Journal of The Cardiovascular Thoracic Anaesthesia and Intensive Care Society

GKDA Derg 2025;31(1):38-46
Doi: 10.14744/GKDAD.2025.57983

RESEARCH ARTICLE

Diaphragm Paralysis After Congenital Heart Surgery: A Single Center Experience

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ABSTRACT

Objectives: Phrenic nerve injury following congenital heart surgery has become the most common cause of diaphragm paralysis in children. In this single-center study, we aimed to determine the incidence of diaphragm paralysis after congenital heart surgery and to identify the risk factors for prolonged mechanical ventilation in this unique patient population.

Methods: We retrospectively reviewed the records of all patients diagnosed with diaphragmatic paralysis after congenital heart surgery between January 2018 and May 2023.

Results: The incidence of diaphragm paralysis was 3.13%. The median age and weight of the patients were 2.5 (IQR: 0.3–7) months and 4.2 (IQR: 3.2–7.25) kg. The median duration of mechanical ventilation was 10 (IQR: 5–28) days. Mechanical ventilation was prolonged in 30 (34.1%) patients. Infection, chylothorax, ECMO requirement, and unplanned cardiac reintervention significantly increased the risk of prolonged mechanical ventilation ($p<0.05$). After initial surgery, 50% underwent diaphragm plication at a median of 18 days (IQR: 12–27.5 days). In this group, infection, chylothorax, and late plication (>14 days) increased the risk of prolonged mechanical ventilation ($p<0.05$). The time between diaphragm plication and index surgery was significantly longer in cases with prolonged mechanical ventilation ($p<0.05$).

Conclusion: Phrenic nerve injury can cause significant morbidity after congenital heart surgery. The relationship between diaphragm paralysis and prolonged mechanical ventilation may have enormous clinical implications. Some patients may recover with conservative strategies; however, others require plication. Therefore, tailoring management strategies according to the patient's age, clinical condition, and need for positive pressure ventilation may help improve outcomes.

Keywords: Congenital heart disease, congenital heart surgery, diaphragm paralysis, prolonged mechanical ventilation

Please cite this article as: "Hekim Yılmaz E, Çiçek M. Diaphragm Paralysis After Congenital Heart Surgery: A Single Center Experience. GKDA Derg 2025;31(1):38-46".

Introduction

Phrenic nerve injury resulting in transient or permanent diaphragmatic dysfunction is a well-known complication of congenital heart surgery. Phrenic nerve injury and associated diaphragm paralysis (DP) may be the result of extensive dissection, adhesions inherent to previous operations, stretching, or thermal injury.[1] The incidence is highly variable, ranging from 0.3% to 12.8%.[2,3] Neonates and infants are particularly susceptible to the effects of diaphragm dysfunction, as breathing is majorly dependent on the diaphragm at younger ages.[4] Diaphragm dysfunction may be asymptomatic or present with respiratory distress, atelectasis, recurrent lung infections, or failure to wean from mechanical ventilation (MV), and is associated with increased postoperative morbidity and mortality.[4–6] Management strategies for diaphragm dysfunction are either conservative or surgical (diaphragm plication). Nowadays, the length of postoperative hospital stay is accepted as a surrogate for the quality of care in congenital heart surgery.[7] Therefore, the primary aim

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Submitted: October 15, 2024 **Revised:** December 06, 2024 **Accepted:** January 07, 2025 **Available Online:** March 17, 2025

The Cardiovascular Thoracic Anaesthesia and Intensive Care - Available online at www.gkdaybd.org

of this study was to determine the incidence of DP and to identify the risk factors for prolonged mechanical ventilation in patients with DP following congenital heart surgery. We also analyzed the risk factors for prolonged MV in the group who underwent diaphragm plication (DPL).

