Original Article

Use of oxygenation, ventilation indices, and pulmonary hypertension as selection parameters for thoracoscopic repair of congenital diaphragmatic hernia, improved outcome: A retrospective study

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ABSTRACT

Background: Many reports describing the thoracoscopic repair (TR) of congenital diaphragmatic hernia (CDH) have been published in the last two decades. These showed the safety and feasibility of the technique. CDH TR was based on selection criteria relying on authors' experience. Many indices were described to determine preoperative evaluation and prognosis in CDH cases.

Purpose: We aim to settle selection criteria to help in selecting CDH cases to improve the outcome of TR in limited resource centers plus usage of oxygenation and ventilation indices as predictors for the postoperative outcome.

Patients and Methods: Between January 2016 and June 2023, 59 ventilated neonates with posterolateral CDH have been subjected to TR.

Results: A total of 59 cases were included in the study divided into. Group A: Included 47 survivor patients. Group B: Included 12 nonsurvivor patients. The mean values for survivors; mean ventilation index (VI) was 474.75±114.01, mean oxygenation index (OI) was 7.95±2.01, and mean oxygenation saturation index (OSI) was 6.95±3.11. There was a correlation of VI, OI, and OSI with mortality where all dead cases have higher values where VI greater than 500, OI greater than 10, OSI greater than 10, and pulmonary hypertension less than 40 mmHg.

Conclusion: TR of CDH is feasible and safe even in countries with limited infrastructure. The selection criteria for good outcomes are VI less than 500, OI less than 10, OSI less than 10, and pulmonary hypertension less than 40 mmHg added to the clinical patients' criteria and surgical expertise.

Key Words: Congenital diaphragmatic hernia, indices, oxygenation, thoracoscopy, ventilation.

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INTRODUCTION

Congenital diaphragmatic hernia (CDH) presented in the first 12 h of life is associated with a high mortality rate of up to 50%, despite the recent advances in antenatal diagnosis, fetal intervention, and significant improvement in the intensive care of these neonates. Over the last decade, the prognosis has not changed significantly, although improvements in ventilation, use of inotropic drugs, and delaying surgical repair until hemodynamic stability of cases were settled[1-4].

The major factor in mortality and morbidity is the severity of pulmonary hypertension (PH) due to pulmonary hypoplasia[1]. Since the overall outcome and prognosis are highly variable, the management plan is not uniform in all cases[5].

Many indices were described for preoperative evaluation for CDH cases, such as ventilator index (VI) and modified ventilator index (MVI). There are a few literature studies that described the use of these indices for outcome expectations in CDH patients[6–8].

The severity of hypoxemic respiratory failure is estimated and calculated by oxygenation index (OI). The best OI in the first 48 h of life in CDH cases has been shown to predict survival. However, the use of the best OI is not an actual reflection of the severity of the condition. OI is defined as a marker for cardiopulmonary function and is considered the best indicator of morbidity and mortality currently used[9]. Many other indices were included, but the best is not yet determined[9]. We aimed to settle some selection criteria that help in selecting CDH cases for thoracoscopic repair (TR) with favorable outcomes that help the pediatric surgeons in limited resource centers plus

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evaluate the usage of oxygenation, ventilation, and other indices as predictors for postoperative mortality rate.

PATIENTS AND METHODS:

This retrospective study was conducted on children presented with Bochdalek congenital diaphragmatic hernia in the first week of life to the level III Pediatric Surgery Unit in Tanta University Hospital and Qena University Hospital from January 2016 to June 2023. The internal review board approved the study (IRB number: SVU-MED-SUR011-4-24-7-872). We included all neonates diagnosed with CDH admitted to the neonatal intensive care unit (NICU) with the following inclusion criteria; (a) diagnosis of CDH within 24 h of delivery, (b) no associated fatal congenital abnormality and (c) ventilation before surgical repair. All infants were intubated after birth. They were initially ventilated conventionally, but some transferred to high-frequency oscillation (HFO) according to the NICU protocol. For all patients, indwelling arterial catheters were inserted, and continuous pulse oximeter monitoring on the first day of admission was set. PH in patients was clinically assessed by pre and postductal peripheral oxygen saturation (SpO_2) differences of greater than or equal to 10% is considered high PH and confirmed by echocardiograms before and after surgery to assess the degree of PH.

