Intraoperative acidosis and hypercapnia during thoracoscopic repair of congenital diaphragmatic hernia and esophageal atresia/tracheoesophageal fistula

Running head: Acidosis at neonatal thoracoscopy

Research report

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What is already known

• Thoracoscopy in neonates is known to be associated with intraoperative acidosis and hypercapnia.

What this article adds

• Thoracoscopic repair of CDH or EA/TEF may result in more severe intraoperative acidosis and hypercapnia than during open surgery.

Abstract

Background: Intraoperative hypercapnia and acidosis have been associated with thoracoscopic repair of both congenital diaphragmatic hernia (CDH) and esophageal atresia/tracheoesophageal fistula (EA/TEF).

Aim: The aim of the present study was to investigate whether thoracoscopic repair of CDH or EA/TEF was associated with acidosis and hypercapnia in a large group of neonates, and to analyze the effects of acidosis and hypercapnia on early postoperative outcomes.

***Methods*.** We reviewed the charts of neonates who underwent open or thoracoscopic CDH or EA/TEF repair (2004-2014). Patients with available intraoperative arterial gas values were included. Data ($PaCO_2$: mmHg) were compared using paired/unpaired tests and are reported as difference [95% confidence interval].

***Results*.** *CDH*: 187 neonates underwent open (n=153) or thoracoscopic (n=34) repair. Intraoperative arterial gas values were recorded in 96 open and in 23 thoracoscopic operations. Both groups had similar preoperative pH and $PaCO_2$, and developed intraoperative acidosis (open -0.08 [-0.11, -0.05] p<0.001, thoracoscopic -0.14 [-0.24, -0.04] p=0.01) and hypercapnia (open: 7.8 [3.2, 12.4], p=0.002; thoracoscopic: 20.2 [-2.5, 43, p=0.07). Intraoperatively, neonates undergoing thoracoscopic repair developed lower pH than those having open surgery (-0.06 [-0.01, -0.10] p=0.018), but maintained similar levels of $PaCO_2$ (-4.0 [-9.0, 4.4] p=0.39). *EA/TEF*: 205 neonates underwent open (n=180) or thoracoscopic (n=25) EA/TEF repair. Intraoperative arterial gas values were recorded in 62 open and in 14 thoracoscopic operations. Both groups had similar preoperative pH and $PaCO_2$, and developed intraoperative acidosis (open: -0.09 [-0.14, -0.04], p<0.001; thoracoscopic: 0.21 [-0.28, -0.14], p<0.001) and hypercapnia (open: 9.2 [2.6, 15.7] p=0.008; thoracoscopic: 15.2 [1.6, 28.7], p=0.03). Intraoperatively, neonates undergoing thoracoscopic repair developed lower pH than those having open surgery (difference 0.08 [0.01, 0.15], p= 0.02) but maintained similar levels of $PaCO_2$ (difference -1 [-9, 3], p=0.35).

***Conclusions*.** Neonates undergoing operative repair of CDH or EA/TEF develop intraoperative acidosis and hypercapnia, regardless of the approach used. However, this phenomenon is more severe during thoracoscopic repair. Novel modalities to reduce intraoperative gas derangements, particularly during thoracoscopic repair, need to be established.

Keywords: acidemia; hypercapnia, hypercarbia, neonate, thoracoscopy, minimally invasive surgery

Introduction

Since the first reports on the use of thoracoscopy for congenital anomalies in infants (**1-3**), this surgical approach has been shown to be effective, safe, and to result in better cosmetic outcome in comparison to open surgery (**4, 5**). However, intra-operative acidosis and hypercapnia during thoracoscopy have been reported in some retrospective studies in the pediatric age group (**6-11**) and have been confirmed by a pilot randomized controlled trial in neonates undergoing thoracoscopic repair of congenital diaphragmatic hernia (CDH) or esophageal atresia/trachea-esophageal fistula (EA/TEF) (**12**). Carbon dioxide (CO_2) is the gas most commonly used to insufflate the body cavities during minimally invasive surgery and may be absorbed, leading to increased arterial CO_2 and increased CO_2 elimination from the lungs (**13**). Intra-operative acidosis and hypercapnia during thoracoscopy seem to be associated with an excess of CO_2 absorption from thoracic insufflation that, in neonates, is more pronounced than that reported from peritoneal insufflation during pediatric laparoscopy (**12, 14**). Despite previous reports, it is still a matter of debate whether severe intraoperative acidosis in neonates undergoing thoracoscopic surgery influences adversely their postoperative outcomes.