Methods

This is a retrospective and single-center study. It was approved by the local ethics committee (23.10.2023, E-28001928-604.01.01-227441404) and conducted in accordance with the Declaration of Helsinki. The study included all patients diagnosed with DP after congenital heart surgery between January 2018 and May 2023. Phrenic nerve injury was suspected if the patient failed to wean from MV, showed signs of respiratory distress after extubation (which could not be explained by other factors such as residual/additional cardiac lesions, pulmonary pathology, or infection), had paradoxical thoracic movement, or had an elevated hemidiaphragm on chest X-ray. The initial assessment was made at bedside using an echo machine. In all cases, the diagnosis was confirmed by fluoroscopy during spontaneous breathing. Phrenic nerve injury/paralysis of the diaphragm was defined according to the STS-CHSD complication code specification: "Presence of elevated hemi-diaphragm(s) on chest radiograph in association with evidence of weak, immobile, or paradoxical movement assessed by ultrasound or fluoroscopy".[8]

The medical records of these patients were retrospectively reviewed, and demographic data, cardiac pathology, details of surgical procedures, and postoperative course were extracted. Special attention was paid to the duration of positive pressure ventilation (time to final extubation), cardiac intensive care unit (ICU) and hospital stay, and the rate and timing of surgical diaphragm plication. Prolonged MV was defined as the need for positive pressure ventilation for ≥21 days. The Society of Thoracic Surgeons - European Association for Cardio-Thoracic Surgery (STAT) score was used to describe surgical complexity.[9]

Following diagnosis, initially, we preferred a conservative approach with continued ventilatory support and gradual weaning with the support of alternative ventilation methods such as non-invasive positive pressure ventilation and high-flow oxygen therapy. We considered diaphragm plication for patients who failed multiple extubation attempts (maximum three attempts) or who were unable to wean from positive pressure ventilation without an obvious cardiac or pulmonary etiology. Early plication was defined as plication up to 14 days, whereas late plication was defined as plication after 14 days following the index operation. Diaphragm plications were performed using the technique described by Schwartz and Filler.[10]

Statistical Analysis

Statistical analyses were performed using SPSS version 20 (IBM Corp., Armonk, NY, USA). Continuous variables were described using medians and interquartile ranges. Categorical variables were described by the number of patients and relative frequencies. The Mann-Whitney U test was used to compare continuous variables between two groups. Categorical variables were analyzed using the chi-squared test or Fisher's exact test, as appropriate. Associations between individual variables and the outcome of interest (prolonged mechanical ventilation) were initially assessed using univariate binary logistic regression. Variables showing a significant association in the univariate analysis were considered for inclusion in the multivariate model. Multivariable analysis was performed using binary logistic regression to identify independent predictors of outcome. The selection of variables for the multivariate model was based on their significance in the univariate analysis, clinical relevance, and the absence of multicollinearity. A p value<0.05 was considered statistically significant.

Results

A total of 2814 patients underwent surgery during the study period. Of them, eighty-eight (3.13%) were diagnosed with DP. The clinical characteristics of the patients are outlined in Table 1. The median duration of ventilation was 10 (IQR: 5–28) days, and MV was prolonged in 34.1% of the patients. The risk of prolonged MV significantly increased in younger patients and those with low body weight (p<0.05). DP was most commonly left-sided (72.7%), but the laterality of the injury had no significant effect on the risk of prolonged MV (p>0.05). Whether the surgery was the initial one or a repetitive one did not have a significant effect on the risk of prolonged MV (p>0.05). Infection, chylothorax, extracorporeal membrane oxygenation (ECMO) requirement, and an unplanned cardiac re-intervention significantly increased the risk of prolonged MV (p<0.05). The complexity of the surgical procedure had no effect on the duration of MV (p>0.05). ICU and hospital stays were significantly longer, and mortality was significantly higher in patients with prolonged MV (p<0.05). When these variables were included in the multivariate analysis, the association between the site of infection (ventilatory-associated pneumonia (VAP) associated with bloodstream infection) and prolonged MV persisted (p<0.05, Table 2). The majority of the group (75%) had undergone biventricular heart surgery. The patients' primary cardiac pathologies and operations are summarized in Figure 1 and 2.

