

## **The effect of surgery on lung volume and conventional monitoring parameters in ventilated newborn infants**

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**Running head title:** FRC measurements in ventilated newborns following surgery

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**Abstract:**

In newborn infants, thoraco-abdominal surgery is a serious intervention with respect to gas exchange and lung mechanics. This prospective clinical study compared surgery-induced changes in functional residual capacity (FRC) and ventilation homogeneity indices (VI) with changes in conventional monitoring parameters.

**Methods:** Of 29 ventilated newborns (mean weight  $2770 \pm 864$ g at surgery), 13, 9 and 7 underwent thoracic, abdominal or congenital diaphragmatic hernia (CDH) surgery, respectively. The multiple breath washout technique (MBWO) using heptafluoropropane (HFP) as tracer gas (Babylog 8000, Fa. Dräger) was performed <6 h before surgery, 22-24 h after surgery and <6 h before extubation. Gas exchange, respiratory mechanics, FRC and VI index data were recorded.

**Results:** Thoraco-abdominal surgery resulted in changes to FRC and VI indices in a procedure-specific manner, however, these changes were not reflected in conventional mechanical or ventilatory monitoring parameters. FRC decreased in non-CDH infants, while FRC increased and VI decreased in CDH infants. Despite improvements, the differences in FRC and VI indices between CDH and non-CDH infants indicated persistent impaired lung function in the former.

**Conclusion:** MBWO can be advantageously used to measure the effect of surgery on the lung. While FRC and VI indices changed following surgery, conventional monitoring parameters did not.

## Abbreviations

AMDN <sub>1</sub>	Alveolar mean dilution number 1
AMDN <sub>2</sub>	Alveolar mean dilution number 2
C <sub>resp</sub>	Respiratory Compliance
ET	Endotracheal tube
f	Respiratory rate
FiO <sub>2</sub>	Fraction of inspired oxygen
FRC	Functional residual capacity
HFP	Heptafluoropropane
ICU	Intensive care unit (for newborn infants)
LCI	Lung clearance index
MBWO	Multiple breath washout
M <sub>1</sub> /M <sub>0</sub>	First-to-zeroth moment ratio
M <sub>2</sub> /M <sub>0</sub>	Second-to-zeroth moment ratio
PaCO <sub>2</sub>	Arterial partial pressure of carbon dioxide
PaO <sub>2</sub>	Arterial partial pressure of oxygen
PEEP	Positive end-expiratory pressure
PIP	Peak inflation pressure
V <sub>D</sub>	Deadspace volume
V <sub>Dapp</sub>	Apparatus deadspace volume
V <sub>T</sub>	Tidal volume

## **Introduction**

Survival in newborn infants following corrective surgery for serious cardiac [1, 2] or abdominal wall defects [3] or for congenital diaphragmatic hernia (CDH) [4] has improved over the last decade. Nevertheless, opening the thoracic cavity and/or abdominal wall remains a significant intervention with respect to temporary alterations in gas exchange and lung volume.

In addition to ventilator monitoring, blood gas analyses and repeated x-rays are usually performed in ventilated infants to monitor clinical development. Meanwhile, commercial equipment is available to assess lung aeration by measuring functional residual capacity (FRC) and ventilatory inhomogeneity (VI) [5-7]. This non-invasive method is based on the multiple breath washout (MBWO) measurement technique using a tracer gas [8]. However, the equipment used for simultaneously measuring airflow and molar mass of the breathing gas is generally bulky and cumbersome for routine applications in intubated newborns or premature infants, and requires significant floor space [9]. We have recently validated a prototype of an extended neonatal ventilator for MBWO analysis in small ventilated piglets [10]. This apparatus uses a miniaturized lightweight gas sensor and heptafluoropropane (HPF) as the tracer gas.

We hypothesized that this technique can be advantageously used in a clinical setting to measure the effect of surgery on the lung. The aim of the present prospective clinical study was the use of the HPF-MBWO technique to investigate the effect of thoraco-abdominal surgery on the lung, and to compare the changes in FRC and VI indices with the changes in conventional monitoring parameters.

## **Materials and Methods:**

### *Patient characteristics*

This prospective clinical study was performed in the ICU of the Clinic of Neonatology, Charité Universitätsmedizin Berlin, Campus Mitte. Sixty-two newborn infants born between November 2006 and June 2008 and requiring surgery were potentially eligible for the study. The inclusion criteria were anticipated surgery and written parental consent. Due to the equipment apparatus dead space ( $V_{Dapp}$ ) of 4.5 mL, only infants with a tidal volume ( $V_T$ ) > 10 mL as measured after intubation by the Babylog 8000 (Fa. Dräger, Lübeck, Germany) were included. Thirty-three infants were excluded due to no requirement for mechanical ventilation after surgery (10 infants), measurements not able to be performed according to the protocol (11 infants), a  $V_T < 10$  mL (7 infants), or parents refusing to give consent (5 infants).