The aim of the present study was to investigate whether thoracoscopic repair of CDH or EA/TEF was associated with acidosis and hypercapnia in a large group of neonates, and to analyze the effects of acidosis and hypercapnia on early postoperative outcomes.

Patients and Methods

We performed a retrospective review of the medical charts of all neonates who underwent open or thoracoscopic repair for posterolateral CDH or EA/TEF between August 2004 and October 2014 at The Hospital for Sick Children, Toronto, Canada. Open repair was via laparotomy for

CDH patients and via thoracotomy for EA/TEF patients. Only patients with available intraoperative arterial gas values were included in the present study.

Data included patient demographics, preoperative and intraoperative arterial gas values (nadir pH, nadir PaO_2, and zenith $PaCO_2$), effect of intraoperative pH on conversion to open surgery, length of postoperative ventilation, and postoperative complications (hernia recurrence, esophageal stricture). Patients who were converted to open surgery (laparotomy for CDH, thoracotomy for EA/TEF) were considered in the thoracoscopic group for the analysis.

Statistics

Data were tested for normality distribution using the Kolmogorov-Smirnov test and were compared using parametric (t-test) or non-parametric tests (Mann-Whitney), accordingly; dichotomous data were compared using Fisher's exact test. Intraoperative acidosis was correlated with postoperative ventilation duration using linear regression analysis. Data are reported as mean ± SD or median (range). Differences in mean and median are also reported with 95% confidence intervals (CI), dichotomous data report odds ratios and their 95% CIs.

Results

During the study period, 392 neonates underwent surgery for CDH (n= 187) or EA/TEF (n=205).

Congenital Diaphragmatic Hernia

Of the 187 neonates who underwent CDH repair, 153 had open surgery and 34 thoracoscopic repair. Intraoperative arterial gas values were recorded in 96 (63%) open and in 23 (68%) thoracoscopic operations. There were no differences in gender (OR 1.5

[0.6, 3.7] p=0.5), birth weight (difference -213 [-540, 115] p=0.2), gestational age (difference -0.6 [-2.0, 0.9] p=0.4), or side of the defect (OR 1.1 [0.3, 4.1] p=1) between those undergoing open and thoracoscopic repair [**Table 1**]. Neonates who underwent thoracoscopic repair were younger than the ones who had an open repair (difference -2 [-3, 0], p<0.004) [**Table 1**]. The length of thoracoscopic repair (163 [71,282] min) was longer than that of open surgery (115 [46, 252] min, (difference in medians -48 [-67, -22], p=0.0003).

There were no differences in preoperative arterial pH, $PaCO_2$ or PaO_2 values between neonates who underwent open or thoracoscopic CDH repair (**Table 2**). During surgery, the arterial pH values of open and thoracoscopic groups were lower than the preoperative values, whereas the arterial $PaCO_2$ values had the opposite trend (**Figure 1A-D**). In addition, the intraoperative nadir arterial pH values of neonates undergoing CDH thoracoscopic repair were significantly lower than those of neonates who underwent open surgery (**Figure 1E**). However, the intraoperative zenith arterial $PaCO_2$ values were not different between those undergoing open and thoracoscopic CDH repair (**Figure 1F**). Similarly, intraoperative nadir PaO_2 values were similar between infants undergoing open surgery and those undergoing thoracoscopy (**Table 2**).

Thoracoscopy was converted to open surgery in 8/34 (24%) patients, but only in one neonate was this due to severe intraoperative acidosis. Median postoperative ventilation was 4 days (1-78) after open surgery and 5 days (1-40) after thoracoscopic repair (difference -1[-3, 0], p=0.14). There was a weak correlation between intraoperative acidosis and postoperative ventilation duration (r^2= 0.06 [0.00, 0.18, p=0.01).

At a median follow-up of 3.6 years, there were 6/153 patients (4%) in the open surgery group and 7/34 (21%) in the thoracoscopic group that developed a diaphragmatic hernia recurrence; this difference was significant (odds ratio 0.15, 95% CI 0.05, 0.5 p=0.0028). The nadir intraoperative pH at the time of the initial surgery of patients who then developed a hernial recurrence were not different to that who did not recur (difference 0.02 [-0.12, 0.16], p= 0.7).