50% of the patients underwent diaphragm plication at a median of 18 days (IQR: 12–27.5 days) after the initial operation (Fig. 3). Although the median age and weight of

Table 1. Characteristics of the study population

Characteristics	All patients (n=88)		MV Prolonged (n=30)		MV not prolonged (n=58)	
	n	%	n	%	n	%
Age at surgery, median (IQR) months	2.5 (0.3–7)		0.75 (0.2–3)		5 (0.4–11)	
Age group						
Neonates (0–30 days)	37	42	17	56.7	20	34.5
Infants (31 days–1 year)	37	42	12	40	25	43.1
Others (>1 year)	14	16	1	3.3	13	22.4
Gender, male	55	62.5	17	56.7	38	65.5
Weight at surgery, median (IQR) kg	4.2 (3.2–7.25)		3.7 (3.1–4.2)		5.45 (3.5–8)	
Laterality of diaphragm injury						
Left	64	72.7	21	70	43	74.1
Right	22	25	7	23.3	15	25.9
Bilateral	2	2.3	2	6.7	0	0
Ventricular physiology						
Univentricular	22	25	8	26.7	14	24.1
Biventricular	66	75	22	73.3	44	75.9
First sternotomy	67	76.1	26	86.7	41	70.7
STAT score						
1	0	0	0	0	0	0
2	13	14.8	3	10	10	17.2
3	36	40.9	11	36.7	25	43.1
4	31	35.2	11	36.7	20	34.5
5	8	9.1	5	16.7	3	5.2
DPL	44	50	28	93.3	16	27.6
Time between DPL and index operation, median (IQR), days	18 (12–27.5)		21.5 (16.5–36)		12.5 (8.5–17.5)	
DPL>14 days after index operation	29	65.9	24	85.7	5	31.3
Length of MV, median (IQR) days	10 (5–28)		38.5 (28–72)		7 (3–10)	
Unplanned cardiac re-intervention	17	19.3	13	43.3	4	6.9
Post-operative ECMO support	11	12.5	9	30	2	3.4
Chylothorax	25	28.4	15	50	10	17.2
Length of ICU stay, median (IQR) days	20.5 (12.25–41)		36 (60.5–83)		14 (9–20)	
Length of hospital stay, median (IQR) days	29 (20.25–46.75)		66 (44–96)		22.5 (18–31)	
Tracheostomy	17	19.3	15	50	2	3.4
Mortality	6	6.8	5	16.7	1	1.7
Documented infection	55	62.5	27	90	28	48.3

MV: Mechanical ventilation; IQR: Interquartile range; ICU: Intensive care unit; STAT: The Society of Thoracic Surgeons - European Association for Cardio-Thoracic Surgery; DPL: Diaphragm plication; ECMO: Extracorporeal Membrane Oxygenation

Table 2. Analysis of risk factors for prolonged MV

	Univariate			Multivariate		
	p	OR	95% CI for the OR	p	OR	95% CI for the OR
Age at surgery	0.034	0.892	0.803–0.992	0.66		
Sex, male	0.416	NA				
Body weight	0.011	0.735	0.58–0.932			
Laterality	0.138	NA				
First sternotomy	0.096	NA				
STAT score	0.284	NA				
DPL	<0.001	36.75	7.833–172.42			
Time between DPL and index operation	0.005	1.236	1.065–1.433			
DPL>14 days after index operation	0.001	13.2	2.957–58.921			
Length of MV	<0.001					
Unplanned re-intervention	<0.001	10.324	2.969–35.895			
ECMO	0.003	12	2.393–60.164			
Chylothorax	0.002	4.8	1.787–12.894	0.111		
Length of ICU stay	<0.001					
Length of hospital stay	<0.001					
Mortality	0.03	11.4	1.266–102.67			
Documented infection	0.001	9.643	2.63–35.355			
Source of infection						
Infection is not present	Reference category					
VAP	0.046	4.521	1.028–19.879	0.845		
BSI+VAP	0.000	62	9.188–418.380	0.010	17.068	1.949–149.443
BSI	0.562			0.513		
Surgical site infection	0.999			0.999		
Mediastinitis	1.000			1.000		

MV: Mechanical ventilation; OR: Odds ratio; CI: Confidence interval; STAT: The Society of Thoracic Surgeons - European Association for Cardio-Thoracic Surgery; DPL: Diaphragm plication; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit; BSI: Bloodstream infection; VAP: Ventilator-associated pneumonia; NS: Not significant.

patients who underwent DPL were lower in the group with prolonged MV, this was not statistically significant (p>0.05). Chylothorax and infection significantly increased the risk of prolonged MV (p<0.05). When analysis was performed according to the site of infection, VAP and VAP associated with bloodstream infection (BSI) significantly increased the risk of prolonged MV (p<0.05). The risk of prolonged MV was significantly higher in those who had late plication (>14 days) (p<0.05). Multivariate analysis supported the association between the timing of plication and prolonged MV (p<0.05) (Table 3). Six patients died. Three of them died due to sepsis. Two patients who initially underwent biventricular repair had to be switched to single ventricle repair and died. The other one was suffering from bronchopulmonary dysplasia, which impeded weaning from positive pressure ventilation.

