Insufflation in minimally invasive surgery: is there any advantage in staying low?

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Abstract

Aim: Minimally invasive repair of oesophageal atresia with trachea-oesophageal fistula (OA/TOF) and congenital diaphragmatic hernia (CDH) is feasible and confers benefits compared to thoracotomy or laparotomy. However, carbon dioxide (CO_2) insufflation can lead to hypercapnia and acidosis. We sought to determine the effect of lower insufflation pressures on patients' surrogate markers for CO_2 absorption – arterial partial pressure of CO_2 ($PaCO_2$), end tidal CO_2 ($EtCO_2$) and pH.

Methods: Single centre retrospective review, including neonates without major cardiac anomaly. Selected patients formed 2 groups: Historical pressure (HP) group and low pressure (LP) group. We reported on the patients' preoperative characteristics that potentially confound the degree of CO_2 absorption or elimination. Outcome measures were perioperative $PaCO_2$, $EtCO_2$, arterial pH and anaesthetic time.

Results: 30 patients underwent minimally invasive surgery for CDH and 24 patients for OA/TOF with similar distribution within the HP and LP group. For CDH patients as well as for OA/TOF patients, there were no significant differences in their preoperative characteristics or surgery duration comparing HP and LP groups. With a decrease in insufflation pressure in CDH patients, there was a significant decrease ($p=0.002$) in peak $PaCO_2$ and an improvement in nadir pH ($p=0.01$). For the OA/TOF patients, the decrease in insufflation pressure was associated with a significant decrease ($p=0.03$) in peak $EtCO_2$. Considering all 54 patients, we found $EtCO_2$ highly significantly inversely correlated with pH and positively correlated with intraoperative $PaCO_2$ ($p<0.001$). Baseline Hb was inversely correlated with mean $EtCO_2$ ($p<0.001$).

Conclusion: With lower insufflation pressures, CDH patients had significantly improved hypercapnia and acidosis, whilst OA/TOF patients had significantly reduced $EtCO_2$. $EtCO_2$ was correlated with acidosis and hypercapnia.

Introduction

Minimally invasive repair of congenital diaphragmatic hernia (CDH) and oesophageal atresia with tracheo-oesophageal fistula (OA/TOF) in infants have first been described in 1995 and 1999, respectively[1-3], and are increasingly being performed in many paediatric surgical centres[4,5]. Controversy still exists concerning outcome of either approach regarding specific complications such as recurrence in CDH or, leak or stricture in OA/TOF, respectively[6-9]. Advocates of the minimally invasive approach claim advantages such as superior visualisation, less traumatic lung injury from retraction and avoidance of the thoracotomy incision allowing for a quicker postoperative recovery [6,10]. Critics of minimally invasive surgery (MIS) are concerned about the risk of insufflation-induced hypercapnia, acidosis and hypoxia with resultant decreased cerebral oxygenation[11-17]. The neonatal brain, with its immature autoregulatory system, seems to be particularly vulnerable to the aforementioned pathophysiologic changes[18]. In MIS, higher insufflation pressures often increase the working space and can thus be applied to improve the field of vision and to increase the instruments' intracorporal range of motion. We have previously performed the first randomized trial showing higher CO_2 levels in patients undergoing thoracoscopy repair[15]. However, in our initial experience, we failed to minimize CO_2 insufflation pressure during the procedure.

Our aim in this study was to test our hypothesis that lower CO_2 insufflation pressure would reduce end-tidal CO_2 ($EtCO_2$) and arterial partial pressure of CO_2 ($PaCO_2$) and increase arterial pH.

Methods

This was a single centre, retrospective review of patients undergoing minimally invasive repair of CDH or OA/TOF. The study was approved by the institution's audit and governance board (Registration number 2305).

Patients

Patients undergoing a completely minimally invasive primary repair of Bochdalek-type CDH or oesophageal atresia (OA) with tracheo-oesophageal fistula (TOF) in between January 2007 and April 2019 were included in the study. Further inclusion criteria were postnatal age of less than one month and a normal renal function.

Patients operated on in the years 2007 to 2012 were assigned to the "historical pressures" (HP) group, where CO_2 insufflation pressures ranged from 5 up to 10 mmHg; 10 patients in this group were included in a previous randomized controlled trial[15]. Cases during the period of 2014 to April 2019 were assigned to the "low pressures" (LP) group, where insufflation pressures ranged from 4 to 7 mmHg, reflecting the change in institutional practice towards keeping insufflation pressure as low as practicable. We excluded patients older than one month, patients with major cardiac anomalies, patients converted from MIS to open surgery as well as patients with a primary open operation. Since patients with CDH have a cardiorespiratory physiology that can be quite different from patients with OA/TOF, we decided to study the two pathologies separately.