Esophageal atresia/tracheoesophageal fistula

During the study period, 205 neonates underwent open (n=180) or thoracoscopic (n=25) EA/TEF repair. Intraoperative arterial gas values were recorded in 62 (34%) open and in 14 (56%) thoracoscopic operations. Although there was a trend towards those operated thoracoscopically having a higher birthweight and later gestational age, these differences were not significant (difference -438 [-1038, 1626], p=0.2 and difference -2.6 [-5.3, 0.1], p=0.06 respectively; **Table 1**). The two groups had similar ages at repair (difference 0 [-1, 1] p=0.8; **Table 1**). All neonates in both groups had type C EA/TEF according to the Gross classification. Overall, the length of thoracoscopic repair [244 ± 16 min;] was longer than that of open surgery [189 ± 8 min; difference in means -55 (-94 to -17) p=0.006).

There were no differences in preoperative arterial pH, $PaCO_2$ or PaO_2 values between neonates who underwent open or thoracoscopic EA/TEF repair (**Table 2**). The intraoperative arterial pH values of open and thoracoscopic groups were lower than the preoperative values, whereas the arterial $PaCO_2$ values had the opposite trend (**Figure 2A-D**). The neonates who underwent thoracoscopic repair had significantly lower nadir intraoperative pH values than those who underwent open surgery (**Figure 2E**), whereas there were no differences in intraoperative zenith arterial $PaCO_2$ values (**Figure 2F**).

There were no differences in intraoperative lowest PaO_2 values between neonates undergoing open surgery and those undergoing thoracoscopy (**Table 2**).

Five (20%) patients required a conversion from thoracoscopic to open surgery; however, these were not due to ventilatory concerns. Median postoperative ventilation was 2 days (0-21) after open surgery and 3 days (1-8) after thoracoscopy (difference in medians -1, [-2, 2], p=1.0). There was a weak correlation between intraoperative acidosis and postoperative ventilation duration (r^2=0.07 [95% CI 0.00, 0.24], p=0.04).

At a median follow-up of 46 months, 10/180 (6%) patients in the open surgery group and 6/25 (24%) in the thoracoscopic group had developed an esophageal stricture that required balloon dilatation; this difference was significant (odds ratio 0.19 [0.06, 0.57] p=0.006). The levels of intraoperative acidosis at the time of the first surgery were not different between those patients who developed a stricture and those who did not (difference -0.02 [-0.22, 0.18] p= 0.8).

Discussion

The current study shows that, whilst open repair of CDH or EA/TEF is associated with an intraoperative alteration of blood gases, neonates undergoing thoracoscopic repair develop a greater degree of intraoperative acidosis. Overall, the results of the current study support previous reports in the literature addressing the occurrence of intraoperative acidosis in the same population of neonates (**Table 3**). However, some of these previous studies included only patients repaired thoracoscopically, some were not comparative, and most comprised a small number of patients (**Table 3**).

The hypercapnia during thoracoscopy was first reported in 2009 by Bliss *et al*. (**6**). The authors described it as a common phenomenon during thoracoscopic CDH repair, but

concluded that in their series it did not result in clinically evident deterioration. McHoney *et al*. (**8**) confirmed the phenomenon, and also reported that end-tidal CO_2 levels were higher in infants undergoing thoracoscopic repair of CDH than in those undergoing open surgery. This study recommended a close monitoring of intraoperative arterial blood gases and advocated for a randomized trial to assess the effect of thoracoscopy on ventilation and CDH recurrences (**8**). Almost concomitantly, Fishman *et al*. reported that patients with CDH repaired thoracoscopically developed similar intraoperative acidosis levels to those repaired with open surgery (**9**). However, careful scrutiny of the pH values reported in that series reveals the intraoperative degree of acidosis to reach levels as low as 6.61 (**9**). In addition, arterial blood gases are not taken at specified times during the procedures, so that there may be more blood gases values measured during thoracoscopic procedures, both due to the longer operative times and the perceived higher risk of acidosis, resulting in a bias in comparison of open and thoracoscopic blood gas values.

So far there has been only a single pilot randomized controlled trial that compared open versus thoracoscopic surgery addressing the issue of intraoperative acidosis (**12**). The findings of this trial did not support the use of thoracoscopy for CDH repair with CO_2 insufflation and conventional ventilation, calling into question the safety of this practice (**12**). On the other hand, as there were no significant differences in $PaCO_2$ or pH between neonates undergoing open and thoracoscopic repair of EA/TEF, the authors concluded that the effect of thoracoscopy on blood gases in this population required further evaluation, as only 10 EA/TEF had been compared in the pilot study (**12**).