Discussion

Phrenic nerve injury may occur after congenital heart surgery and is associated with prolonged ventilation and ICU stay.[11–14] Historically, the primary quality measure for congenital heart surgery has been postoperative mortality. However, with improving results in surgery, mortality has become a less sensitive marker, and postoperative length of stay has emerged as a surrogate for quality of care.[7] Therefore, the present study was designed to define the risk factors for prolonged MV in the presence of diaphragmatic dysfunction. We also aimed to present our experience with phrenic nerve injury and its relevant variables.

The incidence of diaphragmatic paralysis in our population was 3.13%, which is comparable with the incidence reported in the literature, ranging from 0.3% to 12.8%.[2,3,12,15] The duration of MV was prolonged in 34.1% of the population. The risk of prolonged MV decreased with increasing age. Factors such as the relative weakness of the intercostal muscles, greater chest wall compliance, and increased mediastinal mobility make younger children more vulnerable to respiratory complications in the presence of diaphragmatic dysfunction.[12]

Previous studies have reported that some surgical procedures (TOF repair, arterial switch operation, unifocalization of pulmonary arteries, Glenn anastomosis) requiring extensive dissection or harvesting of autologous

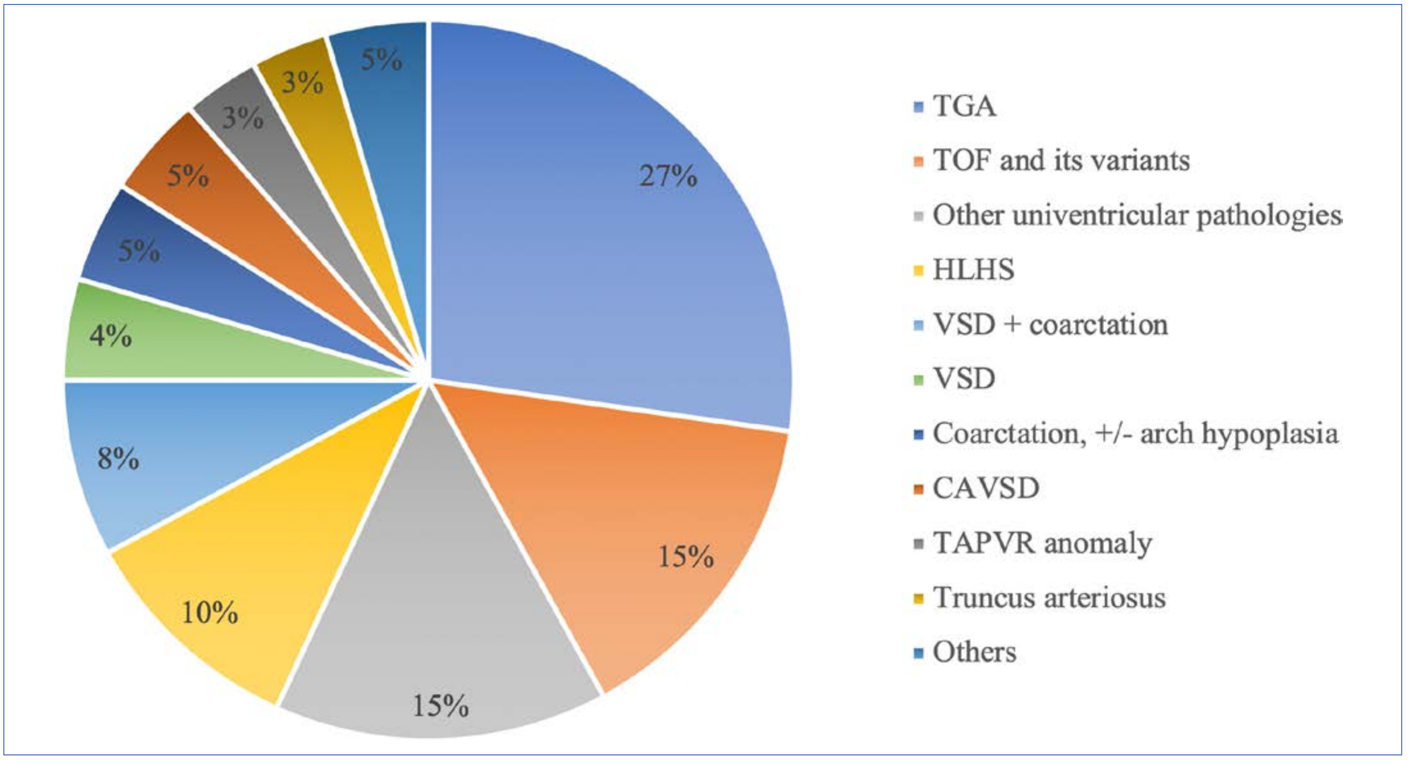

Figure 1. Primary cardiac pathologies of patients with diaphragm paralysis.

TGA: Transposition of great arteries; TOF: Tetralogy of fallot; HLHS: Hypoplastic left heart syndrome; VSD: Ventricular septal defect; CAVSD: Complete atrioventricular septal defect; TAPVR: Total anomalous pulmonary venous return.

