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Long-term neurodevelopmental outcomes of congenital diaphragmatic hernia survivors not treated with extracorporeal membrane oxygenation ☆

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Abstract

Background/Purpose: Although there has been a marked improvement in the survival of children with congenital diaphragmatic hernia (CDH) in the past 2 decades, there are few reports of long-term neurodevelopmental outcome in this population. The present study examined neurodevelopmental outcomes in 10- to 16-year-old CDH survivors not treated with extracorporeal membrane oxygenation (ECMO).

Methods: Parents of 27 CDH survivors completed questionnaires assessing medical problems, daily living skills, educational outcomes, behavioral problems, and executive functioning. Fifteen CDH survivors and matched full-term controls completed standardized intelligence, academic achievement, phonological processing, and working memory tests.

Results: Non–ECMO-treated CDH survivors demonstrated high rates of clinically significant difficulties on standardized academic achievement measures, and 14 of the 27 survivors had a formal diagnosis of specific learning disability, attention deficit hyperactivity disorder, or developmental disability. Specific problems with executive function, cognitive and attentional weaknesses, and social difficulties were more common in CDH patients than controls. Perioperative hypocapnia was linked to executive dysfunction, behavioral problems, lowered intelligence, and poor achievement in mathematics.

Conclusions: Non–ECMO-treated CDH survivors are at substantial risk for neurodevelopmental problems in late childhood and adolescence.

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Congenital diaphragmatic hernia (CDH) refers to an anatomical anomaly in which there is herniation of the abdominal viscera into the thoracic cavity because of incomplete closure of the pleuroperitoneal membrane. Presence of the abdominal contents in the thoracic cavity during fetal development interferes with normal lung development. Mortality rates of 40% to 60% were reported a decade ago [1]; with changes in medical management, these rates have now dropped to approximately 17% in Canadian centers [2].

Treatment for CDH varies. Once the infant is stabilized, surgical repair of the hernia occurs. Depending on the severity of respiratory difficulty, the infant may receive ventilation, supplemental oxygen, vasodilators, narcotic analgesics, or paralyzing agents. In some centers, extracorporeal membrane oxygenation (ECMO) is offered to infants unlikely to survive with standard medical treatment [3]. At the time the present cohort of survivors was born, hyperventilation and alkalinization therapy were also commonly used in treatment to reduce persistent pulmonary hypertension, despite the fact that they may reduce cerebral blood flow and exacerbate hypoxemia [4]. Complications including perinatal asphyxia, hypoxemia, and intracranial bleeding secondary to systemic heparinization treatment given in conjunction with ECMO use all increase the risk of brain injury among high-risk survivors (ie, those whose condition manifested within the first 24 hours) [3].

Studies examining the neurodevelopmental outcomes of CDH survivors have typically focused on the short-term development of survivors who received ECMO therapy [5-9]. Comparable studies of non–ECMO-treated CDH survivors suggest that they may experience fewer problems as young children than those treated with ECMO. In 3 studies examining outcome of non–ECMO-treated survivors from 2 to 5.5 years, 8% to 9.5% were hearing impaired [4,6], 8% to 13% had brain abnormalities [6,10], and 0 to 19% were developmentally delayed [4,10]. Long-term outcomes for non–ECMO-treated survivors may not be so positive. Bouman et al [11] reported a mean IQ of 85 (1 SD below age expectations) for their 8- to 12-year-old patients; 45% had poor academic achievement, and 50% were rated as having emotional and/or behavioral problems. Peetsold and colleagues [12] reported average IQ ratings for their sample of 33 CDH survivors, but 39% of survivors demonstrated problems with sustained attention and concentration, and 21% were reported to have behavioral problems. Together, these findings raise the possibility that neurocognitive difficulties emerge as CDH children mature, placing them at higher than normal risk of learning difficulties.

The present study was designed to add to the limited body of information regarding the long-term neurodevelopmental outcomes of non–ECMO-treated CDH survivors. We obtained information regarding the medical and developmental histories of a group of survivors born between 1981 and 1987 and assessed their intelligence, academic achievement, phonological processing, working memory, executive functioning, and behavior using standardized tests and questionnaires. Relationships between early medical variables and outcomes in different areas were also explored.

1. Method

1.1. Participants

A cohort of 56, 10- to 16-year-old, CDH survivors was identified from the medical records at the Hospital for Sick Children in Toronto, ON, Canada; this represented the entire cohort of survivors born during a 6-year period. At the time these individuals were born, our institution used high-frequency oscillating ventilation as a rescue therapy [13]. Although ECMO was available, it was considered a treatment of last resort restricted to babies who were not expected to survive without such treatment. None of the youth we identified from our records received ECMO treatment in infancy.

One of the CDH survivors identified was excluded because of a lack of proficiency in English, 9 refused to participate, 19 could not be contacted, and 1 had died in childhood. The remaining 27 survivors (18 male, 9 female; mean age, 13.3 years; range, 10.0-16.8 years) and their parents agreed to participate in some or all aspects of the study protocol.

As described below, scores obtained by the CDH participants on the experimental measures were compared with published norms. As an additional step, however, we also collected data from a control group of typical peers. We felt that this was important because many of the tests that we used were developed and normed on American children, and no Canadian normative data are available. There is a growing body of literature indicating significant differences in the mean composite scores of American and Canadian standardization samples on a variety of cognitive and academic achievement measures [14-19]. Significant differences in both mean scores and standard deviations have also been observed recently on the Ages and Stages Questionnaires, Second Edition, when comparing Quebcois and American norms [20], and inadequate sensitivity and specificity rates for several American screening tests, including the Ages and Stages Questionnaires, Second Edition, have also been documented when these tests are used with Canadian preschoolers at risk for developmental delays [21]. For the most part, the American standardization samples have demonstrated significantly lower scores than the Canadian standardization samples—a finding that appears to be related to differences in the educational systems of the 2 countries, given that when the samples are matched on the basis of race/ethnicity and parent education level, far fewer composite and scaled score differences are observed [17-19].