Preoperative ventilation respiratory rate (RR), peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), and preductal arterial oxygen tension (PaO_2). Also, arterial carbon dioxide tension ($PaCO_2$), fractional inspired oxygen concentration (FiO_2), and preductal SpO_2 were all recorded 6 h before surgery. The mean airway pressure (MAP) was calculated from PIP, PEEP values. The MAP was calculated if the conventional ventilator mode was used, from the following equation: MAP=PEEP+[(PIP–PEEP)/3]. If the high-frequency oscillatory ventilator mode was applied, the MAP of the actual ventilator setting was used directly.

Preoperative OI and VI indices are predictors of physiological stability achieved, denoting progression from birth to surgery. These 7 indices were calculated in all patients who were subjected to thoracoscopic CDH repair. Values are measured 6 h before surgery according to the following equations:

(a) VI=RR X (PIP – PEEP).

(b) MVI=(RR x PIP X $PaCO_2$) / 1000.

(c) Respiratory severity score (RSS)=MAP×FiO_2.

(d) OI=(MAP X FiO_2 X 100) / PaO_2.

(e) OSI: substitutes PaO_2 with oxygen saturation as measured by pulse oximetry (SpO_2) in the OI equation mentioned before and is calculated as:

$OSI = MAP \times FIO_2 \times 100 / SpO_2$

(f) OVI=(PaO_2/FiO_2) – $PaCO_2$.

(g) PaO_2/FiO_2 (P/F) ratio.

All cases included in this series have been repaired by TR, and patients were followed until discharge and divided according to the outcome into two groups: group (A) survivors and group (B) of nonsurvivors. Total numbers and results are used for statistical analysis using ROC analysis. sensitivity/ specificity model plus positive and negative predictive values were calculated. Logistic regression analysis was used to test the correlation of each of these indices in relation to each other as a mortality predictor and as an isolated predictive parameter.

RESULTS:

A total of 77 neonates were diagnosed with CDH and admitted to the NICU during the study period; 61 of them were diagnosed prenatally without any need for prenatal therapy. Out of 59, 44 male and 15 female cases were included in the analysis. The rest of the cases were not ventilated before surgical repair, associated with a fatal congenital malformation, or cases with a birth weight less than 2.5 kg not suitable for thoracoscopy, so they were excluded. The patients were divided into two groups; group A: survivors 47 (79.7%). Group B: nonsurvivor 12 (20.3%). We had 43 cases with type B defects, 12 cases with type A defects, and four cases with type C defect. Most cases were type B and A defects so primary repair was applicable. We needed mesh repair in only two cases with large defects that could not be repaired by primary suturing. The demographic data of all cases repaired by the thoracoscopic approach was depicted in (Table 1). No statistical difference was found in any of these data except for the length of hospital stay which is less in the nonsurvivor group.

Pre-operative mean and range values of RR, PIP, PEEP, PaO_2, $PaCO_2$, FiO_2, and SpO_2 were recorded 6 h before surgery. The MAP was calculated from PIP and PEEP values before surgery, as shown in (Table 2). All cases were started on conventional mechanical ventilation initially, but seven cases needed HFO; three before TR, and four after surgical repair.

The seven OI and VI used in this study were calculated in all patients who underwent thoracoscopic CDH repair. Preoperative mean and range values are measured 6 h before surgery in both survivors and nonsurvivors and are represented in (Table 3). All cases that died (nonsurvivor group) postoperatively had higher mean values of all indices that were statistically significant in addition to higher pulmonary pressure values on echocardiography.

