Extracorporeal Life Support in Patients with Congenital Diaphragmatic Hernia: How Long Should We Treat?

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BACKGROUND: Congenital diaphragmatic hernia (CDH) is a frequently lethal birth defect and, despite advances, extracorporeal life support (ie, extracorporeal membrane oxygenation [ECMO]) is commonly required for severely affected patients. Published data suggest that CDH survival after 2 weeks on ECMO is poor. Many centers limit duration of ECMO support.

STUDY DESIGN: We conducted a single-institution retrospective review of 19 years of CDH patients treated with ECMO, designed to evaluate which factors affect survival and duration of ECMO and define how long patients should be supported.

RESULTS: Of two hundred and forty consecutive CDH patients without lethal associated anomalies, 96 were treated with ECMO and 72 (75%) survived. Eighty required a single run of ECMO and 65 survived (81%), 16 required a second ECMO run and 7 survived (44%). Of patients still on ECMO at 2 weeks, 56% survived, at 3 weeks 46% survived, and at 4 weeks, 43% of patients still on ECMO survived to discharge. After 5 weeks of ECMO, survival had dropped to 15%, and after 40 days of ECMO support there were no survivors. Apgar score at 1 minute, Apgar score at 5 minutes, and Congenital Diaphragmatic Hernia Study Group predicted survival all correlated with survival on ECMO, need for second ECMO, and duration of ECMO. Lung-to-head ratio also correlated with duration of ECMO. All survivors were discharged breathing spontaneously with no support other than nasal cannula oxygen if needed.

CONCLUSIONS: In patients with severe CDH, improvement in pulmonary function sufficient to wean from ECMO can take 4 weeks or longer, and might require a second ECMO run. Pulmonary outcomes in these CDH patients can still be excellent, and the assignment of arbitrary ECMO treatment durations <4 weeks should be avoided. (J Am Coll Surg 2014;218:808−818. © 2014 by the American College of Surgeons)

Congenital diaphragmatic hernia (CDH) is a severe birth defect with a broad spectrum of severity. Fortunately, many patients are born with low- and moderate-severity defects and are cared for with standard ventilatory techniques. Patients with more severe CDH, however, often require extracorporeal life support (ie, extracorporeal membrane oxygenation [ECMO]) to maximize survival potential.[1,2] Although gentle ventilatory techniques have proven to be a necessary component of successful therapeutic strategies,[3] advances in ventilatory support, protocolized care, and wider use of nitric oxide and other pulmonary vasodilators have been unsuccessful in eliminating the need for ECMO in CDH patients.[4-7]

In CDH patients who require ECMO, survival rates are lower and complication rates are higher, which is intuitive, given that patients who require ECMO represent more severe disease than those who do not. Extracorporeal membrane oxygenation is associated with a myriad of additional risks, including bleeding, renal dysfunction, embolic phenomena, and compromised neurologic

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Abbreviations and Acronyms

CDH = congenital diaphragmatic hernia
CDHSG = Congenital Diaphragmatic Hernia Study Group
ECMO = extracorporeal membrane oxygenation
LHR = lung-to-head ratio
VA = veno-arterial
VV = veno-venous

outcomes.[8-10] Based on published and center-specific data, it is not uncommon for centers to limit the total time of ECMO support in CDH patients who do not improve within assigned time frames. Tiruvoipati and colleagues found an 18% survival rate in CDH patients supported on ECMO >2 weeks[11] and, in discussions with other centers, we have found 2 weeks to be a common reference point for CDH survival on ECMO.

We were early adopters of the gentle ventilatory techniques taught by Wung and colleagues[12] and Boloker and colleagues,[13] and helped define the negative effects of hyperventilation.[14] These ventilation techniques form the foundation of our treatment strategy, and we have offered ECMO to patients who could not be adequately supported with these techniques, regardless of the severity of the underlying CDH physiology.

In this study, we review 19 consecutive years of CDH treatment at our institution to evaluate which patient factors affect survival and duration of ECMO, to evaluate the success of second ECMO runs when needed, to define the ECMO duration required for more severe CDH patients to recover, and to ask if there is a point at which additional ECMO support becomes futile.

METHODS

This is a retrospective review of consecutive patients with CDH treated at the University of Florida's Health and Shands Hospital for Children between September 1992 and December 31, 2011. A total of 268 CDH patients were identified from the cross reference of 2 separate medical record queries with operative records, autopsy records, a divisional database, and 2 prenatal evaluation databases. Patients with Morgagni CDH, diaphragmatic eventration, and patients in whom the diagnosis of CDH was missed and delayed more than 48 hours after delivery were not included. All patients were symptomatic in the first 6 hours of life. Of 268, twenty-eight (10%) were judged to have lethal associated anomalies.[15] One hundred and five patients of the total were treated with ECMO, 9 of which were eventually judged to have associated lethal anomalies and are reported here for completeness and transparency, but are not analyzed further. Ninety-six CDH patients, without lethal associated anomalies, were treated with ECMO and comprise the subjects of this study, which was approved by the University of Florida Institutional Review Board.

Clinical care

The majority of patients were prenatally diagnosed and counseled at our facility. Termination of CDH pregnancies did not occur in patients with nonlethal associated anomalies, regardless of severity, and, as such, terminations did not affect the survival results reported here. All patients were treated with strict limitation of ventilation pressures, avoidance of hyperventilation, and use of mild sedation as described previously.[14] Medical oversight throughout the series was uniform, leading to a high degree of therapeutic consistency.

Extracorporeal membrane oxygenation was used for standard indications (oxygenation index > 40) and only when available modalities to avoid it (eg, pressors, nitric oxide, steroids, and milrinone) had failed. Either veno-venous (VV) or veno-arterial (VA) ECMO was used, and patients who declined on VV ECMO were converted to VA. As the experience matured, VA ECMO was used preferentially for those patients judged by anatomy, lung-to-head ratio (LHR), and initial blood gas values to have more severe pulmonary hypoplasia.

Management on ECMO was not considered different from standard. Nitric oxide, if started before ECMO, was weaned off within 24 hours of initiating ECMO. Patients on high-frequency oscillatory ventilation were generally transitioned to conventional ventilation. Ultrafiltration and dialysis were strictly avoided. Representative resting ventilator settings were synchronized intermittent mandatory ventilation (SIMV) 30, inspiratory time of 0.6 seconds, PEEP of 6 cm H_2O, peak inspiratory pressure (PIP) of 22 cm of H_2O, and fraction of inspired O_2 of 0.4. Desired standards for discontinuing ECMO were satisfactory blood gases on SIMV $\leq$60 and fraction of inspired O_2 of $\leq$0.50. Patients successfully weaned from ECMO but who later declined and again met ECMO criteria were considered for a second run of ECMO. During the first 6 years of the study, patients were decannulated at ECMO cessation, and recannulated if a second ECMO run was necessary. Since then, we have perfused the ECMO cannulas with heparinized saline for 48 to 72 hours after cessation of ECMO before removing them, in case a second run of ECMO is needed. Second-run ECMO was also either VV or VA.

Patients were removed from ECMO when they met discontinuation criteria and when complications or additional organ failure made the likelihood of recovery appear dismal, but not for arbitrarily defined time end points.