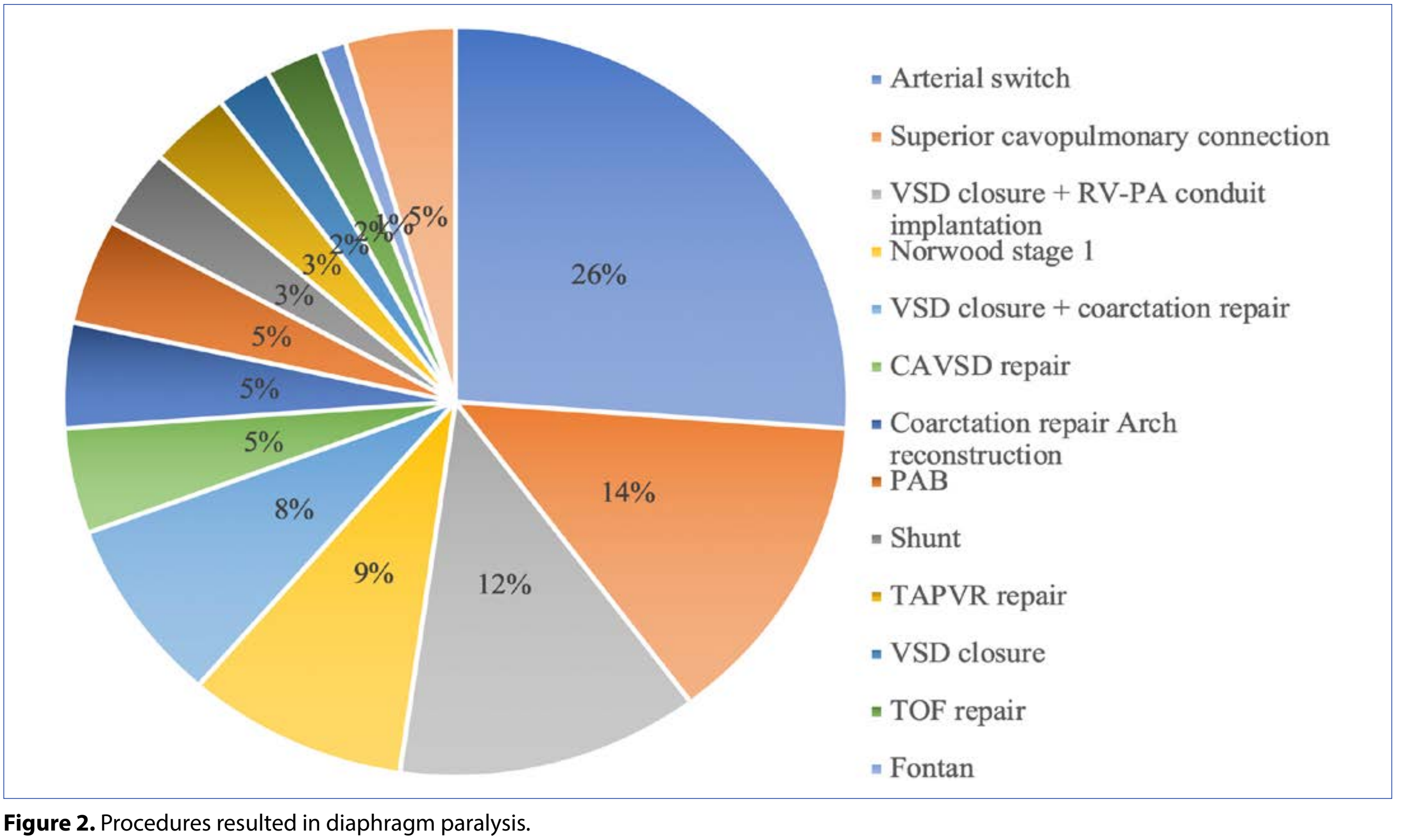

Figure 2. Procedures resulted in diaphragm paralysis.

VSD: Ventricular septal defect; RV-PA: Right ventricle-pulmonary artery; CAVSD: Complete atrioventricular septal defect; PAB: Pulmonary artery banding; TAPVR: Total anomalous pulmonary venous return; TOF: Tetralogy of fallot.

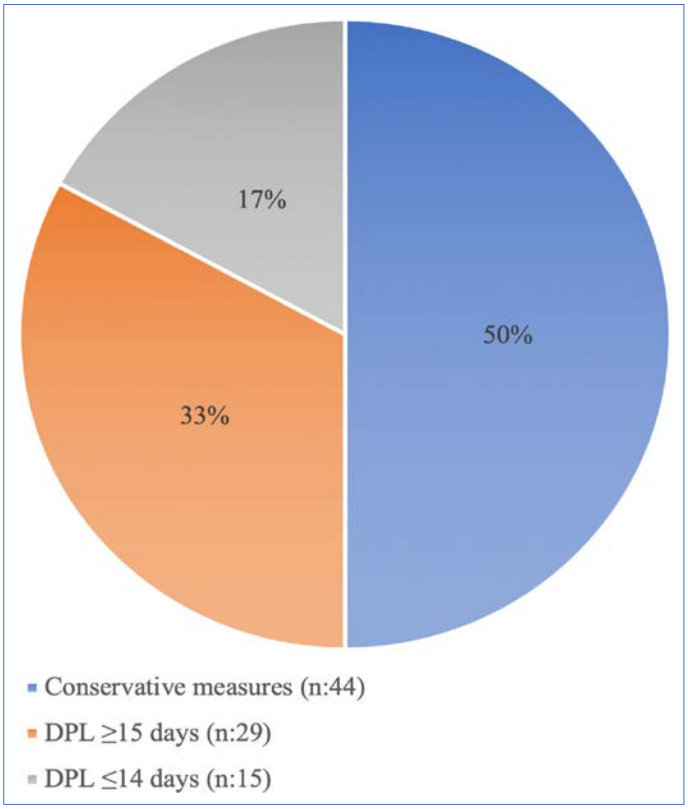

Figure 3. Modes of treatment.
DPL: Diaphragm plication.

pericardium are associated with a higher incidence of DP.[2,5,12,16,17] Similar to these studies, we observed DP most frequently after arterial switch operation in those who underwent biventricular repair and after Glenn surgery in those who underwent single ventricle palliation. However, univentricular or biventricular repair did not significantly affect the risk of prolonged MV.

As a consequence of adhesions and altered anatomical relationships of mediastinal structures, reoperative cardiac surgery has been reported as a risk factor for phrenic nerve injury.[12,14] Whether the sternotomy was the first or a repetitive one did not affect the duration of MV in our population. However, virgin patients underwent DPL more frequently. This can be attributed to the fact that virgin patients constituted the majority of our population and were generally younger, and younger patients tended to be more symptomatic. We did not routinely screen patients for diaphragmatic dysfunction unless they were symptomatic. As redo patients were generally older than virgin ones, even if diaphragmatic dysfunction was present, it may have been well tolerated and gone unnoticed.