Most of the studies published on this topic have attempted to answer the question

whether the presence of intraoperative acidosis has had a negative clinical impact upon patients. To date, none of the reported studies has ever documented a clinical compromise of the neonates during the intra- or post-operative period. In our current study, we have shown that only one infant undergoing CDH repair developed such a profound acidosis that conversion to open surgery was required. The other 12 converted cases were the result of other reasons. This is similar to the experience reported in the randomized trial, where there were no cases of thoracoscopy for CDH or EA/TEF converted to open surgery due to ventilatory concerns (**12**).

In the current study we also determined that neither the thoracoscopic approach, nor the levels of intraoperative acidosis, influenced the duration of postoperative mechanical ventilation. This is similar to that reported in the pilot randomized trial, where there was no difference in days of postoperative ventilation and intensive care unit stay between the open and the thoracoscopic group (**12**).

The current study also looked at whether severe levels of acidosis during thoracoscopy in neonates could result in higher postoperative complication rates, namely hernial recurrence for CDH patients and esophageal stricture for EA/TEF. At follow-up, there appears to be a significantly higher rate of hernia recurrences in the CDH group and esophageal stricture of the anastomosis in the EA/TEF group. The high recurrence rate in thoracoscopic CDH repair has been previously reported in a meta-analysis (**19**), but an association with intra-operative acidosis is unlikely. Likewise, thoracoscopic repair has been reported as one of the factors associated with increased risk of clinically significant stricture formation after EA/TEF repair (**20**).

The issue of whether severe intraoperative acidosis has an impact on the infant developing brain is still a matter of debate. Bishay *et al*. (**15**) measured the regional cerebral oxygen saturation using near-infrared spectroscopy in six infants undergoing thoracoscopic CDH or EA/TEF repair and reported that intraoperative acidosis was associated with a decrease in cerebral hemoglobin oxygen saturation. More recently, Tytgat *et al*., studying the impact of thoracoscopy for EA/TEF at a low CO_2 insufflation pressure (5 mmHg), confirmed a reversible decrease in oxygen saturation and pH, and an increase in $PaCO_2$ (**16**). The authors concluded that the regional cerebral oxygen saturation remained stable and within normal limits during and after the CO_2 pneumothorax, suggesting no hampering of cerebral oxygenation by thoracoscopy (**16**).

It remains unknown whether acidosis and hypercapnia in the presence of normoxia are detrimental for infantile neurodevelopment. In the preliminary study by Bishay *et al*., as well as in the randomized controlled trial, arterial oxygenation was well maintained throughout (**12, 15**). Similarly, in our current study, patients who underwent thoracoscopy did not have changes in arterial oxygenation. It could be that maintaining a good cerebral oxygen saturation prevents cerebral damage, regardless of the changes in the other gas parameters.

As the acidosis phenomenon is now recognized, strategies to prevent it have been proposed. Acidosis could arise either due to respiratory compromise during thoracoscopic procedures due to, for example, lung collapse to allow a working space, or direct absorption of insufflated CO_2 from the thorax. On the other hand, the lower intraoperative pH levels found in neonates undergoing thoracoscopy in comparison to those having open surgery could be due to a component of metabolic acidosis. An acid-

base imbalance, mostly of a metabolic type, has been reported in patients undergoing laparoscopy [**21**], but to the best of our knowledge it has not been reported in neonates undergoing thoracoscopy. Data from Bishay *et al*. suggest that direct absorption of insufflated CO_2 from the thorax is an important factor, as during thoracoscopic procedures up to 50% of expired CO_2 originated from the insufflated gas (**12**). Mortellaro *et al*. (**10**) recommended the use of high-frequency oscillating ventilation to facilitate CO_2 elimination and to prevent acidosis in neonates undergoing thoracoscopic CDH or EA/TEF repair. Studies focused upon the optimal insufflation gas for laparoscopy have proposed the use of nitrous oxide, helium, argon, or air for insufflation. However, a systematic review of the literature found no randomized controlled trials comparing CO_2 pneumoperitoneum to any other gas pneumoperitoneum and could not demonstrate any advantage of alternative gases over CO_2 (**17**). Other gases may introduce additional risks of potentially greater clinical significance, such as embolism. The best strategy to minimize intraoperative hypercapnia and acidosis would be to use CO_2 insufflation at very low pressures, possibly insufflating only at the beginning of the operation, especially in CDH.