We used multivariate analysis to study the effect of more than one variable as VI, MVI, RSS, OI, OSI, OVI, P/F R, and PH in correlation to each other and mortality. The results of the multivariate analysis showed a significant correlation between VI, OI, OSI, PH., and mortality, as all dead cases had a high VI (more than 500), OI (more than 10), OSI (more than 10) and moderate to severe PH (more than 45 mmHg). The mean of the results of these parameters is depicted in (Table 4). Higher VI, OI, OSI, and PH associate higher odds of death with significant values, where odds ratios were = 5.062, 51.329, 402.104, and 4.235, respectively. Ninety-five % confidence interval: 1.995–12.845, 17.430–151.158, 77.929–2074.793, and 1.652–10.860, respectively, with a statistically significant *P value* of less than 0.001* using logistic regression analysis.

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The results of the total analysis of the different parameters were used to determine which baby has a higher survival possibility and which is likely not. This indicates salvageable cases using the previously described indices that were shown in (Table 5), where the sensitivity, specificity, positive predictive value, and negative predictive value to predict survivors and non-survivors were presented. The former data with the related ROC curve confirmed these results as shown and clarified in the curve with (Table 5). Our results showed that VI, OI, OSI, and PH were associated with higher accuracy with values of 96.38, 91.38, 97.76, and 93.32% respectively, with the highest accuracy with VI and OSI.

Table 1: Demographic data, ventilator days, and operation day poststabilization

	Survivors	Nonsurvivors	T test	*P* value
Gestational age at delivery (weeks)				
Range	35–40	34–39	0.478	0.630
Mean±SD	38.61±3.86	37.77±9.3		
Birth weight (g)				
Range	2650–3300	2500–3100	0.541	0.595
Mean±SD	3018±715	2,898.33±581.85		
Length of hospital stay (days)				
Range	10–45	12–17	1.586	0.118
Mean±SD	14.43±10.66	9.25±7.18		
Ventilator days				
Range	4–25	6–15	0.981	0.334
Mean±SD	9.43±10.66	6.25±7.18		
Operation day poststabilization				
Range	3–9	5–8	2.643	0.011*
Mean±SD	2.84±1.52	4.35±2.56		

*: significant result.

Table 2: Preoperative mean and range values of ventilation and oxygenation parameters

	Survivors	Nonsurvivors	*T* test	*P* value
PIP (Cm/H_2O)				
Range	18–24	20–28	4.119	0.001*
Mean±SD	20.63±2.45	24.00±2.83		
PEEP (Cm/H_2O)				
Range	5–7	5–9	3.269	0.001*
Mean±SD	5.75±0.71	6.50±0.71		

RR (Cycle/min)				
Range	25–35	30–44	7.549	0.001*
Mean±SD	31.63±3.29	39.00±1.41		
$PaCO_2$ (mmHg)				
Range	30–62	49–70	10.849	0.001*
Mean±SD	46.83±3.49	59.63±4.25		
PaO_2 (mmHg)				
Range	75–120	55–80	13.776	0.001*
Mean±SD	90.63±6.93	61.63±4.29		
MAP (Cm/H_2O)				
Range	7–14	12–22	11.558	0.001*
Mean±SD	10.83±2.05	18.22±1.63		
FiO_2%				
Range	20–80	70–100	17.131	0.001*
Mean±SD	43.72±4.89	69.80±3.85		
SpO_2%				
Range	25–35	30–44	7.549	0.001*
Mean±SD	31.63±3.29	39.00±1.41		

FiO_2, fractional inspired oxygen concentration; MAP, mean airway pressure; $PaCO_2$, arterial carbon dioxide tension; PaO_2, preductal arterial oxygen tension; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; RR, respiratory rate; SpO_2, pre-ductal peripheral oxygen saturation.
*: significant result.

Table 3: Oxygenation and ventilation indices and pulmonary pressure values

	Survivors	Nonsurvivors	T test	*P* value
VI				
Range	325–630	520–608	2.338	0.023*
Mean±SD	474.75±114.01	564.00±132.94		
MVI				
Range	20–64	42–84	0.749	0.456
Mean±SD	47.85±74.01	64.07±13.87		
RSS				
Range	5–17	12–22	1.312	0.194
Mean±SD	14.925±3.00	17.22±3.54		
OI				
Range	4–10	12–20	9.980	0.001*
Mean±SD	7.95±2.01	15.67±3.57		
OSI				
Range	3–9	12–18	7.279	0.001*
Mean±SD	6.95±3.11	14.65±3.86		
OVI				
Range	−27 – −40	−39 – −49	1.208	0.232
Mean±SD	−37.6±29.2	−48.2 ±15.9		
P/F R				
Range	250–410	170–380	1.568	0.102
Mean±SD	315.95±53.91	284.75±43.66		