Chylothorax is a serious problem that complicates the intensive care process.[18] In patients with DP and concomitant chylothorax, it is not surprising that the duration of MV support was longer.

After congenital heart surgery, revision of the primary repair and unplanned cardiac catheterization independently prolong hospital stay.[7] Similarly, in patients with DP, unplanned reinterventions, either surgical or transcatheter, prolonged the duration of MV.

In our group, VAP significantly increased the risk of prolonged MV. Diaphragmatic dysfunction reduces the tidal volume of the affected side, facilitates lung collapse, and predisposes to pneumonia. VAP has a high burden on ICU and is associated with adverse outcomes, including prolonged duration of MV, increased length of ICU stay, and mortality.[19] However, in this clinical setting, VAP can be a contributing factor or an unwanted consequence of prolonged MV. Diagnosis of DP requires weaning from MV, experience, and clinical suspicion. Sometimes the diagnosis may be delayed, especially in patients with poor general condition and in neonates. Factors other than DP (hemodynamic instability, residual cardiac pathology, pulmonary pathologies, infection) that may hinder the success of extubation should always be considered. Treatment options for DP are a conservative approach or surgical plication of the hemidiaphragm.[2,3,5,12] Spontaneous recovery of diaphragm function may occur within days to months after injury; however, some patients may not recover, suggesting an unpredictable trajectory.[20] Following diagnosis, determining a reasonable time limit to predict the absence of spontaneous recovery of diaphragmatic function before scheduling diaphragmatic plication is crucial, but this limit remains unknown.

Diaphragm plication appears to be an established method in patients with DP and respiratory insufficiency, but its proper timing remains unclear. In our institution, regardless of age and diagnosis, we attempt to wean the patient from MV—if necessary, with the support of alternative ventilation methods—before performing DPL. With this approach, we observed that half of the patients were able to breathe spontaneously without plication. However, this process can sometimes take a long time, making the patient vulnerable to the long-term consequences of MV and ICU stay. Diaphragm paralysis requiring plication has been reported as an independent predictor of prolonged hospital stay.[7] In our study, patients who required DPL spent more time on positive pressure ventilation and had longer ICU and hospital stays. Furthermore, late plication (>14 days) emerged as a risk factor for prolonged MV. Prolonged time to plication has been reported as a risk factor for prolonged length of stay and increased medical costs.[16]

Denamur et al.[21] identified the duration of mechanical ventilation (≥21 days) as an independent risk factor for unsuccessful conservative strategy. ICU and hospital stays were significantly longer when conservative measures failed.

Table 3. Analysis of risk factors for prolonged MV in patients who had DPL

	Prolonged MV (n=28)		MV not prolonged (n=16)		Univariate			Multivariate		
	n	%	n	%	p	OR	95% CI for the OR	p	OR	95% CI for the OR
Age at surgery, median (IQR), months	0.5 (0.2–3)		2 (0.25–6.5)			0.245				
Sex, male	16	57.1	11	68.8	0.447	NA				
Body weight, median (IQR), kg	3.55 (3.05–4.1)		4.1 (3.3–7.5)			0.109				
Laterality					0.136	NA				
Left	19	67.9	15	93.8						
Right	7	25	1	6.3						
Bilateral	2	7.1	0	0						
First sternotomy	26	92.9	12	75	0.097	NA				
STAT score					0.730	NA				
1	0	0	0	0						
2	3	10.7	2	12.5						
3	10	35.7	8	50						
4	11	39.3	5	31.3						
5	4	14.3	1	6.3						
Time between DPL and index operation, median (IQR), days	21.5 (16.5–36)		12.5 (8.5–17.5)		0.005	1.236	1.065–1.433	0.032	1.664	1.045–2.651
DPL>15 days after index operation	24	85.7	5	31.3	0.001	13.2	2.957–58.921			
Length of MV, median (IQR), days	38.5 (28–69)		10.5 (9–13)		<0.001					
Unplanned reintervention	12	42.9	0	0	0.999					
ECMO	9	32.1	0	0	0.999					
Chylothorax	14	50	1	6.3	0.014	15	1.738–129.488	0.176		
Length of ICU stay, median (IQR), days	60.5 (38.5–81.5)		21.5 (15.5–24)		<0.001					
Length of hospital stay, median (IQR), days	66 (44.5–89.5)		27.5 (21–32.5)		<0.001					
Mortality	5	17.9	0	0	0.073					
Documented infection	26	92.9	7	43.8	0.002	16.714	2.920–97.679			
Source of infection										
Infection is not present	2	7.1	9	56.3		Reference category				
VAP	8	8.6	4	25	0.039	7.875	1.105–56.123	0.344		
BSI+VAP	11	39.3	1	6.3	0.03	49.5	3.838–638.404	0.399		
BSI	3	10.7	2	12.5	0.577					
Surgical site infection	2	7.1	0	0	0.999					
Mediastinitis	2	7.1	0	0	0.999					