We acknowledge the limitations of the current study, mainly due to its retrospective nature. In our series, not all patients had arterial gas values checked and recorded intraoperatively and the ones available were not taken at set time points. Nonetheless, if gas values were available for all patients we believe that the degree of intraoperative acidosis and hypercapnia could have been even greater. Moreover, in this study we have compared patients allocated to open surgery or thoracoscopy on clinical grounds, which implies a selection bias whereby neonates allocated to thoracoscopic surgery typically have a more robust preoperative physiology. Yet, we have recorded a greater change in

pH and PaO2 values in this population of neonates.

In conclusion, the present study shows that neonates undergoing surgical repair of CDH or EA/TEF develop intraoperative acidosis and hypercapnia regardless of the approach used. However, this phenomenon is more severe during thoracoscopic repair. Although the finding of acidosis is concerning, we found no association of intraoperative acidosis with any other postoperative outcome of immediate interest. The effects of acidosis and hypercapnia on cerebral development are unknown, but maintaining adequate arterial oxygenation could be key to prevent damage. It would be important for future prospective studies to document intra-operative acidosis systematically, and to establish whether there are any long-term effects on neurological or other relevant outcomes. This would be difficult to do except as a multi-centre randomized controlled trial, as there are likely to be several confounders influencing neurodevelopmental outcomes in these groups of infants.

This study highlights that even in a large volume center a noticeable proportion of neonates undergoing thoracoscopic surgery did not routinely have arterial blood gas levels checked intraoperatively. The findings of the current study have made surgeons and anesthetists aware of the occurrence of intraoperative acidosis and hypercapnia, prompting the surgeons to use low insufflation settings and the anesthetists to meticulously check neonatal physiology intraoperatively.

We advocate for a large multicenter randomized controlled trial of open versus thoracoscopic CDH or EA/TEF repair at low CO_2 insufflation pressures.

Ethics

The study was registered with the institutional Ethics committee (REB1000046560 and REB1000046653),

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Disclosures

The authors have nothing to disclose.

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Table 1. *Demographics of neonates who underwent open or thoracoscopic CDH or EA/TEF repair.*

	Open	**Thoracoscopic**	**Difference (95% CI),**	**Odds ratio (95% CI)**	**p-value**
CDH (n)	96	23			
Gender (M:F)	63 : 33	13 : 10		1.5 (0.6, 3.7)	0.5
Birth weight (grams)	3115 ± 597	3327 ± 565	-213 (-540, 115)		0.2
Gestational age (weeks)	38.2 ± 2.6	38.8 ± 1.6	-0.6 (-2.0, 0.9)		0.4
Side of defect (left)	84 (88%)	20 (87%)		1.1 (0.3, 4.1)	1
Age at repair (days)	4 (3-8)	2 (2-4)	-2 (-3, 0)		0.004
EA/TEF (n)	62	14			
Gender (M:F)	37 : 25	6 : 8		2.0 (0.6, 6.4)	0.4
Birth weight (grams)	2623 ± 766	3060 ± 608	-438 (-1038, 1626)		0.2
Gestational age (weeks)	37 ± 3.5	39 ± 1.5	-2.6 (-5.3, 0.1)		0.06
Type of atresia	C = 100%	C = 100%			1
Age at repair (days)	2 (1-4)	2 (1-3)	0 (-1, 1)		0.8

Mean ± SD or median (IQ range); CI= confidence interval

***Table 2**. Preoperative and intraoperative arterial pH and $PaCO_2$ for neonates who underwent open or thoracoscopic CDH or EA/TEF repair.*