The remaining 29 infants were divided in three groups according to the field of surgery: 13 infants had thoracic operations (congenital heart disease or esophageal atresia), 9 infants had abdominal surgery (gastroschisis, omphalocele or volvulus) and 7 infants had CDH where both cavities were opened.

The study was approved by the Ethical Committee of the Charité Universitätsmedizin Berlin.

### *Equipment for FRC measurement*

FRC was measured using a modified Babylog (BL) 8000. Briefly, a previously described infrared HFP sensor [10] was placed between the flow sensor of the BL 8000 and the endotracheal tube (ET). The constant flow of the ventilator ranged from 8-16 L/min depending on the ventilatory pressure required. Using a mechanical valve, HFP (medical grade HFP, Solvay, Hannover Germany) from a gas cylinder was fed into the inspiratory limb of the ventilatory circuit to achieve a constant HFP concentration of 0.8%. FRC was

calculated according to the MBWO technique using the flow signal (flow sensor, BL 8000) and the concentration signal (HFP sensor) by a software developed by Fa. Dräger. The lung clearance index (LCI) was calculated as the number of turnovers required to lower the end tidal tracer gas concentration to  $1/40^{\text{th}}$  of the starting concentration. The first three moments ( $M_0$ ,  $M_1$ ,  $M_2$ ) of the washout curve and moment ratios ( $M_1/M_0$ ,  $M_2/M_0$ ) and the alveolar mean dilution numbers ( $AMDN_1$ ,  $AMDN_2$ ) were derived from calculations that commenced at the  $0^{\text{th}}$  breathing cycle and ended if concentrations fell below  $1/40^{\text{th}}$  of the initial concentration. All VI indices were calculated by purpose-built software using the data of the BL 8000 as described recently [11]. The time delay between flow sensor signal and HFP concentration was compensated for electronically. The sample rate was 125 Hz and all signals were stored.

FRC measurements were commenced manually and stopped automatically after N cycles when the amount of ventilated alveolar air  $(V_T - V_D) \cdot N$  exceeded the calculated FRC by a factor of ten. In each case, the minimum number of cycles was set at  $N=40$ .  $V_D$  was calculated from the HFP signal by the Draeger software using the Bohr equation. An electronic two-point calibration of the HFP sensor using internal light signals and a one-point flow sensor calibration of the BL 8000 as recommended by the manufacturer was performed prior to every FRC measurement, and the equipment was also checked using a lung model before each measurement [10].

### *Protocol*

All measurements were performed with the patient in a supine position at three defined time points: within 6 h before surgery, 22-24 h after surgery, and within 6 h prior to extubation.

The study protocol did not specify any ventilatory parameters, except that the mode had to be conventional or synchronized Intermittent Mandatory Ventilation (no High Frequency

Ventilation). Ventilation and  $\text{FiO}_2$  were adjusted aiming for a  $\text{paCO}_2$  between 35 and 55 torr [4.67-7.33 kPa] and normoxia according to clinical diagnoses (e.g., cyanotic heart failure). For each FRC measurement respiratory rate ( $f$ ), tidal volume ( $V_T$ ), ET leakage and respiratory compliance ( $C_{\text{resp}}$ ), which was calculated by linear regression analysis, were taken from the BL 8000.

Beside MBWO parameters (FRC, LCI,  $M_1/M_0$ ,  $M_2/M_0$ ,  $\text{AMDN}_1$ ,  $\text{AMDN}_2$ ), ventilatory pressures (PIP, PEEP) and blood gases were recorded. Additionally,  $\text{FiO}_2$ ,  $\text{PaO}_2/\text{FiO}_2$ ,  $\text{paCO}_2$ ,  $\text{SaO}_2$ , blood pressure and heart rate (M1166A; Philips Medical Healthcare, Hamburg, Germany) were recorded at each of the three scheduled time points for evaluation of circulatory parameters following surgery. Data obtained from patient charts included gestational age, birth weight, sex, multiple births, prenatal administration of steroids, mode of delivery and APGAR scores at 1 and 5 minutes.

FRC measurements were performed identically at each of the three scheduled time points. After preparation and calibration of the equipment with identical adjustment of the modified BL 8000, the ET of the infant was clamped to avoid FRC destabilization. Within 5 seconds the modified BL 8000 was connected and a stabilization period of 15 minutes was allowed with continuing mechanical ventilation. Arterial blood samples for blood gases (ABL 800Flex, Radiometer Medical ApS; Bronshoj, Denmark) were then taken and FRC measurements were commenced with an HFP washin procedure ( $\text{FRC}_{\text{washin}}$ ) and a consecutive washout procedure ( $\text{FRC}_{\text{washout}}$ ). Such a cycle was accepted for evaluation and a mean value of  $\text{FRC}_{\text{washin}}$  and  $\text{FRC}_{\text{washout}}$  was calculated if the deviation between  $\text{FRC}_{\text{washin}}$  and  $\text{FRC}_{\text{washout}}$  was lower than 20% and the  $V_T$  was higher than 10 mL due to the increased  $V_{\text{Dapp}}$ . All lung function measurements were repeated three times for each of the three situations.

