Pediatric Surgery International (2019) 35:1265–1270
https://doi.org/10.1007/s00383-019-04548-4

ORIGINAL ARTICLE

Left congenital diaphragmatic hernia-associated musculoskeletal deformities

Emrah Aydın[1,2] · Oğuz Özler[2] · Patricia Burns[1] · Foong-Yen Lim[1] · Jose Luis Peiró[1]

Accepted: 27 August 2019 / Published online: 3 September 2019

Abstract

Aim With the advancement in the treatment strategies of congenital diaphragmatic hernia (CDH), there is an increase in the survival rates. This fact leads to an increase in the morbidity and extrapulmonary complications in the long term such as failure to thrive, hernia recurrence, neurodevelopmental delay, gastrointestinal problems, and musculoskeletal anomalies. Herein, we aim to investigate the association between the long-term musculoskeletal complications in CDH patients regarding the defect size, repair type, and perinatal parameters.

Methods After Institutional Review Board approval was obtained (2017-6361), a retrospective chart review was performed on CDH patients from 2003 to 2016. Patients who were operated due to left-sided isolated congenital diaphragmatic hernia and survived to date were included in the study. Data were collected on demographics, preoperative characteristics, operative interventions, and postoperative outcomes. Statistical analysis was performed with IBM SPSS Statistics 20.0.0 (Chicago, IL).

Results There were 98 patients with left CDH of whom 33 (33.7%) had primary repair, 25 (25.5%) had patch repair, and 40 (40.8%) had muscle flap repair. The median age of the patients was 6.00 ± 3.83 years. 45 patients (45.9%) had large diaphragmatic defects, 28 patients (28.6%) had at least one type of musculoskeletal deformities, 2 of which were pectus carinatum, 16 were pectus excavatum, and 18 were scoliosis. CDH patients who had small diaphragmatic defects and repaired with a patch were less likely develop musculoskeletal deformities while who had primary abdominal closure after ventral hernia significantly have more pectus excavatum.

Conclusion Although there was a trend towards an increased risk of the pectus deformity and scoliosis in patients repaired with muscle flap, it did not reach statistical significance. There is a correlation between musculoskeletal deformities and the severity of the CDH.

Keywords Congenital diaphragmatic hernia · Muscle flap · Prosthetic patch · Outcomes · Scoliosis · Pectus excavatum · Musculoskeletal complications

Introduction

Congenital diaphragmatic hernia (CDH) is a severe condition characterized by the defective formation of diaphragm musculature, which causes protrusion of abdominal organs into the thoracic cavity [1]. It is seen approximately 1 in 2500–5000 live births [2]. One theory speculates that migration of the abdominal content into the thorax compresses the developing fetal lung causing pulmonary hypertension and pulmonary hypoplasia, which have high mortality rates [3]. The type and technique of repair in CDH patients were mostly determined by the surgeon's experience and the defect size, as well as the general condition of the patient. Most of the time, small defects can be repaired primarily, while larger defects require patch repair or muscle flap [3, 4]. With the advancement in the treatment strategies of CDH, there is now an increase in the survival rates ranging from 53 to 90% [5]. These higher survival rates have also led to an increase in the morbidity and extrapulmonary complications in the long term. Failure to thrive, hernia recurrence, neurodevelopmental delay, gastrointestinal problems, and musculoskeletal anomalies are the most common

✉ Emrah Aydın
dremrahaydin@yahoo.com

[1] Division of Pediatric General and Thoracic Surgery, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, MLC 11025, Cincinnati, OH 45229-3039, USA

[2] Department of Pediatric Surgery, Koç University School of Medicine, Istanbul, Turkey

complications [6]. According to the literature, floppy use of synthetic patch has decreased the prevalence of musculoskeletal anomalies in these patients compared to patients operated with muscle flap repair [7–9].

Chest wall deformities and vertebral deformities compromise the central aspect of musculoskeletal anomalies. The prevalence of idiopathic scoliosis, which is defined as the curvature of the spine greater than 10°, is 2–4% in adolescents. Pectus deformity is also seen approximately 1% of adolescents [10]. Of the CDH survivors, 31% have chest wall deformities, mainly pectus excavatum, and 13% have spinal deformities, mainly scoliosis [11]. There are studies in the literature that demonstrate the coexistence of the musculoskeletal anomalies with CDH; however, there is not much study that compares the effect of repair type on this comorbidity [6, 10, 12, 13]. Therefore, the hypothesis of this study is that most severe diaphragmatic hernias are intrinsically associated with musculoskeletal deformities independent of the type of repair. We aim to compare the long-term musculoskeletal outcomes of CDH patients in a selected population per type of repair.