	Open	**Thoracoscopic**	**Difference (95% CI)**	**p-value**
CDH (n)	96	23		
Preoperative pH	7.35 ± 0.06	7.38 ± 0.05	-0.03 (-0.07, 0.01)	0.19
Preoperative $PaCO_2$ (mmHg)	43 (34-79)	41 (35-52)	2 (-2, 8)	0.30
Preoperative PaO_2 (mmHg)	88.5 (31-186)	85.5 (40-128)	3 (-20, 27)	0.82
Intraoperative pH	7.27 ± 0.09	7.22 ± 0.11	0.06 (0.01, 0.10)	0.018
Intraoperative $PaCO_2$ (mmHg)	53.0 (31.7-93.6)	57.0 (28.3-133)	-4.0 (-9.0, 4.4)	0.39
Intraoperative PaO_2 (mmHg)	109 (25-274)	139 (27-330)	-30 (-50, 2)	0.07
EA/TEF (n)	62	14		
Preoperative pH	7.37 ± 0.05	7.39 ± 0.04	-0.02 (-0.06, 0.02)	0.25
Preoperative $PaCO_2$ (mmHg)	40 (32-55)	41 (33-76)	-1 (-9, 3)	0.35
Preoperative PaO_2 (mmHg)	51 (38-105)	51 (34-108)	0 (-15, 13)	0.6
Intraoperative pH	7.28 ± 0.11	7.20 ± 0.11	0.08 (0.01, 0.15)	0.02
Intraoperative $PaCO_2$ (mmHg)	50.6 (22-91.3)	58.8 (30-91.7)	-8.3 (-18.5, 2.2)	0.1
Intraoperative PaO_2 (mmHg)	74 (55-360)	82 (58-320)	-8 (-38, 0.9)	0.06

Mean ± SD or median (range); CI= confidence interval

Table 3*. Studies addressing intraoperative acidosis in neonates undergoing thoracoscopic CDH or EA/TEF repair.*

Reference	Study type	Pathology	Thoracoscopic	Open	Conclusions
Bliss et al 2009 [**6**]	Retrospective	CDH	31	/	Acidosis does not result in clinically evident compromise
McHoney et al 2010 [**8**]	Retrospective	CDH	13	35	Thoracoscopic CDH repair is feasible. Arterial blood gases to be closely monitored.
Fishman et al 2011 [**9**]	Ambispective	CDH	12	9	Similar acidosis levels between open and thoracoscopic surgery
Mortellaro et al 2011 [**10**]	Retrospective	CDH EA/TEF	5 12	/	HFOV allows CO_2 elimination to prevent acidosis
Bishay et al 2011 [**15**]	Prospective	CDH EA/TEF	6 2	/	Possible association of acidosis and decreased cerebral O_2 saturation
Ma et al 2012 [**18**]	Prospective	EA/TEF	18	15	Thoracoscopic repair is safe and tolerable in selected patients
Bishay et al 2013 [**12**]	Prospective RCT	CDH EA/TEF	5 5	5 5	No support for CDH thoracoscopic repair. No conclusive results for EA/TEF repair
Okazaki et al 2015 [**11**]	Retrospective	CDH	20	10	Thoracoscopy is safe for the treatment of selected cases
Tygat et al 2015 [**16**]	Prospective	EA/TEF	15	/	Cerebral oxygenation is not hampered by CO_2 insufflation at 5 mmHg
Zani et al current	Retrospective	CDH EA/TEF	23 14	96 62	

CDH= congenital diaphragmatic hernia;
EA/TEF= esophageal atresia/trachea-esophageal fistula;
HFOV= High frequency oscillatory ventilation.

Figure legends

Figure 1: Arterial gas values for neonates undergoing open or thoracoscopic CDH repair.
A) Pre- vs. intra-operative pH values in the open surgery group;
B) Pre- vs. intra-operative pH values in the thoracoscopic surgery group;
C) Pre- vs. intra-operative $PaCO_2$ values in the open surgery group;
D) Pre- vs. intra-operative $PaCO_2$ values in the thoracoscopic surgery group;
E) Intraoperative pH values in neonates undergoing open vs. thoracoscopic surgery for CDH;
F) Intraoperative $PaCO_2$ values in neonates undergoing open vs. thoracoscopic surgery for CDH.

Figure 2: Arterial gas values for neonates undergoing open or thoracoscopic EA/TEF repair.
A) Pre- vs. intra-operative pH values in the open surgery group;
B) Pre- vs. intra-operative pH values in the thoracoscopic surgery group;
C) Pre- vs. intra-operative $PaCO_2$ values in the open surgery group;
D) Pre- vs. intra-operative $PaCO_2$ values in the thoracoscopic surgery group;
E) Intraoperative pH values in neonates undergoing open vs. thoracoscopic surgery for EA/TEF;
F) Intraoperative $PaCO_2$ values in neonates undergoing open vs. thoracoscopic surgery for EA/TEF.

