Surgery 166 (2019) 854–860

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

Pediatrics

Presented at the Academic Surgical Congress 2019

Predictors of in-hospital mortality in newborn conjoined twins

Brent A. Willobee, MD, Michelle Mulder, MD, Eduardo A. Perez, MD, Anthony R. Hogan, MD, Ann-Christina Brady, MD, Juan E. Sola, MD, Chad M. Thorson, MD, MSPH*

Dewitt-Daughtry Family Department of Surgery, Division of Pediatric Surgery, University of Miami Miller School of Medicine, Miami, FL

ARTICLE INFO

Article history:
Accepted 25 June 2019
Available online 8 August 2019

ABSTRACT

Background: Conjoined twins are rare developmental anomalies. There is a paucity of literature other than case reports and small case series. The aim of this study was to examine national outcomes and identify predictors of mortality in newborn conjoined twins.

Methods: We reviewed data on newborn conjoined twins from the Kids' Inpatient Database (1997–2012).

Results: A total of 240 patients were identified for a nationally weighted incidence of 1 per 100,000 live births. The majority of conjoined twins were female ($n = 190$ [81%]). The most commonly associated anomalies were cardiac ($n = 87$ [36%]), gastrointestinal ($n = 41$ [17%]), and abdominal wall ($n = 32$ [13%]) defects. Fifty-six (23%) patients underwent operative procedures, including 28 (12%) neonatal separation surgeries. The overall mortality rate was 61%; most deaths occurred within 24 hours (99 of 146 [68%]) to 48 hours (129 of 146 [88%]) after birth. Mortality was higher in female compared with male children (66% vs 38%, $P = .025$), premature compared with full-term children (72% vs 44%, $P = .007$), and in children with extremely low birth weight (95% vs 59%, $P = .002$). Congenital diaphragmatic hernias were seen in 15 (6%) patients and were uniformly fatal (100% vs 58%, $P = .029$). Mortality was highest in hospitals not designated as children's hospitals (72%) compared with children's hospitals (44%) ($P = .007$).

Conclusion: Conjoined twins are rare anomalies who are susceptible to extremely high perinatal mortality, especially in female children, those who are premature, or those who have low birth weight. These data support caring for these complex patients at hospitals equipped to care for this fragile population.

Introduction

Conjoined twins are rare developmental anomalies that likely result from aberrant embryogenesis. Popularly known as Siamese twins, conjoined twins are uncommon, have a higher predisposition toward the female sex (3:1 ratio), and have a described incidence of 1 in 50,000 births.[1] Up to 60% of the cases of conjoined twins are stillborn, and 35% of live births do not survive past 48 hours.[2,3] Therefore, the true incidence may be closer to 1 in 200,000 live births.[1]

Conjoined twins are an exceptional and challenging group of patients with variable presentations. They can be fused on the ventral (87%) or dorsal (13%) sides and are classified according to the most prominent site of fusion.[4,5] Additional congenital anomalies are frequently present in conjoined twins. Owing to their unique medical and surgical needs, these patients require specialty treatment from a multitude of disciplines. There is a paucity of literature other than case reports and small case series surrounding this remarkable topic. The aim of this study was to examine national outcomes and identify predictors of mortality in newborn conjoined twins.

Methods

We identified all cases of newborn conjoined twins (International Classification of Diseases [ICD]-9, clinical modification, code 759.4) aged 0 to 30 days from the Kids' Inpatient Database (KID) from 1997 to 2012. KID is a national sample of pediatric inpatient admissions, maintained by the Healthcare Cost and Utilization Project and sponsored by the Agency for Healthcare Research and Quality. It is released triennially and is available from 1997 to 2016. KID is the largest publicly available database in the United States for

Presented at the 14th Annual Academic Surgical Congress, Houston, TX.

* Reprint requests: Chad M. Thorson, MD, MSPH, Division of Pediatric Surgery, PO Box 016960 (R-51), Miami, FL.