### *Statistics*

CDH is a too rare diagnosis (approx. 1:3.500 births) for a sample size calculation. A sample size of 22 was calculated only for non-CDH infants as being required to detect a FRC difference of 2 ml/kg after surgery, assuming an SD of the FRC differences (based on a pilot study) of 3.8 ml/kg and an alpha error of 0.05 and a beta error of 0.1.

Patient characteristics between the patient groups were compared using chi-square tests and ANOVA, as appropriate. Apgar scores, age at time of surgery and duration of intubation and surgery are expressed as median and range and were compared using Kruskal-Wallis tests. All physiological parameters are presented as means (SDs) in tables and means with 95% CIs in figures. Differences between patient groups were tested using ANOVA with Student-Newman-Keuls post hoc test. ANOVA for repeated measurements with Dunnett's post hoc test (comparison with base line) was used to analyze parameter development. Bonferroni correction of the p-value for multiple within- and between group comparisons was used. Statistical analysis was performed using Statgraphics Centurion software (Version 15.0, Statpoint Inc., Herndon, Virginia, USA) and GraphPad PRISM (Vers. 4. San Diego, California, USA). Statistical significance was defined as a p value <0.05.



## **Results**

### *Subjects*

The three patient groups (i.e., thoracic, abdominal and CDH surgery) were similar in terms of preoperative patient characteristics (Table 1). Only 4/29 (13.8%) infants had received prenatal steroids, while 2/29 (6.9%) had undergone surfactant treatment. While the mean body weights were similar for all three groups there was a wide scatter in the time of surgery without statistically significant differences in the median after Bonferroni correction (Table 2).

### *Ventilatory parameters, blood gases and circulatory parameters*

The between group comparison showed that before and after surgery ventilatory parameters (PIP, PEEP, f,  $V_T$ , oxygenation index and ventilatory efficacy index), blood gas parameters ( $paO_2/F_iO_2$ ,  $paCO_2$ ,  $SaO_2$ ) and circulatory parameters (heart rate, systolic and diastolic blood pressure) were not statistically significant different between the three patient groups. Only in CDH infants compared with the other two patient groups f was significantly higher ( $p < 0.001$ ) before surgery and  $V_T$  significantly lower ( $p < 0.001$ ) before as well as after surgery.

The within-group comparison showed in all three patient groups no statistically significant effect of surgery on ventilatory, blood gas and circulatory parameters, respectively.

### *Effect of surgery on lung function*

The preoperative  $C_{resp}$  and FRC for each patient group are shown in Fig. 1. In CDH infants, both parameters were lower while there were no significant differences between thoracic and abdominal surgery infants. Most preoperative VI indices were higher in the

CDH infants, whereas there were no significant differences between the other two patient groups (Fig. 2).

The development of lung function after surgery differed between patient groups (Table 3). There were distinct differences in parameter progression between thoracic, abdominal and CDH surgery infants. Thoracic surgery resulted in changes in FRC, LCI and moment ratios, while  $C_{resp}$  remained nearly constant. At 24 h after thoracic surgery, FRC was lower and ventilatory VI indices, LCI and  $M_1/M_0$  were higher ( $p<0.05$ ). Before extubation, all pulmonary parameters returned to baseline values except for FRC, which remained elevated ( $p<0.001$ ).

At 24 h after abdominal surgery, FRC was lower, but recovered to baseline by the time of extubation.  $C_{resp}$  also decreased after abdominal surgery, but only marginally. However, prior to extubation,  $C_{resp}$  exceeded the baseline ( $p<0.001$ ). No significant differences were observed in the VI indices.

Parameter development differed between CDH and non-CDH infants. Besides  $C_{resp}$ , there was an improvement in all pulmonary parameters after surgery. Compared to baseline, FRC increased ( $p<0.01$ ) and all VI indices (LCI,  $M_1/M_0$ ,  $M_2/M_0$ ,  $AMDN_1$ ,  $AMDN_2$ ) decreased ( $p<0.05$ ).

$C_{resp}$  and FRC were compared between patient groups prior to extubation (Fig. 3). There were no significant differences in the infants following thoracic or abdominal surgery. However, despite the trend of increased  $C_{resp}$  and improvement in FRC in CDH patients, both parameters remained lower compared to the other patient groups. At extubation, there were no significant differences in VI indices between the three patient groups.

## Discussion

The study has shown that HFP-MBWO is a suitable technique to measure the effect of surgery on the lung. The main finding was that FRC and VI indices measured during mechanical ventilation were more affected by surgery than conventional monitoring parameters. Furthermore, the effect on FRC and VI indices was procedure-specific.