PH (mmHg)				
Range	20–40	45–65	19.718	0.001*
Mean±SD	26.55±3.77	51.22±4.25		

MVI, Modified ventilator index; OI, Oxygenation index; OSI, Oxygenation saturation index; OVI, Oxygenation ventilation index; P/F R, PaO_2/FiO_2 ratio; PH, pulmonary hypertension; RSS, Respiratory severity score; VI, Ventilatory index.
*: significant result.

Table 4: Correlative multivariate analysis of the seven respiratory indices and pulmonary hypertension with mortality

	Chi-Square				
Mortality	X^2	*P* value	Odds Ratio	95% CI	*P* value
VI	13.000	< 0.001*	5.062	1.995–12.845	< 0.001*
MVI	0.051	0.821	1.086	0.530–2.227	0.821
RSS	3.170	0.075	1.672	0.820–3.408	0.157
OI	105.88	< 0.001*	51.329	17.430–151.158	< 0.001*
OSI	137.34	< 0.001*	402.104	77.929–2074.793	< 0.001*
OVI	3.020	0.082	1.968	0.912–4.245	0.085
P/F R	2.638	0.104	1.805	0.882–3.694	0.106
PH	17.000	0.002*	4.235	1.652–10.860	< 0.001*

MVI, Modified ventilator index; OI, Oxygenation index; OSI, Oxygenation saturation index; OVI, Oxygenation ventilation index; P/F R, PaO_2/FiO_2 ratio; PH, pulmonary hypertension. RSS, Respiratory severity score; VI, Ventilatory index.
*: significant result using logistic regression analysis (significant *P<0.05*).

Table 5: Accuracy of oxygenation, ventilation indices, and pulmonary pressure values

	Chi-Square						
	X^2	*P*-value	Sens.	Spec.	PPV	NPV	Accuracy %
VI	13.000	< 0.001*	94.33	93.00	95.25	94.55	96.38
MVI	0.051	0.821	90.00	70.00	82.23	77.23	79.23
RSS	3.170	0.075	90.00	32.00	67.92	66.67	67.69
OI	105.88	< 0.001*	96.25	94.00	96.25	94.00	91.38
OSI	137.34	< 0.001*	96.87	94.44	96.28	93.51	97.76
OVI	3.020	0.082	76.25	38.00	66.30	50.00	61.54
P/F R	2.638	0.104	62.50	52.00	67.57	46.43	58.46
PH	17.000	0.002*	93.45	92.44	93.85	91.76	93.32

MVI, modified ventilator index; OI, oxygenation index; OSI, oxygenation saturation index; OVI, oxygenation ventilation index; P/F R, PaO_2/FiO_2 ratio; PH, pulmonary hypertension; RSS, respiratory severity score; VI, ventilatory index.
*: significant result.

DISCUSSION

To our knowledge, this is the first study that evaluates the different OI and VI and correlates them to the postoperative survival rate following TR of CDH. In our study, we calculated all these indices 6 h before thoracoscopy. The parameters and values of indices selected were based on authors' experience from the former data in our institution and literature data.

VI index is easy in the calculation using simple ventilation parameters, which are PIP, PEEP, and RR. There was a significant correlation between VI and survival as all cases that survived had a lower VI of less than 500. Higher VI was associated with statistically a significant positive correlation with mortality and a higher accuracy of 96.38%. Paret *et al*., concluded that the VI provides a reliable prognostic marker for bad outcomes and mortality studies where VI had a specificity with a positive predictive value of greater than 90% on days 3–9[10].

There are few literature studies that describe the use of MVI in the evaluation of pediatric surgical patients. Both Numanoglu *et al*., and Oliver *et al*., reported that the survival rate was 91% if the MVI score was less than 40 in patients with CDH[6,11], which goes in agreement with our results. Içe and colleagues found that if the MVI score was under 40, the survival rate was 100%, contrary to the MVI score value of greater than 80, where all patients died. In their study, a significant difference between the early

and late scores was reported between the survivors and nonsurvivors. They concluded that MVI is a good prognostic parameter in CDH patients[12].