E-mail address: cthorson@med.miami.edu (C.M. Thorson).

https://doi.org/10.1016/j.surg.2019.06.028
0039-6060/

Table I
Demographics

Characteristics	Total	
	n (%)	95% Confidence Interval (*n* [%])
Total	240 (100)	
Sex		
Female	190 (81)	163–218 (70–88)
Male	46 (19)	23–69 (12–30)
Race		
White	101 (53)	74–127 (41–65)
Black	33 (17)	10–56 (9–31)
Hispanic	30 (16)	14–47 (9–26)
Other	13 (7)	0.1–27 (3–18)
Insurance status		
Medicaid	108 (45)	83–132 (36–55)
Private/HMO	95 (40)	69–121 (31–50)
Self-pay	17 (7)	7–27 (4–13)
Household income by quartile*		
First quartile ($1–$24,999)	54 (23)	35–74 (16–33)
Second quartile ($25,000–$34,999)	70 (30)	47–93 (22–40)
Third quartile ($35,000–$44,999)	70 (30)	44–96 (21–40)
Fourth quartile (>$45,000)	41 (18)	24–58 (11–26)
Hospital bed size†		
Small	12 (8)	5–1 (5–14)
Medium	28 (19)	20–36 (14–24)
Large	111 (73)	92–130 (66–79)
Hospital location/teaching status		
Rural	1 (1)	1 (1)
Urban nonteaching	43 (28)	30–55 (22–36)
Urban teaching	107 (71)	130–173 (63–78)
Children's hospital designation‡		
Children's hospital	95 (60)	72–118 (48–71)
Non–children's hospital	63 (40)	42–84 (29–52)
In-hospital birth		
Yes	185 (78)	162–208 (71–83)
No	53 (22)	38–69 (17–29)
Birth term		
Premature (<37 weeks' gestation)	144 (60)	121–167 (51–69)
Full	96 (40)	68–123 (31–50)
Post	0	0
Birth weight		
Low (<2,500 g)	66 (27)	44–87 (20–37)
Very low (<1,500 g)	17 (7)	8–27 (4–13)
Extremely low (<1,000 g)	26 (11)	17–35 (8–15)

HMO, Health Maintenance Organization.
* Actual dollar amounts are approximations across all year ranges and are adjusted yearly for inflation.
† Definition varies slightly by region.
‡ Children's hospital designation refers to a free-standing children's hospital or general hospital with children's ward; only recorded in 158 patients (denominator $n = 158$ was used for percentage calculations)

all-payer pediatric inpatient care.[6] The database includes more than 4,200 hospitals in the United States and samples normal newborns at a rate of 10% and complicated newborns at a rate of 80%, making it ideal for investigating rare conditions.

Information regarding demographics (sex, race, primary payer, income), associated anomalies (anatomic, perinatal factors), and hospital characteristics (bed size, region, children's hospital designation) were recorded. A hospital was considered to have a children's designation if it was a free-standing children's general or specialty hospital or a children's unit in a general hospital. Only data points from the first 30 days of life were included in the study.

To produce national or regional estimates, discharge weights are developed and provided in KID datasets. Records are poststratified by hospital ownership or control, bed size, teaching status, urban or rural location, and US region, with the addition of a stratum for free-standing children's hospitals. Statistical analysis must be performed accounting for this complex sampling.[7] Statistical analysis was performed using IBM SPSS Statistics Premium, version 26 (IBM Corporation, Armonk, NY). Weighted national estimates accounting for hospital strata (KID_STRATUM, STRATUM), clustering (HOSPID, HOSPNUM), and discharge weight (DISCWT, DISCWT_U) were calculated using the Complex Samples module of SPSS.[8–10] This accounts for the hierarchical structure of the data; patients were nested within hospitals.

Investigating newborn twins poses unique challenges because there are 2 unique patients. Because KID samples 80% of complicated newborns, all patients may not have a pair represented in the database. Therefore, individual patients were analyzed for the purpose of the study. There were 84 unique patients (42 pairs) confirmed in the database. The remaining 68 patients could not be confirmed as a pair owing to incomplete information in the database to link records. Nonetheless, there were 152 patients identified, and after appropriate weighting this resulted in a sample size of 240.