The three patient groups were similar with regard to clinical characteristics (Table 1 and 2). The wide scatter in the age of the infants undergoing thoracic and abdominal surgery reflected the diagnosis and the clinical requirements, whereas all CDH infants underwent surgery on the 2<sup>nd</sup> postnatal day based on our standard protocol.

Before surgery, lung function measurements were similar for the infants requiring abdominal or thoracic surgery, probably because the lung was only indirectly affected. In contrast, CDH infants with impaired prenatal lung development [12] had lower FRC and  $C_{resp}$  and higher VI indices, indicating impaired ventilation homogeneity. Although lungs in infants requiring abdominal or thoracic surgery are thought likely to be normal, we found both groups had relatively low FRC values ( $16.38 \pm 4.0$  and  $17.12 \pm 3.9$  mL/kg, respectively). These observations may be explained by the findings of Ungern-Sternberg et al. [8] in a study of 14 anesthetized young infants (2.76–7.5 kg; age 0-6 months) that demonstrated that neuromuscular blockade led to a decrease in FRC from  $21.3 \pm 4.7$  mL/kg to  $12.2 \pm 4.8$  mL/kg, which could be restored by additional PEEP of 3 cmH<sub>2</sub>O. In our study, PEEP was applied prior to neuromuscular blockade and not changed, and FRC measurements prior to and 24 h after surgery were performed under neuromuscular blockade.

We found that the effect of surgery on lung function measurements was procedure-specific. Within 24 h after surgery, FRC decreased in infants who underwent thoracic or abdominal surgery, VI indices increased in infants who underwent thoracic surgery, while FRC and VI indices improved in CDH infants (Table 4). Few studies on respiratory mechanics in newborn infants measured parameters both pre- [13] and post operatively

[14, 15]. Dimitriou et al. [16] demonstrated in infants with abdominal wall defects that primary closure and surgical repositioning of the herniated viscera into the abdomen was associated with deterioration of  $C_{\text{resp}}$ . Since this observed effect was only temporary, they interpreted the decrease in  $C_{\text{resp}}$  with an increase in intra-abdominal pressure. While it appeared the same  $C_{\text{resp}}$  trend was observed in the abdominal surgery infants in our study, the findings did not reach statistical significance.

The differences in lung function measurements between CDH and non-CDH infants were not the result of any differences in volume load, duration of operation or anesthesia, which were similar for all three patient groups (Table 2). Dinger et al. [17] demonstrated in 5 patients with congenital CDH that FRC increased over time depending on PEEP and suctioning of the chest tube. The present FRC and  $C_{\text{resp}}$  data are similar to those reported by Dinger et al, however we did not change the PEEP after surgery and chest tubes are not routinely inserted due to side-effects [4]. Dinger et al. [17] explained the increase in FRC in CDH infants after surgery as an over distension of hypoplastic lungs. However, Fehrenbach et al. [18] and Weibel [19] described lung growth following pneumonectomy in adult mice as an effect of neoalveolarization. Which of these effects is responsible for the FRC gain in our CDH infants following surgical repair remains unknown and warrants further study.

At the time of extubation, the differences in lung function measurements between CDH and non-CDH infants had reduced, yet remained. The observed faster increase in FRC compared to  $C_{\text{resp}}$  in CDH infants agrees with a recent study by Roehr et al. [20] showing that despite apparently well-inflated lungs, CDH patients had worse tidal breathing parameters and lower  $C_{\text{resp}}$  after discharge compared to non-CDH patients. Thoracic and abdominal surgery infants had similar FRCs at extubation ( $19.04 \pm 6.0$  and  $18.88 \pm 4.0$  mL/kg, respectively). Although all infants were successfully extubated and the neuromuscular blockade was removed, the FRC values were slightly lower than that

reported by Ungern-Sternberg et al. [8] in intubated infants prior to anesthetic procedures ( $21.3 \pm 4.7$  mL/kg). However, the infants in the present study were younger and lighter than those in the Ungern-Sternberg et al. study, and the present FRC values are consistent with those for ventilated preterm infants [21, 22] and non-ventilated full term control infants (18.4 mL/kg) [23].

Performing MBWO techniques in ventilated infants is difficult because the measurements are susceptible to any ET leakage [24, 25]. While this problem can be easily overcome in ventilated older patients by using cuffed ETs (Ungern-Sternberg et al. [8]), uncuffed ETs are advised in neonates both to protect airways and to avoid subglottic stenosis [26]. In our study we could exclude a substantial effect of ET leakage on FRC measurements. During measurement we tried to avoid any ET leakage, if necessary the head position was changed. In a previous *in-vitro* study we found that the absolute value of the relative FRC error was <3% for ET leakages <20% and 6% for ET leakages < 40%. In our study the ET leakage was <20% in 95% of all infants and ET leakages of 40% were never exceeded.