Perioperative factors and outcome

Data collected were weight, gestational age and postnatal age, gender, preoperative haemoglobin, use of inhaled nitric oxide (NO), high frequency oscillation ventilation (HFOV) or extracorporeal membrane oxygenation (ECMO). We also recorded findings from the preoperative echocardiogram. These factors were chosen because they might affect patients' cardiorespiratory physiology and thus influence the intraoperative degree of hypercapnia or acidosis. Duration of the operation was also recorded. Measured endpoints were pH and

$PaCO_2$, which were obtained from intraoperative arterial blood gas analysis (BGA). We also recorded $EtCO_2$ which was continuously monitored and recorded at intervals on the anaesthetic chart during surgery. Since ventilation pressures were largely not available, we calculated the Carrico index (PaO_2/FiO_2 ratio) from the recorded fraction of inspired oxygen (FiO_2) and arterial partial pressure of oxygen (PaO_2). Although blood gas analyses (BGA) were done a minimum of three times during each of the procedures, the samples were not taken at standardized intervals.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 25 (SPSS Inc., Chicago, IL, USA). Due to the small sample size and since most variables were not normally distributed – as assessed using the Shapiro-Wilk Test – we compared continuous factors and outcome variables using the Mann-Whitney Test and Fisher's exact test for dichotomous factors, respectively. Numerical results were graphically presented using boxplots, the box encompassing the interquartile range from the first quartile to the third quartile, and the bold transverse bar representing the median. The whiskers mark maximum and minimum values. Outliers represented by a circle (o) are more than a 1.5-fold interquartile range away from quartile 1 or 3, respectively. Correlation analysis was performed using Pearson's correlation. The significance of difference between correlation coefficients was assessed using Fisher's r-to-z transformation. Probability values of ≤ 0.05 were considered significant, values <0.001 were considered highly significant.

Results

During the observation time, a total of 54 patients underwent successful congenital diaphragmatic hernia (CDH) or primary repair of oesophageal atresia (OA), with trachea-oesophageal fistula (TOF), using minimally invasive surgery (MIS). During the same period, 37 patients had a primary open repair of OA while thoracoscopic repair was converted to an open operation in another 10 patients; 28 patients underwent primary open repair of CDH with 6 patients converted from MIS to open.

Among the 30 patients with CDH operated thoracoscopically, 15 underwent patch repair; only 1 patient had a right sided hernia. 24 patients presented with OA/TOF. Body weight corrected gestational age at the time of the operation, haemoglobin levels, gender distribution, use of NO or HFO were similar when comparing the historical (HP) and low pressures (LP) groups of patients with CDH or patients with OA/TOF, respectively (Table 1). Preoperative median FiO_2, median PaO_2 and median Carrico index were similar in the HP compared to the LP group for both, OA/TOF as well as CDH patients. However, the use of a patch in CDH repair was more common in the more recent LP group (p=0.03).

We found less acidosis and decreased $PaCO_2$ with lower insufflation pressures in patients with CDH. Median nadir pH in the LP group was higher with 7.20 compared with 7.03 in the HP group (p=0.01; Figure 1). Additionally, peak $PaCO_2$, as well as end-operative $PaCO_2$, were significantly lower in the LP group compared to the HP group (median 9.3 kPa and 7.6 kPa vs 15.7 kPa and 9.6 kPa, p=0.002 and p=0.02, respectively; Figure 2). Peak $EtCO_2$ were similar in the LP group compared to the HP group.

$EtCO_2$ was reduced with lower insufflation pressures in patients with OA/TOF. Median peak $EtCO_2$ in the LP group was significantly lower by 29% compared to the HP group (7.05 kPa vs 5.55 kPa, p=0.04; Figure 3). However, there was no significant difference in nadir pH or $PaCO_2$ between these groups (Figure 1 and Figure 2). In CDH patients, median FiO_2 was significantly lower in the LP compared to the HP group (0.47, range 0.34-0.7 vs 0.5, range 0.39-0.9; p=0.04); however, no difference in median FiO_2 was found in OA/TOF patients.

In CDH patients $EtCO_2$ was positively correlated with simultaneously measured $PaCO_2$ and inversely correlated with arterial pH (Figure 4 A+C). These correlations of $EtCO_2$ with $PaCO_2$ and $EtCO_2$ were tested for the first three intraoperative BGA and were found to be highly significant ($p<0.001$). Interestingly, no such correlation was seen in OA/TOF patients (Figure 4 B+D). The intraoperative Carrico index, however, was not correlated with acidosis in CDH patients, whereas in OA/TOF patients it showed a highly significant correlation with pH ($p<0.001$, cc=0.4; Figure 5 A+B) and a significant correlation with $PaCO_2$ (p=0.002, cc=0.31).