Denominators for calculation of incidences were taken from the US Census Bureau website.[11] Frequency data are presented as *n* (%) with 95% confidence intervals to provide appropriate population estimates of variance. Univariate associations were analyzed with the Pearson χ^2 statistic. Multivariate logistic regression models were constructed for identification of independent predictors of mortality with demographic, clinical, and comorbidity indicators. Overall model performance is reported as a Nagelkerke pseudo-R2

Table II
Associated anomalies*

Characteristics	Total	
	n (%)	95% Confidence interval (*n* [%])
Total	240 (100)	
Major cardiac†	87 (36)	59–114 (27–47)
Ventricular septal defect	22 (9)	9–36 (5–17)
Atrial septal defect	21 (9)	10–32 (5–15)
Transposition/double outlet right ventricle	12 (5)	4–20 (3–9)
Other congenital heart anomaly	70 (29)	43–98 (20–40)
Gastrointestinal	**41 (17)**	**23–58 (11–25)**
Anorectal malformation/imperforate anus	21 (9)	8–34 (5–16)
Other anomaly of intestine	24 (10)	9–38 (5–18)
Unspecified anomaly of intestine	14 (6)	2–26 (3–13)
Genitourinary	**30 (13)**	**16–44 (8–19)**
Ureteral obstruction	11 (5)	0–23 (0–13)
Cystourethral anomaly	11 (5)	1–22 (2–11)
Other genitourinary anomaly	16 (7)	6–26 (4–12)
Abdominal wall defects	**32 (13)**	**18–46 (8–20)**
Musculoskeletal	**24 (10)**	**10–37 (6–17)**
Brain/central nervous system	**16 (7)**	**4–29 (3–14)**
Congenital diaphragmatic Hernia	**15 (6)**	**5–25 (3–12)**
Pulmonary	**10 (4)**	**2–17 (2–9)**
ENT	‡	‡
Multiple major anomalies§	**65 (27)**	**47–82 (20–35)**

Bold values denote major categories.
ENT, Ear, Nose and Throat.
* Numbers and percentages within subcategories are not additive as patients often had multiple anomalies.
† Excluding patent foramen ovale or ductus arteriosis.
‡ Cell censored because $n < 10$ as per Healthcare Cost and Utilization Project guidelines.
§ Defined by the presence of ≥2 defects involving the above categories.

and the area under the receiver-operator curve. Significance for all analyses was determined at $\alpha = .05$. The University of Miami Institutional Review Board considered this national retrospective review as exempt from full review.

Results

A total of 240 patients were identified for a nationally weighted incidence of 1 per 100,000 live births. There also was a female sex predilection ($n = 190$ [81%]). Prematurity ($n = 144$ [60%]) and low birth weight ($n = 109$ [45%]) were frequently encountered. The majority of patients ($n = 150$ of 152 [99%]) were treated in urban centers, but only 60% ($n = 95$ of 158) were hospitalized at centers designated for children. Additional baseline demographic data are shown in Table I.

Associated congenital anomalies were relatively common and are shown in Table II. Overall, cardiac defects were seen most often (36%), especially septal defects (18%) and great vessel transposition (5%). Other cardiac anomalies encountered were pulmonary artery anomalies, valvular atresia, common ventricle, coarctation, endocardiac cushion defect, total anomalous pulmonary venous return, and truncal anomalies. Gastrointestinal defects were also common (17%), with the majority being anorectal malformations (9%). Additional gastrointestinal anomalies were malrotation, atresias (esophageal, small-bowel atresia), and Meckel's diverticulum. Other common anomalies were genitourinary, abdominal wall, musculoskeletal, central nervous system, and congenital diaphragmatic hernia (Table II). The presence of multiple major anomalies was seen in more than a quarter of patients.