Tracer gas MBWO characteristics (e.g.,  $V_{Dapp}$ , gas-sensors used, properties of tracer gases and number of evaluated breathing cycles during tracer gas washin and washout) are also highly method-dependent. Most MBWO measurements in ventilated newborns are performed using custom-made equipment and nitrogen [27], helium [28] or SF<sub>6</sub> [7] as tracer gases. The commercial system for MBWO in ventilated patients [9] used by Ungern-Sternberg et al. [8] is based on ultrasound spirometry with SF<sub>6</sub> as the tracer gas. That equipment has a high  $V_{Dapp}$  and a bulky and heavy measuring head, and its use was shown to be feasible predominantly in ventilated older infants or preschool children aged from 13 months to 7 years [29-31]. By comparison, our HFP measuring head was designed for use in small lungs and is smaller and lighter. While HFP and SF<sub>6</sub> are both inert gases, the former has a higher molecular weight (170.03 vs. 146.05 g/mol), water

solubility (0.23 vs. 0.04561 g/L) and specific (air=1) gravity (5.9 vs. 5.114) and a lower vapor pressure (4 vs. 21.5 bar). Furthermore, tracer gas concentrations are lower for HFP compared to SF<sub>6</sub> (0.8 vs. 4% [9, 32]). We recently investigated the in-vitro accuracy of HFP-MBWO in ventilated piglets [10] and found that it allowed for reproducible measurements of FRC and VI indices, and no relevant accumulation of HFP was observed [33].

The present study found that HFP-MBWO was a valuable tool for monitoring the effect of surgery on lung function. A limitation of the study was the relatively low number of patients in each treatment group, which may have limited the statistical power for comparing differences in lung function and increased the risk of the type II error. The calculated sample size was only reached for non-CDH infants. Secondly, the still relatively high  $V_{Dapp}$  of the combined flow and HFP sensor meant that only patients with tidal volumes greater than 10 mL could be investigated, which reduced the number of eligible patients. Hopefully, technical progress and increased efforts by the manufacturers will lead to new, lightweight mainstream sensors with a  $V_{Dapp} < 1$  mL that will enable reliable measurements even in premature infants. Thirdly, the extent to which FRC monitoring could be used to optimize ventilator settings and to realize the “open lung concept” [34] remains unknown even in these small patients.

In conclusion, the HFP-MBWO is a suitable technique to assess the effect of thoraco-abdominal surgery on the lung. The study has shown that infants with CDH have low FRC values and impaired gas mixing before surgery, improving, but not normalizing thereafter. In contrast, infants receiving thoracic surgery showed a temporary decline after surgery whereas in infants receiving abdominal surgery little variation took place. These changes were not reflected in mechanical or ventilatory variables. A prerequisite for clinical use of HFP-MBWO is that the measuring heads be miniaturized so that measurements in

premature infants are possible and that this technique is integrated into the standard monitoring of neonatal ventilators.

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H.P., O.F., S.Y. and C.C.R conducted the measurements; H.P., G.S. and R.R.W. planned and calculated the study. C.B. and P.D. were responsible for prenatal diagnosis and surgery, respectively. The paper was written by H.P. and G.S., who was responsible for statistics.

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Table 1: Patient characteristics at birth

	<b>Thoracic surgery N=13</b>	<b>Abdominal surgery N=9</b>	<b>Surgery of CDH N=7</b>	<b>p-value</b>
Birth weight (g)	2742 (1076)	2076 (855)	2695 (556)	0.224
Gestational age (weeks)	36.6 (3.5)	34.4 (4.3)	37.9 (1.6)	0.134
Inborn	9/13 (70%)	7/9 (78%)	5/7 (71%)	0.905
Boys	9/13 (69%)	3/9 (33%)	4/7 (54%)	0.248
Sectio	10/13 (77%)	8/9 (89%)	6/7 (86%)	0.847
Prenatal steroids <sup>1)</sup>	3/11 (27.3%)	0/8 (0%)	1/7 (14%)	0.265
Surfactant	1/13 (7.7%)	1/9 (11%)	0/7 (0%)	0.678
Apgar 1min	8 (2 to 10)	7 ( 2 to 9)	5 ( 1 to 9)	0.078
Apgar 5 min	9 (3 to 10)	8 (7 to 9)	7 (5 to 8)	0.149

<sup>1)</sup> Reduced total number due to missing data of admitted patients.  
Data represent mean (SD) or n (%) or median (range)

Table 2: Patient characteristics at surgery

	<b>Thoracic surgery N=13</b>	<b>Abdominal surgery N=9</b>	<b>Surgery of CDH N=7</b>	<b>p-value</b>
Body weight at time of surgery (g)	2992 (754)	2581 (997)	2680 (539)	0.462
Age at time of surgery (days)	9 (1 to 113)	2 (1 to 103)	2 (2 to 2)	0.022
Duration of surgery (min)	145 (60 to 235)	150 (45 to 540)	100 (30 to 120)	0.091
Duration of intubation (days)	10.5 (3 to 23)	9.0 (4 to 25)	8.0 (6 to 22)	0.914
Total amount of infusion within 24 h post surgery (ml)	474 (296)	593 (210)	741 (140)	0.122

Data represent mean (SD) or median (range).