Methods

Data acquisition

After Institutional Review Board approval was obtained with IRB #2017-6361, a retrospective review was performed of all congenital diaphragmatic hernia repairs from 2003 to 2016 at a single academic pediatric hospital with associated fetal care center. Data were assembled through an institutional database and augmented with the electronic medical record for the hospital. Data were collected on demographics, comorbidities, preoperative characteristics, operative interventions, and complications. Long-term outcome data were achieved prospectively through parental surveys and verified by electronic medical record review. All surveys were distributed at a single point in time regardless of the original surgery date. Phone calls to non-responders allowed for additional data collection for a total inclusion percentage of 93%.

Study population

Patients who were operated due to left-sided isolated congenital diaphragmatic hernia between January 2003 and December 2016 and survived to date were included in the study. The primary outcome of this study was the presence of musculoskeletal and vertebral deformities. The diagnosis was based on the medical records of the patients by primary care physicians, pediatric surgeons, orthopedics and radiologists; and verbal announcements of the parents, which were verified by the latest radiological images of the patients. Patients were categorized by the technique of their CDH repair: primary, patch, and muscle flap. The degree of scoliosis was decided mild for curves less than 25°, moderate for curves between 25° and 45° and severe for the curves over 45°. The diagnosis of pectus deformity was made by Haller Index in radiological studies. Abdominal closure techniques were classified as primary repair, secondary repair (primary repair after intentional temporary abdominal ventral hernia), tertiary repair (primary repair after multiple closures with Silastic or Gore-Tex dual mesh patch, similar to Bogota bag), primary closure with mesh, and secondary closure with mesh (mesh closure after temporary abdominal ventral hernia).

Statistical analysis was performed with IBM SPSS Statistics 24.0.0 (Chicago, IL). The characteristics of the study sample were summarized by descriptive statistics, with dichotomous or ordinal data presented as percentages, and continuous data as medians with standard deviations. Kolmogorov–Smirnov test was used to demonstrate normal distribution. One-way ANOVA was used for homogeneity of the variables, Student's T test and Pearson correlation were used for parametric data, and Mann–Whitney U, Wilcoxon and Kruskal–Wallis tests and Spearman correlation were used for non-parametric data. Statistical associations were considered significant if the p value was < 0.05.

Results

There were 203 patients who were admitted with a diagnosis of CDH during the study period, of which 114 patients were diagnosed with isolated left-sided CDH. Among these patients, 98 of them (86.0%) survived to date (Table 1).

None of the non-survivals had a musculoskeletal deformity. Among them, 7 (43.8%) were female with a mean birth weight of 2848.13 ± 577.46 g. The defect in the diaphragm muscle was classified as type D per CDH Study Group registry classification in 9 (56.3%) of the patients while the rest were type C. Six (37.5%) patients were repaired with muscle flap, of which 66.7% were type D. The mean age for surgical repair was 19.00 ± 14.12 days.

Of these survivors, 33 (33.70%) had primary repair, 25 (25.50%) had patch repair, and 40 (40.80%) had muscle flap repair. The median age of the patients at the time of the survey was 6.00 ± 3.83 years. 45 patients (45.9%) had large diaphragmatic defects (CDH Study Group registry classification types C and D) (Table 2). 28 patients (28.6%) had at least one type of musculoskeletal deformities, 2 (2%) of which were pectus carinatum, 8 (8.2%) were pectus excavatum, 10 (10.2%) were scoliosis, and 8 (8.2%) patients had both pectus excavatum and scoliosis.