Major operative procedures were required for 23% of patients, and separation surgery during the neonatal period was performed in 12% of patients (shown in Table III). Additional procedures included endotracheal intubation (22%), vascular access (18%), and cosmetic reconstructions (8%). Perinatal complications are also shown in Table III. Overall mortality in the cohort was high (61%), with only 39% of patients surviving to discharge. Most deaths occurred in the first 48 hours ($n = 129$ of 146 [88%]), and the vast majority of these deaths ($n = 99$ of 146 [68%]) occurred within 24 hours of birth.

Female sex, prematurity, and extremely low birth weight were all significantly associated with increased mortality (shown in Table IV). Congenital diaphragmatic hernia ($n = 15$ [100%]) and pulmonary agenesis ($n = 10$ [100%]) were uniformly fatal (both $P < .05$). There was a higher mortality rate in hospitals not designated as children's hospitals (72%) compared with those with a children's hospital designation (44%) ($P < .01$). All deaths ($n = 104$ [100%]) at non–children's hospitals were within 48 hours of birth.

To limit selection bias, patients who were transferred in to the index hospital were excluded from further analysis. Still, higher mortality rates were found in non–children's hospitals (81%) compared with children's hospitals (56%) ($P = .032$). This disparity toward higher mortality was most pronounced for those dying within 24 hours (78% vs 17%, $P < .001$) or 48 hours (81% vs 46%, $P = .006$) of birth. Lastly, multiple logistic regression was performed to identify predictors of mortality. Prematurity (odds ratio 2.3 [1.06–4.84], $P = .034$) and non–children's hospital designation (odds ratio 2.3 [1.09–5.02], $P = .029$) were the only independent predictors of mortality (as seen in Table V).

Discussion

In this retrospective analysis, we have, for the first time, identified several variables predictive of increased perinatal mortality in conjoined twins. This study represents the largest analysis of early outcomes in this patient population. Mortality in the cohort was high and similar to the historically reported rate of 60%.[3,12,13] Those who survive the neonatal period to undergo eventual separation surgery have a mortality rate of around 33%.[12,14] Although we have seen advancements in surgical technique in the last 20 years leading to increased survival from separation surgery, our results

Table III
Procedures and hospital outcomes

Characteristics	Total	
	N (%)	95% Confidence Interval (*N* [%])
Total	240 (100)	
Operative procedures		
Major operating room procedure*	56 (23)	34–78 (16–33)
Twin separation	28 (12)	11–44 (6–20)
Plastic	20 (8)	7–32 (4–15)
Genitourinary	15 (6)	2–29 (3–15)
Ostomy formation	14 (6)	2–27 (3–13)
Major cardiac	13 (5)	3–23 (3–11)
Orthopedic	12 (5)	3–21 (2–11)
Gastrointestinal resection	11 (5)	1–21 (2–11)
Neurologic	—	—
Abdominal wall repair	—	—
Miscellaneous procedures		
Vascular access†	44 (18)	28–60 (13–26)
Endotracheal intubation >96 h	34 (14)	18–50 (9–22)
Endotracheal intubation <96 h	18 (8)	7–30 (4–14)
Perinatal Complications		
Respiratory distress syndrome	78 (33)	58–99 (25–42)
Infection	26 (11)	11–41 (6–19)
Jaundice	23 (10)	10–35 (5–16)
Hematologic disorder	22 (9)	9–35 (5–16)
Endocrine/metabolic derangement	18 (7)	5–31 (4–15)
Birth trauma	—	—
Intraventricular hemorrhage	—	—
Miscellaneous	52 (22)	27–76 (14–33)
Disposition		
Death	146 (61)	118–174 (52–69)
Discharge home	41 (17)	22–60 (11–26)
Transfer to facility	33 (14)	18–50 (9–22)
Home health care	19 (8)	8–30 (4–14)
Died During Hospitalization		
Died at birth	99 (41)	74–124 (32–51)
Died <48 h after birth	30 (13)	28–33 (12–14)
Died >48 h after birth	17 (7)	5–28 (4–13)

* Excludes venous/arterial access and umbilical catheterization.
† Includes arterial and umbilical vein catheterizations.

indicate that there is a need for further study into the early perinatal care of these patients.

