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Contemporary Outcomes in Infants With Congenital Heart Disease and Bochdalek Diaphragmatic Hernia

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Background. **Fifteen percent of infants with congenital diaphragmatic hernia (CDH) are born with a coexisting cardiac anomaly. The purpose of this study was to evaluate contemporary outcomes in this patient population and to identify potential risk factors for in-hospital mortality.**

Methods. **Data from all CDH neonates with congenital heart disease managed at a single pediatric tertiary care referral center between 1997 and 2011 were retrospectively analyzed.**

Results. **Forty (18%) of 216 CDH patients had a cardiac anomaly. This group was associated with a significant decrease in overall survival when compared with patients without cardiac anomaly (55% versus 81%; $p = 0.001$). There was no association between type of cardiac anomaly and mortality based on risk stratification according to the Risk Adjustment for Congenital Heart Surgery and The Society of Thoracic Surgeons–European Association for Cardiothoracic Surgery scoring systems ($p = 0.86$ and $p = 0.87$, respectively). Birth weight was similarly no different between survivors and nonsurvivors (2.8 ± 0.6 kg versus 2.8 ± 0.9 kg, respectively; $p = 0.98$). There was a trend toward increased extracorporeal membrane oxygenation use among nonsurvivors ($p = 0.13$). Infants with hemodynamic stability enabling subsequent cardiac repair were associated with lower mortality ($p = 0.04$). Survivors had a wide spectrum of long-term morbidity, but most had some evidence of neurodevelopmental impairment.**

Conclusions. **This large single-institution series suggests that the overall prognosis of infants with concomitant CDH and congenital heart disease can be quite variable, regardless of the type of heart anomaly. Hemodynamic instability and need for extracorporeal membrane oxygenation correlate with higher mortality. Although some long-term survivors have excellent outcomes, most suffer from chronic, long-term morbidities.**

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Neonates born with both congenital diaphragmatic hernia (CDH) and congenital cardiac anomalies (CA) represent approximately 15% of all CDH patients treated at major pediatric referral centers worldwide [1, 2]. Despite advances in prenatal diagnosis as well as the greater availability of pediatric cardiac surgery and extracorporeal membrane oxygenation (ECMO), the overall survival rate in this subset of CDH patients continues to be low [1, 3]. According to the Congenital Diaphragmatic Hernia Study Group, the overall survival rate for CDH infants with major CA is only 41% compared with survival rates in excess of 70% for CDH infants without major CA [1]. Infants with univentricular anatomy were found to have survival rates of 5.1%.

Recent experience caring for CDH infants with CA at our institution has suggested a more variable prognosis in these patients. Moreover, because an increasing number of CDH patients are now surviving well beyond infancy, there has been increasing focus on understanding the long-term morbidities associated with these anomalies [4–7]. Therefore, we conducted this study to assess clinical outcomes in this patient population and to identify potential risk factors for in-hospital mortality.

Material and Methods

A retrospective review of 216 consecutive CDH patients treated postnatally at the University of Michigan C. S. Mott Children's Hospital between 1997 and 2011 was

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Abbreviations and Acronyms

ASD = atrial septal defect
CA = cardiac anomaly
CDH = congenital diaphragmatic hernia
ECMO = extracorporeal membrane oxygenation
PDA = patent ductus arteriosus
RACHS-1 = Risk Adjustment for Congenital Heart Surgery
STS-EACTS = The Society of Thoracic Surgeons–European Association for Cardiothoracic Surgery
VSD = ventricular septal defect

conducted under an approved Institutional Review Board protocol (0039416). Infants with concomitant CA were identified based on the initial postnatal echocardiograms. Minor heart anomalies, such as a patent foreman ovale or a small patent ductus arteriosis (PDA), were excluded from the analysis. Each CA was reviewed by a staff pediatric cardiologist (C.G.F.) and stratified based on risk for in-hospital mortality according to the Risk Adjustment for Congenital Heart Surgery (RACHS-1) scale 0 to 6 and The Society of Thoracic Surgeons–European Association for Cardiothoracic Surgery (STS-EACTS) scale 0 to 5 classification systems, as described elsewhere [8, 9]. For each case, risk stratification was performed in a blinded fashion by a staff congenital heart surgeon (J.C.H.).