Table 1 Characteristics of CDH patients included in the study

	Primary repair *n* 33	Patch repair *n* 25	Muscle flap repair *n* 40	*p*
Demographics				
Female sex	13 (39.4%)	12 (48%)	21 (52.5%)	0.532
Age of the patient	7.50 ± 3.92	5.00 ± 4.52	5.00 ± 3.11	0.102
Age of mother	27.00 ± 6.50	26.00 ± 4.50	27.00 ± 6.03	0.978
Gestational age at diagnosis	29.71 ± 5.08	25.86 ± 5.34	24.29 ± 4.14	0.100
Gestational age at delivery	38.29 ± 1.15	37.71 ± 1.56	38.07 ± 1.96	0.022
Birth weight	3130.00 ± 505.51	2907.00 ± 465.19	2875.00 ± 469.43	0.104
Perinatal information				
Prenatal diagnosis	22 (66.7%)	16 (64.0%)	38 (95%)	0.003
Large defect size	2 (6.1%)	14 (56%)	29 (72.5%)	0.000
Liver up	3 (9.1%)	11 (50%)	23 (57.5%)	0.000
Hernia sac	7 (21.2%)	1 (4.4%)	5 (12.5%)	0.157
LHR 1	1.60 ± 0.69	1.41 ± 0.58	1.20 ± 0.48	0.010
O/E LHR 1	38.06 ± 11.37	31.93 ± 12.27	30.38 ± 9.11	0.070
O/E TLV 1	27.62 ± 15.24	14.26 ± 11.89	12.10 ± 9.36	0.003
LHR 2	1.86 ± 0.74	1.61 ± 0.48	1.70 ± 0.76	0.135
O/E LHR 2	32.98 ± 11.36	30.07 ± 9.33	32.01 ± 14.26	0.323
O/E TLV 2	37.28 ± 9.32	24.13 ± 11.04	30.60 ± 9.94	0.130
CDH repair				
Repair time (days)	6.00 ± 9.87	8.00 ± 8.39	13.00 ± 10.72	0.028
Gastrostomy	4 (12.1%)	13 (52%)	22 (55%)	0.000
Musculoskeletal outcomes				
Pectus excavatum	4 (12.1%)	4 (16%)	8 (20%)	0.662
Scoliosis	2 (6.1%)	5 (20%)	11 (27.5%)	0.061

Values expressed as medians ± standard deviations or counts (percentage of the group). LHR 1 indicates the lung-to-head ratio before the 30th week of gestation; O/E LHR 1, observed to expected lung-to-head ratio before 30th week of gestation; O/E TLV 1, observed to expected total lung volume before 30th week of gestation; LHR 2 indicates lung-to-head ratio after 30th week of gestation; O/E LHR 2, observed to expected lung-to-head ratio after 30th week of gestation; O/E TLV 2, observed to expected total lung volume after 30th week of gestation

Table 2 Comparison of the repair techniques with diaphragmatic defect size determined by CDH Study Group staging

	Primary repair	Patch repair	Muscle flap repair
A	14	0	0
B	17	11	11
C	2	9	21
D	0	5	8

The majority (89/98, 90.8%) of the patients had primary abdominal closure while only 9 (9.2%) had mesh repair. Among primary abdominal closure patients, five were left with a ventral hernia at the initial surgery, which was followed by primary repair (Table 3). 6 of 89 primary abdominal closure patients were repaired after multiple closures with a synthetic patch similar to Bogota bag. Among patients, those repaired with mesh closure, only 2 (22.2%) of them needed secondary mesh closure. In patients with musculoskeletal deformity, 8 out of 9 abdominal mesh closure patients had large diaphragmatic defect ($p = 0.007$, OR 11.24, 95% CI 1.35–93.78). As the number of concurrent abdominal closures increases, the probability of the musculoskeletal deformity increases; 60% ($p = 0.200$) in patients with primary repair after ventral hernia and 66.7% in patients with primary repair after multiple closures with a Bogota bag ($p = 0.077$, OR 4.47, 95% CI 0.76–25.79). Furthermore, CDH patients who had primary abdominal closure after ventral hernia significantly have more pectus excavatum ($p = 0.007$, OR 7.36, 95% CI 1.41–60.66).

Patient characteristics and postnatal follow-up course are summarized in Table 1. Patient demographics other than gestational age at delivery were comparable between groups. Further analysis demonstrated that CDH patients who had small diaphragmatic defects were less likely to develop musculoskeletal deformities than those with large defects ($p = 0.074$, OR 2.318, 95% CI 0.914–5.880). Although there was a trend towards an increased risk of the pectus deformity and scoliosis in patients repaired with muscle flap, it did

Table 3 Distribution of musculoskeletal deformity types per diaphragmatic repair and abdominal closure type

CDH repair type	Abdominal closure type	Musculoskeletal deformity type			
		PE	Sc	PC	PE&Sc
Primary repair	Primary abdominal closure	2 (50%)	1 (25%)		1 (25%)
	Secondary abdominal closure	1 (100%)			
Prosthetic patch	Primary abdominal closure	2 (28.6%)	3 (42.9%)		2 (28.6%)
Muscle flap	Primary abdominal closure	1 (12.5%)	3 (37.5%)	1 (12.5%)	3 (37.5%)
	Secondary abdominal closure	1 (50%)			1 (50%)
	Tertiary abdominal closure	1 (25%)	2 (50%)	1 (25%)	
	Primary mesh closure		1 (50%)		1 (50%)

PE pectus excavatum, *Sc* Scoliosis, *PC* pectus carinatum

not reach statistical significance (Table 4). The univariate analysis demonstrated that prenatal diagnosis, LHR ratio, O/E TLV after the 30th week of gestation, liver herniation into the thoracic cavity, diaphragmatic defect size and CDH repair type (primary repair and muscle flap repair) were independent risk factors for musculoskeletal deformity in CDH patients. However, the correlation coefficients between each parameter were low.