Conjoined twins are rare. Estimated incidence varies widely and is between 1/50,000 and 1/200,000 in the United States, with the highest incidence being described in Uganda (1/4,200) and India (1/2,800).[15] Conjoined twins occur because of a rare embryologic phenomenon resulting in monozygotic, monoamniotic, monochorionic twins. Although the pathophysiological etiology of conjoined twins is not completely understood, there exist 2 hypotheses as to their pathogenesis. The first theory asserts that incomplete fission of the early embryo produces identical twins with shared anatomic structures.[16] Monozygotic twins occur when an embryo divides before day 13. Therefore, this hypothesis asserts that embryos, which divide on or after day 13, will not divide completely and will remain with fused organs of various degrees, producing conjoined twins. The extent of division and subsequent development will determine the degree of shared anatomy between the twins.[17]

Although the first hypothesis is most commonly accepted in medical literature, a preeminent pediatric surgeon specializing in the care of these patients, Dr. Rowena Spencer, championed a controversial and opposing theory.[18] This second hypothesis states that conjoined twins are the result of an interaction between 2 embryos from completely separated fertilized eggs. The close proximity of these separate embryos results in cellular signaling and subsequent cellular migration and fusion events between 13 and 17 days' gestation.[19] However, her model faced numerous criticisms from pathologists and developmental embryologists and is not commonly accepted.[20]

There is a wide spectrum of severity in conjoined twins, and conventional classification systems are based on site(s) of attachment. Twins may be joined at the head (craniopagus), chest (thoracopagus), abdomen (omphalopagus), or lower abdomen (ischiopagus). Patients may be joined for a variable distance across multiple body compartments (ie, thoraco-omphalo-ischiopagus). In addition, they may be joined dorsally at the lower back (pyopagus), dorsally for a larger distance (rachipagus), or laterally (parapagus).[1,21] Prior studies have suggested that certain defects are associated with worse outcomes. Thoracopagus is often associated with significant underlying cardiopulmonary abnormalities and has been found to have a mortality rate higher than 80%, whereas mortality rates with isolated omphalopagus may be lower than 20%.[12] Unfortunately, although we are able to obtain data on associated anomalies and outcomes for a large volume of patients in the United States with the KID database, there is only 1 ICD-9 code for conjoined twins, which does not provide information about severity or extent of the defect.

Respiratory distress syndrome and congenital pulmonary processes are a serious cause of morbidity and mortality in newborn infants. In our cohort, pulmonary agenesis and congenital diaphragmatic hernia were universally fatal, with all deaths occurring before 48 hours. It is unknown whether their universal mortality was due to an increased severity of these malformations in conjoined twins or whether the combination of these diagnoses in the background of conjoined twins led to the pursuit of a palliative course of treatment.

Most conjoined twins are female. We found that female conjoined twins experience higher mortality rates than male

Table IV
Univariate predictors of mortality*

Variable	Died % (95% confidence interval)	Survived % (95% confidence interval)	*P* value
Sex			
Female	66 (55–75)	34 (25–45)	**.025**
Male	38 (20–60)	62 (40–80)	
Premature birth†			
Yes	72 (61–81)	28 (19–39)	**.007**
No	44 (29–61)	56 (39–71)	
Low birth weight‡			
Yes	72 (53–86)	28 (15–47)	.125
No	57 (47–66)	43 (34–53)	
Very low birth weight‡			
Yes	58 (29–82)	42 (18–71)	.853
No	61 (51–70)	39 (30–49)	
Extremely low birth weight‡			
Yes	95 (71–99)	5 (1–30)	**.002**
No	57 (47–66)	43 (34–53)	
Children's hospital designation			
Non–children's hospital	72 (61–80)	28 (20–39)	**.007**
Children's hospital	44 (29–61)	56 (39–71)	
Congenital diaphragmatic hernia			
Yes	100 (100)	—	**.029**
No	58 (49–67)	42 (33–51)	
Major pulmonary anomaly			
Yes	100 (100)	—	**.047**
No	59 (50–68)	41 (32–50)	
Major cardiac anomaly			
Yes	59 (43–74)	41 (26–57)	.821
No	62 (50–72)	38 (28–50)	
Newborn respiratory distress			
Yes	51 (29–72)	49 (28–71)	.348
No	63 (52–72)	38 (28–48)	
Abdominal wall defect			
Yes	74 (47–91)	26 (9–54)	.274
No	59 (49–68)	41 (32–51)	
Imperforate anus or colonic atresia			
Yes	48 (24–72)	53 (28–76)	.274
No	62 (53–71)	38 (29–47)	
Multiple congenital anomalies			
Yes	60 (42–76)	40 (24–58)	.902
No	61 (51–71)	39 (29–49)	