MV: Mechanical ventilation; DPL: Diaphragm plication; OR: Odds ratio; CI: Confidence interval; IQR: Interquartile range; STAT: The Society of Thoracic Surgeons - European Association for Cardio-Thoracic Surgery; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit; VAP: Ventilator-associated pneumonia; BSI: Bloodstream infection; NA: Non applicable.

Thus, relying on natural recovery of diaphragm function may result in extended and complicated periods of MV. Another concern with the conservative approach is that late surgical plication may be accompanied by diaphragm atrophy, which could even preclude successful surgical plication.[17]

On the other hand, early diaphragmatic plication may result in swift extubation, reduced ICU and hospital length of stay, and improved outcomes.[13] Potential drawbacks of plication include the trauma associated with an additional surgical procedure and concerns about the long-term return of function of the injured diaphragm. A few studies have focused on the long-term function of the plicated diaphragm and reported that normal motion tended to return during follow-up in the majority of patients.[3,15,22] Some studies have recommended early diaphragmatic plication after diagnosis, while others have failed to show an association between early plication and increased success rates.[2,11,23] Although the real benefit of early surgical treatment has not been shown in prospective randomized studies, there is an increasing number of publications suggesting that it may be the right strategy.[7,16]

Therefore, we believe that while deciding on the treatment modality, instead of applying a routine protocol, treatment should be individualized considering the patient's demographic variables, cardiac diagnosis, and clinical conditions. Especially in neonates and small infants, after excluding other pulmonary and cardiac risk factors that may impede MV weaning, earlier consideration of DPL may yield more successful outcomes. However, prospective randomized controlled studies are necessary to support this theory.

Limitations

Our study had several important limitations. First, it was a retrospective observational study and suffered from the inherent limitations of its design. In addition, we did not screen all patients for diaphragm function. Therefore, some patients with DP may have escaped diagnosis due to uneventful recovery and failure to identify an elevated hemidiaphragm on chest X-ray.

Conclusion

In conclusion, the results of the current study confirm that phrenic nerve injury is a potential complication causing significant morbidity after pediatric cardiac surgery. The relationship between DP and prolonged ventilation may have enormous clinical implications, such as an increased risk of infection, prolonged ICU stay, and hospital stay. Although DPL seems to be an established method in patients with diaphragmatic paralysis and respiratory failure, its appropriate timing remains unclear. Therefore, in this clinical context, which complicates the ICU course after congenital heart surgery, tailoring management strategies according to the patient's conditions, including age, clinical status, or need for invasive or non-invasive MV support, may help to improve outcomes. However, prospective randomized studies are necessary to determine the modality and timing of optimal treatment.

Disclosures

Ethics Committee Approval: The study was approved by The Dr. Siyami Ersek Chest Heart and Vascular Surgery Training and Research Hospital Ethics Committee (no: E-28001928-604.01.01-227441404, date: 23/10/2023).

Authorship Contributions: Concept – E.H.Y., M.Ç.; Design – E.H.Y., M.Ç.; Supervision – E.H.Y., M.Ç.; Fundings – E.H.Y., M.Ç.; Materials – E.H.Y., M.Ç.; Data collection &/or processing – E.H.Y., M.Ç.; Analysis and/or interpretation – E.H.Y., M.Ç.; Literature search – E.H.Y., M.Ç.; Writing – E.H.Y., M.Ç.; Critical review – E.H.Y., M.Ç.

Informed Consent: Written informed consent was obtained from all patients.

Conflict of Interest: All authors declared no conflict of interest.

Use of AI for Writing Assistance: No AI technologies utilized.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

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