In RSS, PaO_2 measurements were not needed. Arterial lines are required for the monitoring of PaO_2 in other indices, such as OI, and hence complications may be reported, including thrombosis, infection, and anemia, following frequent blood sampling. When using the RSS, there is no need to do frequent blood sampling, so the risk of sepsis is minimized. Del Vecchio *et al*., suggested that RSS as a respiratory index can be used which is a less invasive intensive care parameter, especially for NICU infants[13]. Ahn and colleagues concluded that the highest RSS value measured within 24 h after birth is correlated to the prognosis of CDH. The advantage of RSS as an index is that it can be calculated from the ventilator setting without invasive tools. Therefore, the RSS as a prognostic predictor is simple and helpful in the management plan of CDH cases[14].

OI is a simple tool using ventilation and oxygenation parameters (MAP, FiO_2, PaO_2). The results of this study showed a significant correlation between OI and morality, as all cases that survived had a lower OI of less than 10. Higher OI values were associated with significantly higher odds of death. Also, a statistically significant positive correlation with mortality and higher accuracy was reported being 91.38%. In Bruns and colleagues the highest OI in the first 48 h of life shows a significant correlation with fatality in cases with isolated left-sided CDH in agreement with our current results. It provides a better correlation with length of stay than prenatal MRI indices. They concluded that OI may be a useful tool added to US and MRI indices to predict survival[15]. Abman and colleagues demonstrated inaccuracy in the calculation of OI due to the frequency of arterial blood gases. This former point may have resulted in a lower number of estimated values so that the true OI could be underestimated. The same holds true for the MAPs that were reported by respiratory therapists at intervals and are only accurate as charting is completed. They observed that OI plays a pivotal role in the clinical decision-making for CDH management[16]. Ghazal *et al*. stated that cases with an OI lower than 6 or an MVI less than 40 can survive with conventional ventilation therapy, with 98 and 96% accuracy, respectively. But when OI was greater than 17.5 or MVI more than 80, the expected rate of death is almost 100% in all cases with conventional ventilation therapy. Therefore, all these babies have a degree of lung hypoplasia, which is incompatible with postnatal life. These infants are unlikely to benefit from therapies used for PH. Cases with less severe values may have significant PH and moderate pulmonary hypoplasia may benefit from using conventional ventilation therapies[17]. Tan *et al*., reported that OI is of high importance in predicting survival based on the best OI on the first day of life or mean OI on the first day of life. They found that serial measurements could play a role in detecting the optimal timing for surgery[18].

OSI is more easily calculated using oxygen saturation measured by pulse oximetry (SpO_2) instead of the need for arterial line and blood gas evaluation. We found a significant correlation between OSI and morality, as all cases that died where OSI was more than 10. Higher OSI was associated with expected significantly higher odds of death. It also denotes a statistically significant positive correlation with mortality and higher accuracy; 97.76%. Hemananda and colleagues used OSI as an indicator of respiratory failure as well as lung injury. OSI can be calculated easily at the bedside, without the need for invasive blood sampling. The current study showed a strong correlation of OI with OSI values of 5–25. Additionally, OI derived from a noninvasive source, such as OSI, is useful to estimate the severity of respiratory failure and response to therapy[19]. Katherine D. *et al*., measured OSI as well as the OI as a predictor of clinical outcomes, OSI was simple to calculate and offered more prognostic information than traditional indicators of severity such as PaO_2/FiO_2 ratio plus avoiding invasive arterial blood gas monitoring[20].

When estimating multiple indices; the OI is a powerful tool to use because the value of PaO_2 is adjusted by both FiO_2 and MAP. $PaCO_2$ values are affected by either respiratory rate or peak inspiratory pressure under conventional ventilation. Also, it is affected by frequency and MAP under HFO ventilation. Since the values under the two different ventilator settings (conventional ventilation and HFO) are different, it is difficult to correct or adjust $PaCO_2$ by the appropriate values. Also using the PaCO2 arises from the timing of the blood sampling[21–24].