Bold values denote major categories.
* All percentages were rounded to the nearest whole percent.
† Defined as birth after <37 weeks' gestation.
‡ Low birth weight is defined as <2.5 kg, very low birth weight is defined as <1.5 kg, and extremely low birth weight is defined as <1.0 kg.

Table V
Logistical regression

Variable	Mortality	
	Odds Ratio (95% confidence interval)	*P* value
Non–children's hospital birth	2.341 (1.091–5.024)	**.029**
Premature birth	2.270 (1.064–4.841)	**.034**
Extremely low birth weight	7.612 (0.919–63.049)	.06
Congenital diaphragmatic hernia	1.15 (0–1.0)	.999
Female sex	2.27 (0.842–6.119)	.105

Bold values denote major categories.
Model R2 = 0.298, area under curve = 0.77, $P < .001$.

conjoined twins, especially in the immediate perinatal period. This is interesting because female children in the United States generally have a lower infant mortality rate than male children, and the difference is most pronounced in the first several weeks after birth.[22] Although there are numerous potential explanations for this disparity, the most widely held belief is that female infants have a survival advantage as a result of an increased tolerance to neonatal respiratory distress syndrome. Numerous studies have demonstrated that male infants have more severe symptoms and die of neonatal respiratory distress syndrome at significantly higher rates than female infants.[23,24] In addition, neonatal respiratory distress syndrome primarily affects infants born preterm and those born with low birth weight (both highly prevalent in our cohort) and is the leading cause of mortality in these children.[25] This reversal in sex-based neonatal survival is likely caused by children in this cohort dying of unrelated complications before sex-based differences in survival from respiratory distress syndrome have the possibility to manifest. In this scenario, female infants who

would have survived respiratory distress die earlier in their course due to other complications of being a conjoined twin. This question could not be definitively answered using our available data. Nevertheless, the increased mortality risk seems to be multifactorial, and the above factors are likely to all play a complex role in the outcomes of these patients.

Because many of the children in our cohort were born at non–children's hospitals without dedicated pediatric wards, it may be that the health care team lacked the equipment and resources necessary to care for children with such complex presentations. The conjoined twin birth is extremely rare and unlikely to be previously encountered by nonspecialized providers or hospitals. This is supported by the fact that although there are more than 4,000 hospitals included in KID sampling clusters, the patients in our database only came from 75 unique hospitals. The presentation of this unfamiliar birth anomaly, combined with the lethal triad of prematurity, low birth weight, and respiratory distress, may have led providers to underestimate the chances for survival. Furthermore, even if heroic efforts were made, there may have simply been a lack of appropriate resources that would otherwise be present in facilities specializing in the care of children.