Table 3: Development of pulmonary parameters after surgery for the three patient groups

	Before surgery	24h after surgery	At extubation	p-value
<b>Thoracic surgery</b>				
C <sub>resp</sub> (ml/kPa/kg)	0.46 (0.16)	0.42 (0.14)	0.46 (0.12)	p=0.541
FRC (ml/kg)	16.38 (4.0)	<b>13.89 (3.9)*</b>	<b>19.04 (6.0)*</b>	<b>p&lt;0.001</b>
LCI	9.25 (2.25)	<b>10.42 (1.79)*</b>	8.67 (2.02)	<b>p=0.001</b>
M <sub>1</sub> /M <sub>0</sub>	2.21 (0.48)	<b>2.46 (0.42)*</b>	2.07 (0.5)	<b>p=0.003</b>
M <sub>2</sub> /M <sub>0</sub>	10.61 (4.87)	<b>12.68 (4.36)*</b>	9.06 (4.86)	<b>p=0.004</b>
AMDN <sub>1</sub>	1.24 (0.3)	1.3 (0.36)	1.17 (0.21)	p=0.341
AMDN <sub>2</sub>	3.46 (2.07)	3.85 (2.82)	2.84 (1.02)	p=0.325
<b>Abdominal surgery</b>				
C <sub>resp</sub> (ml/kPa/kg)	0.46 (0.14)	0.37 (0.08)	<b>0.55 (0.16)**</b>	<b>p=0.001</b>
FRC (ml/kg)	17.12 (3.9)	<b>12.66 (4.3)*</b>	18.88 (4.0)	<b>p&lt;0.001</b>
LCI	9.7 (1.3)	10.57 (2.31)	9.07 (0.97)	p=0.177
M <sub>1</sub> /M <sub>0</sub>	2.32 (0.32)	2.46 (0.41)	2.21 (0.23)	p=0.287
M <sub>2</sub> /M <sub>0</sub>	10.87 (2.58)	12.51 (4.85)	9.95 (1.97)	p=0.285
AMDN <sub>1</sub>	1.17 (0.26)	1.28 (0.49)	1.21 (0.19)	p=0.578
AMDN <sub>2</sub>	3.34 (1.78)	3.79 (3.27)	3.01 (1.01)	p=0.646
<b>Surgery of CDH</b>				
C <sub>resp</sub> (ml/kPa/kg)	0.25 (0.10)	0.26 (0.09)	0.29 (0.09)	p=0.221
FRC (ml/kg)	8.99 (2.07)	<b>11.5 (2.92)*</b>	<b>13.7 (3.61)**</b>	<b>p&lt;0.001</b>
LCI	11.2 (1.21)	<b>9.78 (0.77)*</b>	<b>9.24 (1.08)**</b>	<b>p=0.005</b>
M <sub>1</sub> /M <sub>0</sub>	2.69 (0.36)	<b>2.34 (0.19)*</b>	<b>2.20 (0.25)**</b>	<b>p=0.006</b>

$M_2/M_0$	14.6 (3.65)	<b>11.1 (1.88)*</b>	<b>9.91 (2.09)**</b>	<b>p=0.005</b>
$AMDN_1$	1.57 (0.34)	<b>1.20 (0.36)*</b>	<b>0.98 (0.19)**</b>	<b>p=0.005</b>
$AMDN_2$	5.20 (2.28)	3.06 (1.93)	2.09 (0.91)	p=0.009

\*\* p<0.01, \*p<0.05 when compared with measurements before surgery.

Data represent group means (SD). Statistically significant values after Bonferroni correction are printed in bold.