Figure 1

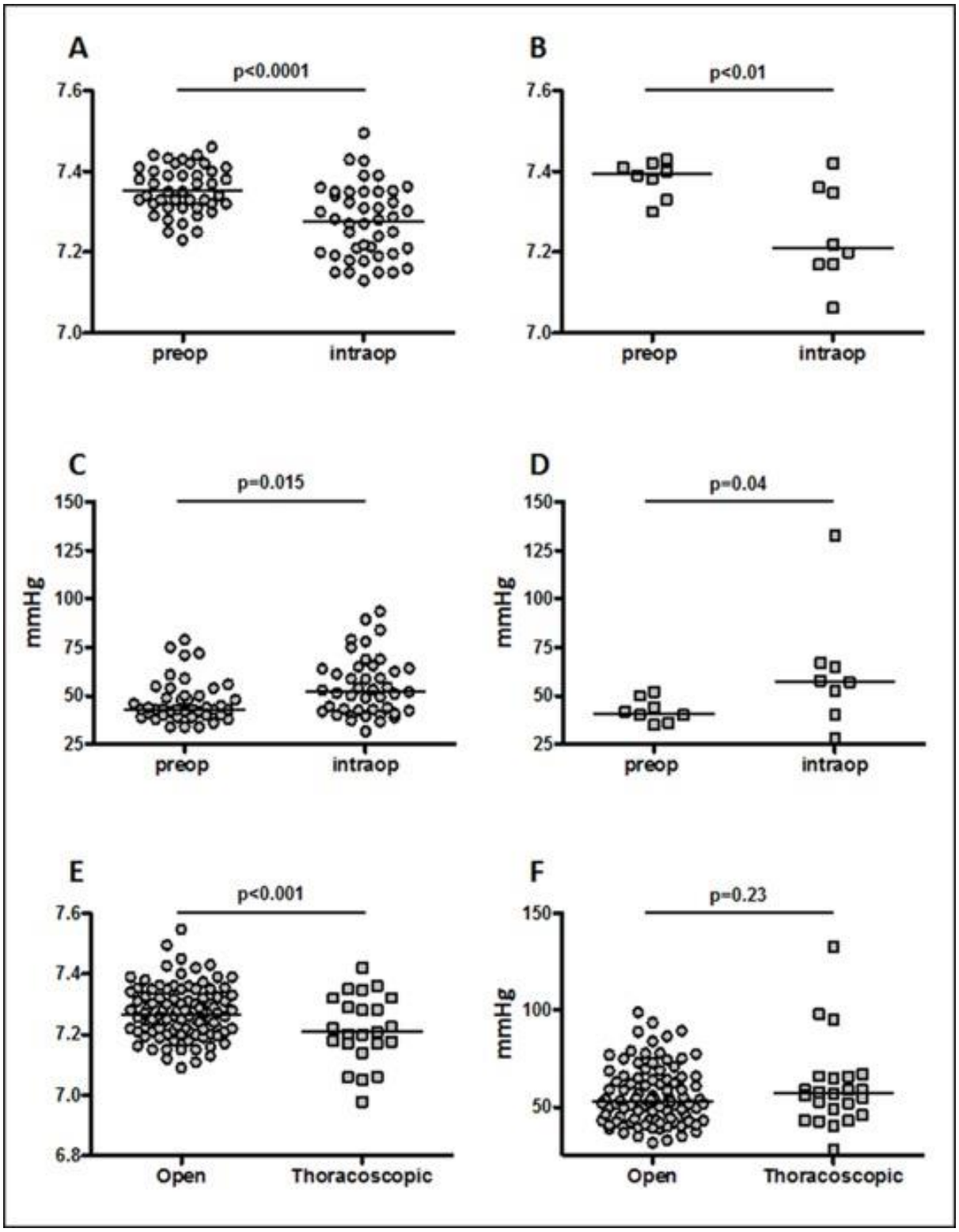
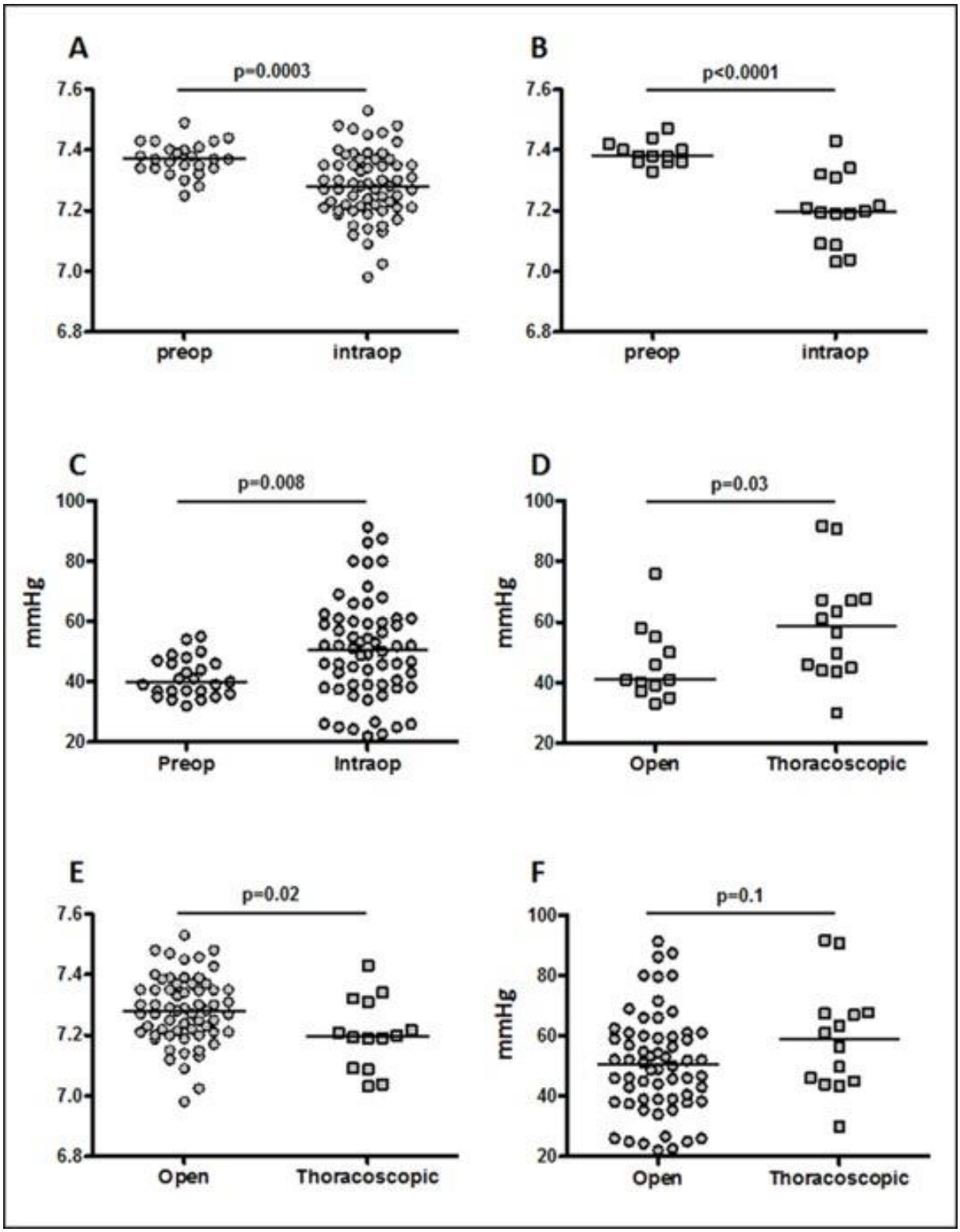

A
p<0.0001
7.6
7.4
7.2
7.0
preop
intraop
B
p<0.01
7.6
7.4
7.2
7.0
preop
intraop
C
p=0.015
150
125
100
75
50
25
mmHg
preop
intraop
D
p=0.04
150
125
100
75
50
25
mmHg
preop
intraop
E
p<0.001
7.6
7.4
7.2
7.0
6.8
Open
Thoracoscopic
F
p=0.23
150
100
50
mmHg
Open
Thoracoscopic

Figure 2


A
p=0.0003
7.6
7.4
7.2
7.0
6.8
preop
intraop
B
p<0.0001
7.6
7.4
7.2
7.0
6.8
preop
intraop
C
p=0.008
mmHg
100
80
60
40
20
Preop
Intraop
D
p=0.03
mmHg
100
80
60
40
20
Open
Thoracoscopic
E
p=0.02
7.6
7.4
7.2
7.0
6.8
Open
Thoracoscopic
F
p=0.1
mmHg
100
80
60
40
20
Open
Thoracoscopic