There is another potential explanation for the disparate outcomes between children's hospitals and non–children's hospitals. It is impossible to know prenatal information (ultrasound findings, associated anomalies, consultations) from the KID database as it is an inpatient sample database. In the modern era, it is presumable that most conjoined twins will be prenatally diagnosed via ultrasound. Some of these patients may have been evaluated at specialized centers and deemed to have severe defects not compatible with long-term survival. Therefore, mothers may have chosen to deliver at their home institution, which may not have been a children's center. This is suggested by the fact that all deaths at non–children's hospitals were within 48 hours of admission. Although it is commonly assumed that children's hospitals have specialty care teams for various rare conditions, this does not necessarily guarantee any consistent level of expertise in caring for patients with conditions as rare as conjoined twinning. We are careful not to overstate the importance of hospital designation given this potential bias. Nonetheless, prior large case series at international referral centers suggest improved outcomes for these patients based on multidisciplinary specialized care.[12,14,26–29]

Our findings are not without limitations. KID is a strictly regulated source of pediatric inpatient information sampled across participating hospitals in the United States. Still, there are possibilities that heterogeneity may exist in the data entry process. Inherently, the analysis is retrospective, and our analyses are limited to information coded in ICD-9 clinical modification classifications. Because there is only 1 ICD code for conjoined twins, we were unable to obtain information about the anatomic region involved or the severity of the conjoined defect. Owing to the large number of very early postnatal deaths, it is possible that the full assessment of associated anomalies was not undertaken. Therefore, our estimates may be an underrepresentation of the severity of associated anomalies. Generalizability of the data may be limited by the fact that patients were cared for in only 75 different hospitals, highlighting the rarity of this condition. Lastly, there is a risk of selection bias when comparing hospital factors because those children healthy enough to transfer to a higher level of care are likely to have increased odds of overall survival. To mitigate this potential bias, we excluded patients who were transferred to tertiary care centers and only considered in-born patients. However, we did not eliminate transferred patients for the entire analysis because this would result in loss of important information regarding associated anomalies, operations, and outcomes that are important for clinicians caring for this population. We continued to observe higher survival in conjoined twins who were born at large urban teaching hospitals designated for the treatment of children. Our results agree with other published literature showing a survival benefit for patients who are cared for at large institutions with a multidisciplinary team.[30,31]

In conclusion, conjoined twins are rare developmental anomalies with a high risk for perinatal mortality. This is especially true for female children, those who are premature, those born with low birth weight, or those with severe congenital pulmonary disease (agenesis, hypoplasia from diaphragmatic hernia). This study suggests that every effort should be made to optimize the perinatal care of these patients at tertiary hospitals designated for the treatment of children because this affords the optimal chance for survival in the early perinatal period.

Funding/Support

The authors have indicated that they have no funding regarding the content of this article.

Conflict of interest/Disclosure

The authors have indicated that they have no conflicts of interest regarding the content of this article.