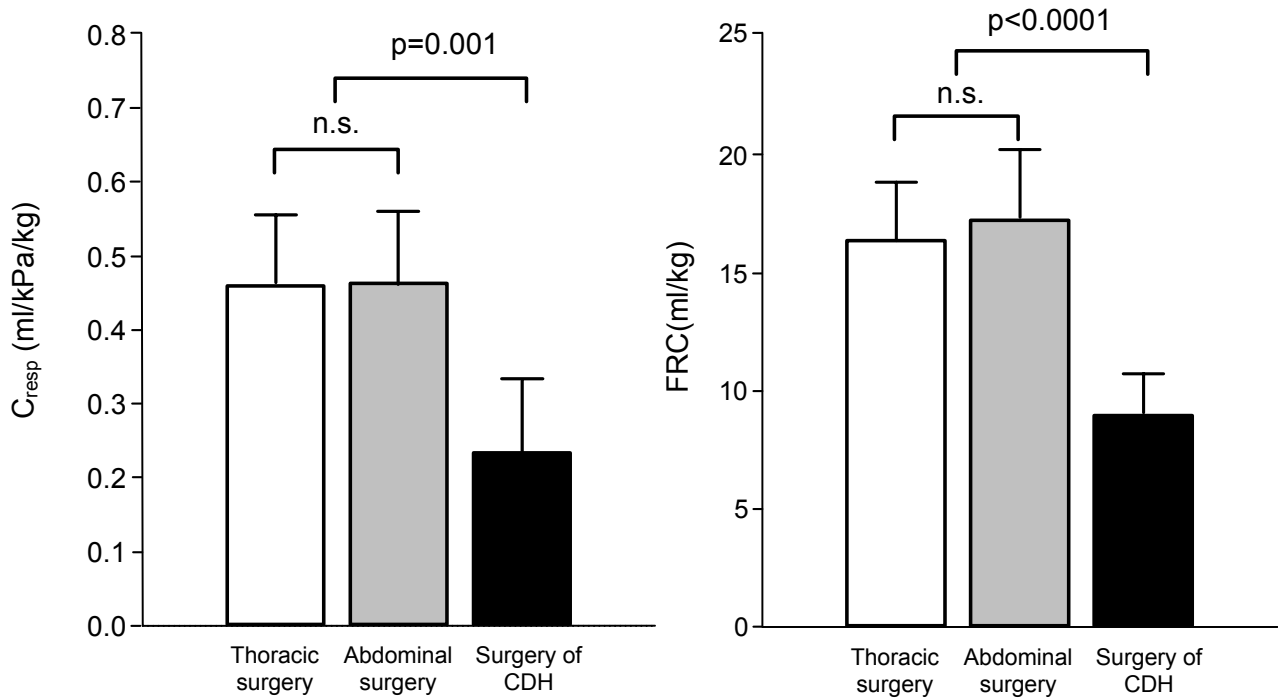


Fig. 1.: Compliance (left) and FRC (right) in infants before thoracic, abdominal or CDH surgery