All CDH infants with CA were initially managed by a multidisciplinary group of surgeons, cardiologists, and intensivists using principles emphasizing minimal pulmonary barotrauma while maximizing cardiac output and oxygen delivery [10]. The ECMO was reserved for neonates with worsening cardiac dysfunction or pulmonary hypertension despite maximal medical therapy. When the patient was clinically stable, CDH repair was performed before the repair of cardiac anomalies, unless a palliative shunt was required. Demographic, perioperative, and long-term outcomes data were collected and compared with data for patients with isolated CDH. Statistical analyses were performed by the independent samples t test for equality of means, the Pearson χ^2 test, the Pearson correlation test, and logistic regression using the SPSS software package (SPSS, Chicago, IL). Significance was defined as p less than 0.05.

Results

Demographics

Of 216 infants with CDH, 40 (18%) had congenital heart disease. Within the CA group, 68% were inborn, and 70% were diagnosed by fetal echocardiogram. Nine (23%) had right-sided CDH. There was a wide spectrum of cardiac disease. Eleven (28%) had an isolated ventricular septal defect (VSD), 5 (13%) had an atrioventricular septal defect, 4 (10%) had a concomitant atrial septal defect (ASD) and PDA, 2 (5%) had an isolated ASD, and 2 (5%) had tetralogy of Fallot. Four (10%) had univentricular anatomy, and 4 (10%) had an isolated large PDA. The mean RACHS-1 and STS-EACTS scores for the entire group were 2.2 ± 1.1 and 2.0 ± 1.3, respectively ($p = 0.46$). For each patient, the RACHS-1 and STS-EACTS scores were significantly correlated ($p < 0.001$).

Comparison With Isolated CDH

There was a significant decrease in the overall survival rate of CDH infants with CA when compared with CDH infants without CA (55% versus 81%, respectively; $p = 0.001$; Table 1). The mortality rate across the entire 15-year study period was stable, thereby suggesting the absence of an era effect with respect to mortality. All deaths occurred during the initial hospitalization. Several known predictors of CDH mortality at birth, including 5-minute Apgar scores and liver position, were not significantly different in the CA group when compared with the group without CA. The CA group had slightly lower mean birth weights (2.8 ± 0.7 kg versus 3.0 ± 0.6 kg, $p = 0.04$) as well as lower estimated gestational ages (37.0 ± 2.2 weeks versus 37.7 ± 2.1 weeks, $p = 0.08$) compared with the group without CA. There was a trend toward increased ECMO use and decreased ECMO survival among infants with CA compared with infants without CA (ECMO use 53% versus 39%, respectively; $p = 0.16$; and ECMO survival 43% versus 61%, respectively; $p = 0.21$; Table 1). These differences were not statistically significant. The most common cause of death among CDH infants with CA supported on ECMO was the inability to wean off support (n = 6). The incidence of patch repair was higher in the CA group ($p = 0.07$; Table 1). Among survivors, patients with CA had significantly prolonged mechanical ventilation days (31.2 ± 21.9 versus 20.0 ± 14.61, respectively; $p = 0.003$) and hospital length of stay (73.0 ± 60.3 days versus 39.4.8 ± 38.9 days, respectively; $p = 0.001$) compared with isolated CDH patients.

Table 1. In-Hospital Outcomes of Infants With Diaphragmatic Hernia

Outcome	No CA n = 176	CA n = 40	p Value
Survival to discharge	143 (81%)	22 (55%)	0.001[a]
ECMO use	69 (39%)	21 (53%)	0.16
ECMO survival	42 (61%)	9 (43%)	0.21
CDH repair done	156 (89%)	31 (80%)	0.19
CDH patch repair	60 (39%)	18 (58%)	0.07
Ventilator days	20.0 ± 14.1	31.2 ± 21.9	0.003[a]
Survivor hospital stay, days	39.4 ± 38.9	73.0 ± 60.3	0.001[a]

[a] Significant ($p < 0.05$).

CA = cardiac anomaly; CDH = congenital diaphragmatic hernia; ECMO = extracorporeal membrane oxygenation.

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