In the subanalysis of musculoskeletal deformity in CDH patients, the majority had a mild deformity, of which 8 (40%) were isolated pectus excavatum, 6 were isolated scoliosis, 1 (5%) was pectus carinatum, and 5 were combined scoliosis and pectus excavatum. Only 7 (25%) patients with a musculoskeletal deformity needed an intervention which is bracing for scoliosis. None of the patients with pectus excavatum or carinatum required surgery.

Discussion

While overall survival rates for neonates with CDH have improved significantly, pulmonary and extrapulmonary complication rates are also increasing [12]. Of the extrapulmonary ones, musculoskeletal problems are essential to consider during follow-up visits with the prevalence ranging between 20 and 48% [13]. In our study, we retrospectively analyzed 98 patients with a left-sided isolated congenital diaphragmatic hernia for associated musculoskeletal anomalies and found that 28 patients (28.6%) have at least one anomaly, mainly scoliosis, and pectus excavatum.

Although there is no definitive mechanism explained for musculoskeletal anomalies in CDH patients, there are some theories. First, these anomalies are primarily associated with CDH given the close relationship between the development of chest wall, thoracic spine, diaphragm, and lungs [3]. To better evaluate the effects of surgical techniques, we did not include any patient with congenital musculoskeletal deformities at birth. Second, musculoskeletal anomalies develop as a complication of CDH. Excessive tension after repair causes chest wall asymmetries and spinal abnormalities. This is supported by the fact that musculoskeletal anomaly incidence is higher in larger defects. To deal with the second theory, patch repair is widely preferred in the larger defect per the floppy patch decreases the tension [10]. In our study, even though more patients had pectus deformity and scoliosis in patients repaired with muscle flap, the statistical significance could not be determined. We speculated that the preference of the surgeons related to the repair type might put a bias on these results per muscle flap repair technique is the most preferred technique in patients with larger defects. Another explanation is that the lungs of the patients with CDH are hypoplastic and have poor compliance. To overcome this compliance problem, increased negative intrathoracic pressure is needed, and it causes inward pulling of the chest wall. This increased work of breathing also creates increased tension on the diaphragm and may cause spinal deformities [10]. This knowledge correlates with our findings in this study. We demonstrated that the severity of the musculoskeletal deformities increases as the prenatal lung measurements decrease.

Table 4 Relation between repair types and musculoskeletal deformity in CDH patients

CDH repair type	Pectus excavatum			Scoliosis		
	RR	95% CI	*p*	RR	95% CI	*p*
Primary	0.66	0.23–1.88	0.422	0.24	0.06–1.01	0.025
Patch	0.97	0.35–2.74	0.959	1.12	0.45–2.84	0.807
Muscle flap	1.45	0.59–3.54	0.414	2.28	0.97–5.37	0.053

RR relative risk, *CI* confidence interval

As stated in the literature, patients with CDH have much higher rates of musculoskeletal deformities compared to the general population. Vanomo et al. [14] found that in patients with CDH, these rates were 27% and 48%, respectively. However, to our knowledge, there has been no other study that investigates the relationship between abdominal wall closure in CDH and musculoskeletal deformities. Since the abdominal organs herniate into the thorax, the abdominal cavity is small in size compared to healthy counterparts. We also speculated that the musculoskeletal deformities were not only resulted from the disease itself or type of repair but also the abdominal closure might affect that. In our study, the majority of patients with musculoskeletal anomalies (92.9%) had primary abdominal closure, which supports our hypothesis per more tension would be caused in these patients.

Our study demonstrated that CDH patients with larger diaphragmatic defects were more likely to develop musculoskeletal deformities than those with smaller defects. It also showed that that prenatal diagnosis, low LHR ratio, low O/E TLV after the 30th week of gestation, liver herniation into the thoracic cavity were risk factors. Besides, it was revealed that the prevalence of a musculoskeletal deformity in CDH patients was higher in patients repaired with muscle flap. The incidence of scoliosis was higher in patients with muscle flap repair than primary repair. However, there is no statistically significant difference in musculoskeletal complication rates between the patch repair and muscle flap repair, which is also compatible with the literature [9, 15].

One limitation of the study other than being a retrospective review which includes inherent bias is the bias on the selection of the surgical technique by the surgeon. If there is not enough muscle to stitch the patch, then costal stitches would be done which probably increase the deformity incidence. To prevent this, the muscle flap technique would be the chosen technique in these patients, which contributes to the high incidence of deformities in this group. Another limitation is relatively short follow-up of the patients per musculoskeletal deformities may develop late in childhood or even adulthood.