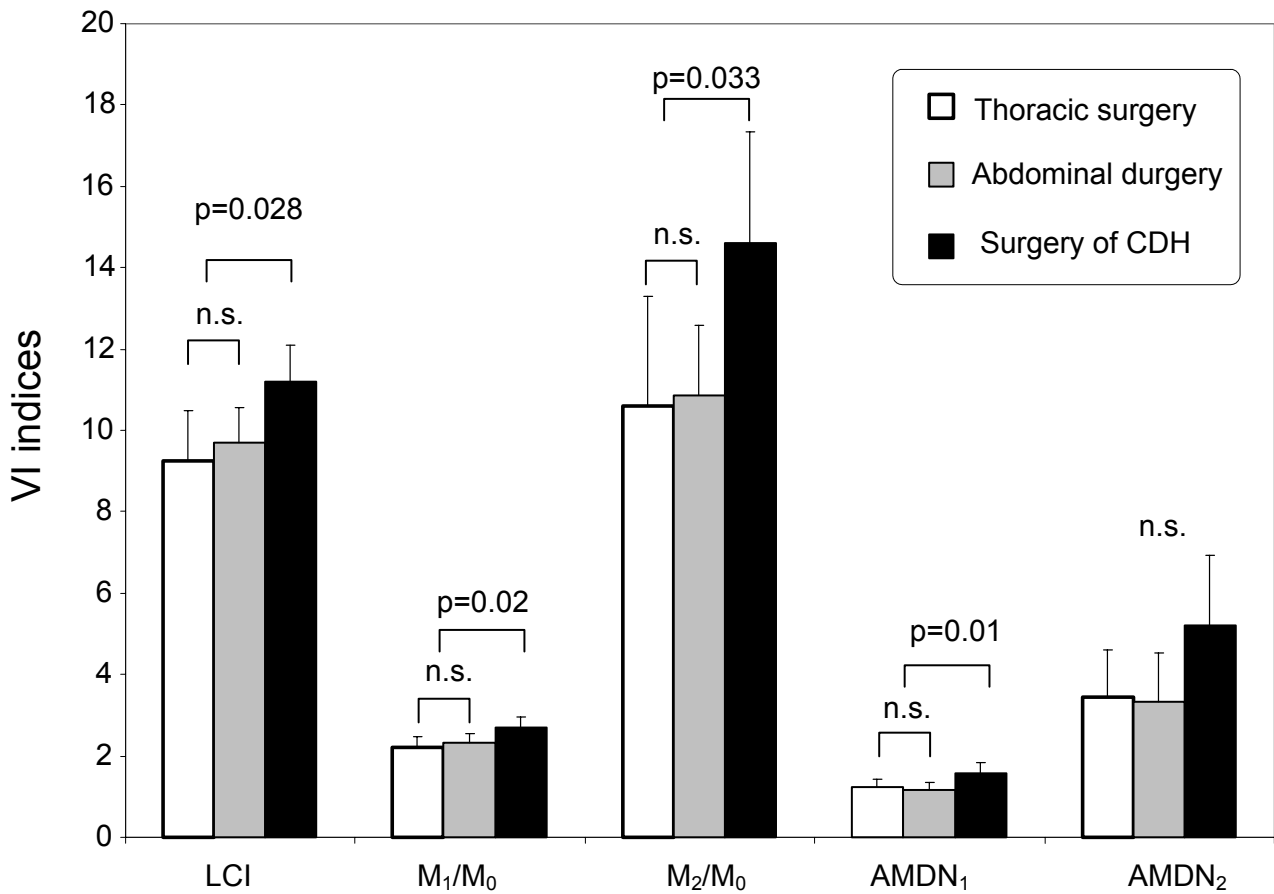


Fig. 2.: Comparison of different VI indices in infants before thoracic, abdominal or CDH surgery

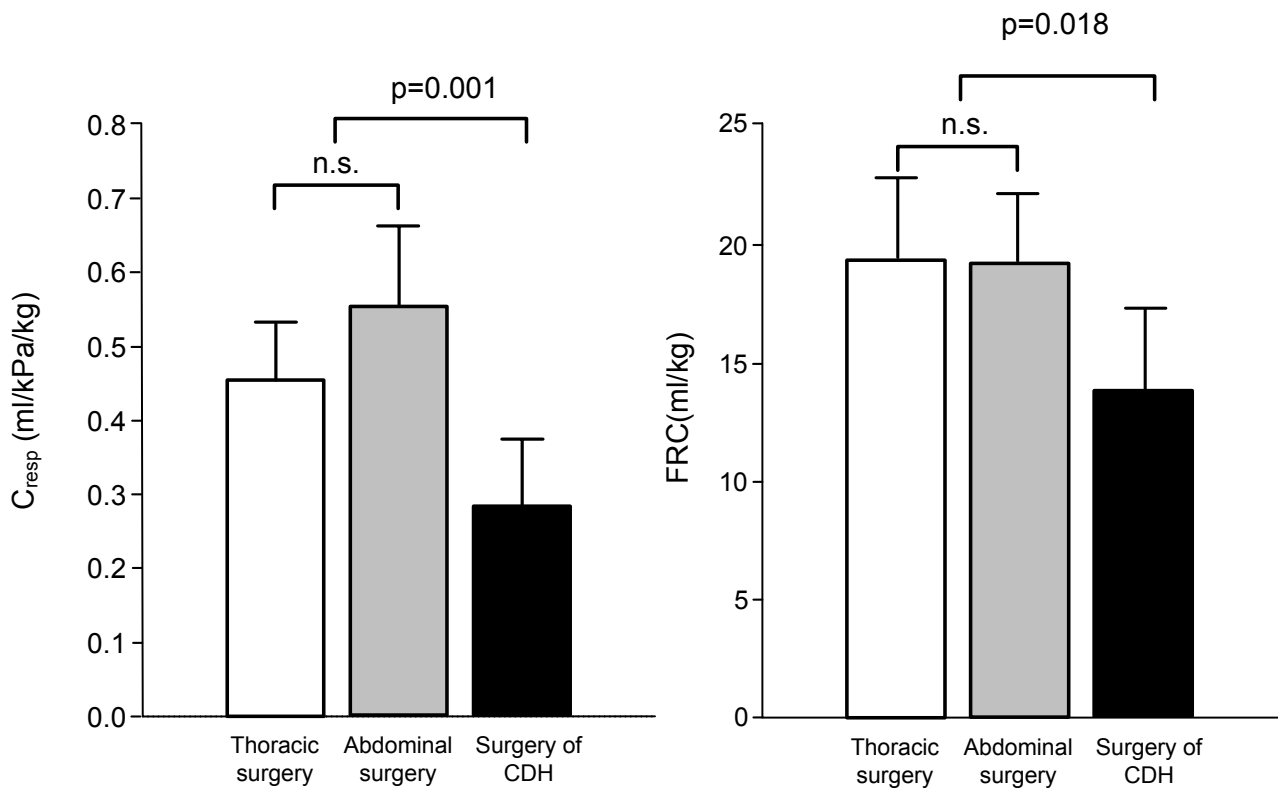


Fig. 3: Compliance (left) and FRC (right) in infants before extubation

**Legends:**

Fig. 1.: Compliance (left) and FRC (right) in infants before thoracic, abdominal or CDH surgery

Fig. 2.: Comparison of different VI indices in infants before thoracic, abdominal or CDH surgery

Fig. 3: Compliance (left) and FRC (right) in infants before extubation

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