The effect of pulmonary pressure and post-thoracoscopy mortality studied here showed that there is a significant correlation between PH and morality, as all cases that died had high pulmonary pressure of more than 45 mm/Hg. Higher values were associated with significantly higher odds of death with a statistically significant P value and significant positive correlation with mortality, as well as higher accuracy; 93.32%. In two literature studies[25,26], the authors found that infants who had persistent pulmonary hypertension, had an increased risk of mortality than infants with a mild degree of PH which goes in agreement with our findings. Our study provides some evidence for the use of well-selected indices as prognostic aids for thoracoscopic CDH repair added to the known standard clinical parameters used by pediatric surgeons.

CONCLUSION

TR of Bochdalek CDH is feasible and safe. Our results showed that Ventilation Index (VI) less than 500, Oxygenation Index (OI) lower than 10, OSI below 10 and PH under 40 mm/Hg can be used as selection parameters for expecting excellent outcomes following thoracoscopic CDH repair. We proposed an algorithm for the management of Bochdalek CDH thoracoscopically based on standard parameters in addition to our newly selected parameters as depicted in (Fig. 1).

The current results and the proposed parameters of this study need to be validated on a wider scale by a larger series including more numbers of patients. Also, we start applying these data and algorithms in a prospective way following this study.

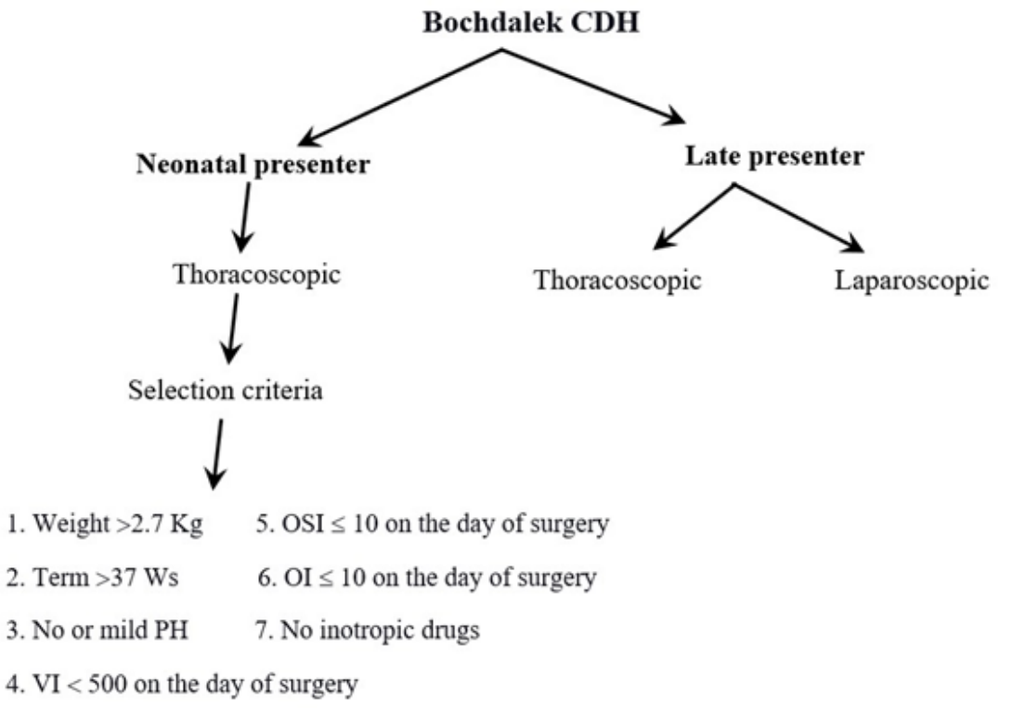

Fig. 1: Graph based on our results from this study we proposed an algorithm for management of bochdalek congenital diaphragmatic hernia thoracoscopically or laparoscopically in early and late presenters with selection to cases undergo thoracoscopy with favourable outcomes.

CONFLICT OF INTEREST

There are no conflicts of interest.

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