In conclusion, we found a 28.6% incidence of musculoskeletal anomalies in CDH patients. Prenatal diagnosis, low LHR ratio, low O/E TLV after the 30th week of gestation, liver herniation into the thoracic cavity, and larger diaphragmatic defect size are risk factors. We also found that muscle flap and patch repair have a higher incidence of scoliosis rate than primary repair.

Acknowledgements This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions All authors have made substantial contributions to the conception and design of the study, acquisition, analysis, and interpretation of data, drafting the article and revising it for important intellectual content and final approval of the version to be submitted.

Compliance with ethical standards

Conflict of interest The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (IRB #2017-6361) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

References

1. Rawat M, Lakshminrusimha S, Madappa R et al (2017) Congenital Diaphragmatic hernia—a review. Matern Heal Neonatol Perinatol 3:6. https://doi.org/10.1186/s40748-017-0045-1
2. Kuroda T (2016) Congenital diaphragmatic hernia and diaphragmatic eventration. Tomoaki T (ed) Operative general surgery in neonates and infants. Springer, Tokyo, p 194
3. Waqar L, Antiel RM, Campbell RM et al (2016) Management and outcomes of scoliosis in children with congenital diaphragmatic hernia. J Pediatr Surg 51:1921–1925. https://doi.org/10.1016/j.jpedsurg.2016.09.013
4. Aydin E, Lim F-Y, Kingma P et al (2019) Congenital diaphragmatic hernia: the good, the bad, and the tough. Pediatr Surg Int 35:303–313. https://doi.org/10.1007/s00383-019-04442-z
5. Crankson SJ, Al Jadaan SA, Namshan MA et al (2006) The immediate and long-term outcomes of newborns with congenital diaphragmatic hernia. Pediatr Surg Int 22:335–340. https://doi.org/10.1007/s00383-006-1643-6
6. Morini F, Valfrè L, Bagolan P (2017) Long-term morbidity of congenital diaphragmatic hernia: a plea for standardization. Semin Pediatr Surg 26:301–310. https://doi.org/10.1053/j.sempedsurg.2017.09.002
7. Barnhart DC, Jacques E, Scaife ER et al (2012) Split abdominal wall muscle flap repair vs patch repair of large congenital diaphragmatic hernias. J Pediatr Surg 47:81–86. https://doi.org/10.1016/j.jpedsurg.2011.10.023
8. Joshi SB, Sen S, Chacko J et al (2005) Abdominal muscle flap repair for large defects of the diaphragm. Pediatr Surg Int 21:677–680. https://doi.org/10.1007/s00383-005-1438-1
9. Nasr A, Struijs MC, Ein SH et al (2010) Outcomes after muscle flap vs prosthetic patch repair for large congenital diaphragmatic hernias. J Pediatr Surg 45:151–154. https://doi.org/10.1016/j.jpedsurg.2009.10.024
10. Russell KW, Barnhart DC, Rollins MD et al (2014) Musculoskeletal deformities following repair of large congenital diaphragmatic hernias. J Pediatr Surg 49:886–889. https://doi.org/10.1016/j.jpedsurg.2014.01.018
11. Hollinger LE, Harting MT, Lally KP (2017) Long-term follow-up of congenital diaphragmatic hernia. Semin Pediatr Surg 26:178–184. https://doi.org/10.1053/j.sempedsurg.2017.04.007
12. Langer JC, Mihailovic A, Coates AL et al (2006) The price of success in the management of congenital diaphragmatic hernia: is improved survival accompanied by an increase in long-term morbidity? J Pediatr Surg 41:888–892. https://doi.org/10.1016/j.jpedsurg.2006.01.026
13. Takayasu H, Masumoto K, Goishi K et al (2016) Musculoskeletal abnormalities in congenital diaphragmatic hernia survivors:

patterns and risk factors: report of a Japanese multicenter follow-up survey. Pediatr Int 58:877–880. https://doi.org/10.1111/ped.12922

14. Vanamo K, Rintala R, Sovijarvi A et al (1996) Long-term pulmonary sequelae in survivors of congenital diaphragmatic defects. J Pediatr Surg 31:1096–1100. https://doi.org/10.1016/S0022-3468(96)90095-0
15. Tsai J, Sulkowski J, Adzick NS et al (2012) Patch repair for congenital diaphragmatic hernia: is it really a problem? J Pediatr Surg 47:637–641. https://doi.org/10.1016/j.jpedsurg.2011.11.054