References

1. Mian A, Gabra NI, Sharma T, et al. Conjoined twins: From conception to separation, a review. *Clin Anat*. 2017;30:385–396.
2. Viljoen DL, Nelson MM, Beighton P. The epidemiology of conjoined twinning in Southern Africa. *Clin Genet*. 1983;24:15–21.
3. Spitz L, Kiely EM. Experience in the management of conjoined twins. *Br J Surg*. 2002;89:1188–1192.
4. Spencer R. Anatomic description of conjoined twins: A plea for standardized terminology. *J Pediatr Surg*. 1996;31:941–944.
5. Baken L, Rousian M, Kompanje EJ, et al. Diagnostic techniques and criteria for first-trimester conjoined twin documentation: A review of the literature illustrated by three recent cases. *Obstet Gynecol Surv*. 2013;68:743–752.
6. Healthcare Cost and Utilization Project. *KID Database Documentation*. Vol 2019. Rockville, MD: Agency for Healthcare Research and Quality; 2018.
7. Quality AfHRa. *HCUP Sample Design: National Databases: Accessible Version. Healthcare Cost and Utilization Project*. Rockville, MD: Agency for Healthcare Research and Quality; 2018.
8. Chu B, Houchens R, Elixhauser A, Ross D. *Using the KIDS' Inpatient Database (KID) to Estimate Trends*. HCUP Methods Series Report #2007-02. Agency for Healthcare Research and Quality; 2007. http://www.hcup-us.ahrq.gov/reports/methods.jsp. Accessed April 5, 2019.
9. Quality AfHRa. *Producing National HCUP Estimates: Accessible Version. Healthcare Cost and Utilization Project*. Rockville, MD: Agency for Healthcare Research and Quality; 2018.
10. Sakshaug JW, West BT. Important considerations when analyzing health survey data collected using a complex sample design. *Am J Public Health*. 2014;104:15–16.
11. US Census Bureau. National Intercensal Datasets; 2016. https://www.census.gov/data/datasets/time-series/demo/popest/intercensal-2000-2010-national.html. Accessed April 5, 2019.
12. Tannuri ACA, Batatinha JAP, Velhote MCP, Tannuri U. Conjoined twins: Twenty years' experience at a reference center in Brazil. *Clinics (Sao Paulo)*. 2013;68:371–377.
13. Spencer R, ed. *Conjoined Twins. Developmental Malformations and Clinical Implications*. Baltimore, MD: Johns Hopkins University Press; 2003.
14. Rode H, Fieggen AG, Brown RA, et al. Four decades of conjoined twins at Red Cross Children's Hospital: Lessons learned. *S Afr Med J*. 2006;96:931–940.
15. Mutchinick OM, Luna-Muñoz L, Amar E, et al. Conjoined twins: A worldwide collaborative epidemiological study of the International Clearinghouse for Birth Defects Surveillance and Research. *Am J Med Genet C Semin Med Genet*. 2011;157C:274–287.
16. Spitz L, Kiely EM. Conjoined twins. *JAMA*. 2003;289:1307–1310.
17. Kaufman MH. The embryology of conjoined twins. *Childs Nerv Syst*. 2004;20:508–525.
18. Spencer R. Conjoined twins: Theoretical embryologic basis. *Teratology*. 1992;45:591–602.
19. Kobylarz K. History of treatment of conjoined twins. *Anaesthesiol Intensive Ther*. 2014;46:116–123.
20. Gasser RF. Dr. J. Bruce Beckwith's review of Dr. Rowena Spencer's Conjoined twins: Developmental malformations and clinical implications. *Pediatr Dev Pathol*. 2004;7:671.

21. Mathew RP, Francis S, Basti RS, et al. Conjoined twins: Role of imaging and recent advances. *J Ultrason*. 2017;17:259–266.
22. Zisk JL, Genen LH, Kirkby S, Webb D, Greenspan J, Dysart K. Do premature female infants really do better than their male counterparts? *Amer J Perinatol*. 2011;28:241–246.
23. Khoury MJ, Marks JS, McCarthy BJ, Zarro SM. Factors affecting the sex differential in neonatal mortality: The role of respiratory distress syndrome. *Am J Obstet Gynecol*. 1985;151:777–782.
24. Perelman RH, Palta M, Kirby R, Farrell PM. Discordance between male and female deaths due to the respiratory distress syndrome. *Pediatrics*. 1986;78:238–244.
25. Millman GC. Fanaroff and Martin's neonatal-perinatal medicine diseases of the fetus and infant, 8th edn, Vols I and II. *Arch Dis Child Fetal Neonatal Ed*. 2006;91:F468.
26. Pai KM, Naidu RC, Raja A, et al. Surgical nuances in the separation of craniopagus twins: Our experience and a follow up of 15 years. *Neurol India*. 2018;66:426–433.
27. Saguil E, Almonte J, Baltazar W, et al. Conjoined twins in the Philippines: Experience of a single institution. *Pediatr Surg Int*. 2009;25:775–780.
28. Al Rabeeah A. Conjoined twins: Past, present, and future. *J Pediatr Surg*. 2006;41:1000–1004.
29. Carlson TL, Daugherty R, Miller A, Wallace R. Successful separation of conjoined twins: The contemporary experience and historic review in Memphis. *Ann Plast Surg*. 2018;80:S333–S339.
30. Donoho DA, Wen T, Liu J, et al. The effect of NACHRI children's hospital designation on outcome in pediatric malignant brain tumors. *J Neurosurg Pediatr*. 2017;20:149–157.
31. Burke LG, Frakt AB, Khullar D, Jha AK. Association between teaching status and mortality in US hospitals. *JAMA*. 2017;317:2105–2113.