

[a] Includes only Swedish citizens.

3. Discussion

The Congenital Diaphragmatic Hernia Study Group (CDHSG) registry contains data from more than 9000 patients (www.cdhsg.net) [22,23]. The survival rate to hospital discharge was 69%. 31% of the patients were treated with ECMO with a survival of 51% [22,24–26]. Only 6.1% of the patients entered in the registry were subjected to a second course ECMO, of whom 41% survived (data courtesy of the CDHSG Registry). In other words the frequency of second course ECMO in our department was high compared to others, which is the background for the present evaluation of results. A high frequency second run ECMO can among other things indicate that indications for decannulation from the first run are too wide, that the care provided after decannulation is suboptimal or that indications for a second run are liberal when the patients deteriorate.

The median length of the first ECMO run in our material was 11.6 days. This is essentially the same as in the CDHSG database (11 days). Together with the fact that ventilator settings were low at decannulation (FiO2 0.40, PIP 21, PEEP 2.5) this indicates that the patients were not decannulated to early. The patients in the later part of the period were all subjected to echocardiography before and after decannulation in order to estimate pulmonary artery pressure. These investigations were, however, performed at different time points from decannulation. The echocardiograms performed while the patients were on ECMO were done at different flow rates of the ECMO pump and at different levels of right atrium filling. Unfortunately, it has therefore not been possible to do any meaningful interpretation of these data.

The total survival of ECMO patients to discharge in the present material was 70% (71/101). The corresponding figure in the CDHSG registry is 51% [24,25,27] and in the Extracorporeal Life Support Organization (ELSO) registry [28] 48.1%. If we theoretically assume that we had not offered re-ECMO there would have been 13 more deaths in the ECMO group. This corresponds to a survival of 58 instead of 71 of the 101 ECMO patients, i.e. 57%. These figures indicate that offering a second course ECMO rather increases the survival rate than that our decannulation criteria or post ECMO care is suboptimal.

There is significant long-term morbidity among survivors of severe CDH including respiratory symptoms, gastrointestinal problems and neurodevelopmental problems [29–35]. Significant mortality during the first year of life and both physical and neurodevelopmental morbidity was seen in the majority of survivors of CDH patients after ECMO treatment [12]. Of the 10 Swedish survivors after second run ECMO in the present material, there were seven long-term survivors. In a previous study we found that children with CDH who required ECMO more than once perceived their physical function as being overall good, and

no differences were found between patients who needed ECMO once or more [19]. They also reported a good health-related quality of life [20] and showed no behavioral or emotional problems [21]. Although, the present material is small, long term morbidity and mortality do not seem to be more pronounced than what is generally seen in severe CDH patients subjected to ECMO treatment.

Some limitations of the study include the fact that this study covers a time period of 28 years, and, although the treatment protocol was the same all over the period, development in the medical treatment for pulmonary hypertension has occurred with more therapies available that may contribute to changes in the outcomes.

In summary, the present investigation shows that it is possible to recannulate the right common carotid artery and internal jugular vein for a second course of venoarterial ECMO in CDH patients, who deteriorate severely after decannulation. The present study also indicates that a second course ECMO may contribute to a higher survival and that the long-term morbidity among survivors is not more pronounced than among survivors after a single course of ECMO. It is therefore suggested that a second course of ECMO should be offered on the same indications as the first course.

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