Preoperative Hb, on the other hand, was weakly inversely correlated with mean $EtCO_2$ and end-operative $PaCO_2$ ($p<0.001$, cc=0.24 or p=0.02, cc=0.12; Figure 5C). However, there was no direct correlation between preoperative Hb and nadir pH.

Corrected gestational age did not correlate either positively or inversely with any of the outcome variables. Furthermore, duration of surgery was not correlated with peak $PaCO_2$ or nadir pH.

Perioperative factors

Corrected gestational age at the time of operation in the HP group ranged from 35+5 weeks to 44+2 weeks while in the LP group it ranged from 34+0 weeks to 43+0 weeks; corrected gestational age was similar comparing the LP group to the HP group of patients with CDH or OA/TOF (Table 1). Insufflation pressures were only available from about one fourth of the patients; median pressures were lower in the LP compared to the HP group when including CDH and OA/TOF patients (p=0.005). Additionally, there were no significant differences in body weight, gender, pre-operative Hb levels, the use of NO and/or HFOV. No patient operated thoracoscopically had previous ECMO. Surgery duration was also not significantly different among groups. However, application of a patch in CDH repair was more common in the more recent LP group compared to the HP group (p=0.03).

Discussion

CO_2 insufflation in minimally invasive surgery, especially in thoracoscopy, goes along with partial absorption of the CO_2[11]. Furthermore, the iatrogenic pneumothorax reduces alveolar ventilation and can alter pulmonary haemodynamic and thus lead to a ventilation-perfusion mismatch. These pathophysiologic changes might be aggravated by pulmonary hypoplasia and pathologic pulmonary vasculature in CDH patients and make maintenance of normocapnia difficult. Ventilation strategies aim at increasing the alveolar minute ventilation to eliminate CO_2 and thus prevent respiratory acidosis and hypercapnia, as both are associated with alterations of cerebral perfusion and oxygen saturation, particularly in neonates and infants[11,13,15,17]. We have previously reported the incidence of high $EtCO_2$ in patients undergoing MIS for CDH and OA/TOF repair[15]. Although many reports advise against the use of high insufflation pressures, there are only very few studies examining the effect of various pressures on acidosis, hypercapnia and cerebral oxygenation[19,20]. The only randomised controlled trial on this topic described the negative impact of $C0_2$ insufflation on worsening acidosis, especially so in a thoracoscopic repair of CDH[15]. Notably, pressures up to 10mmHg were used. However, the trial did not find a negative impact of thoracoscopy on medium term motor, language and cognitive function.

This retrospective study is the first to provide clinical evidence that a decrease in insufflation pressure in thoracoscopic CDH repair significantly reduces intraoperative acidosis and hypercapnia. The pH and $PaCO_2$ values we recorded in our LP group are similar or even less acidotic and less hypercapnic compared to values reported by other recent clinical studies reporting on thoracoscopic repair of CDH [20-22] or OA/TOF [16].

Interestingly, in CDH patients, $EtCO_2$ – as a surrogate for CO_2 absorption – was not significantly affected by the reduction of insufflation pressures, while acidosis and hypercapnia did improve[11,23]. This could be suggesting that the pathophysiology of CDH patient differs from OA/TOF patients whereby raised intrapleural pressures – with resulting haemodynamic alterations and reduced alveolar ventilation – rather than increased CO_2 absorption could be predominantly responsible for acidosis and hypercapnia during thoracoscopy in CDH patients[19]. This finding could also have implication when considering the best strategy to eliminate CO_2 which is still controversial[22]. Measures that have been described to reduce or avoid intraoperative acidosis and hypercapnia include intrapulmonary percussive ventilation in thoracoscopic CDH repair[24], high frequency oscillatory ventilation[22,25], stopping or reducing insufflation after visceral contents were reduced in CDH and lower insufflation pressure in thoracoscopic OA/TOF or CDH repair (Table 2)[16,21,26]. Intrapulmonary percussive ventilation and HFOV, however, cause vibrations making any repair technically more demanding[25]. In one report where insufflation pressures were limited to a maximum of 5 mmHg, cerebral O_2 saturation was still found to be increased during anaesthesia induction, yet then normalised and remained stable during and after surgery for OA/TOF repair[16].

In patients undergoing thoracoscopic repair of OA/TOF on the other hand, we found a marked reduction of peak $EtCO_2$ in our LP group. There are no studies available directly correlating insufflation pressures to $EtCO_2$. Our observation that lower insufflation pressures did reduce $EtCO_2$ in patients with OA/TOF but not significantly with CDH, might be partially due to the smaller gas-absorbing pulmonary surface of their hypoplastic lung compared to the normal lung of a patient with OA/TOF. The latter may suggest that CO_2-absorption during thoracoscopy is more active on the pulmonary surface than on the parietal pleura; which in turn corresponds to the observation that CO_2 absorption is much greater in thoracic CO_2 insufflation than in abdominal insufflation[11].

Furthermore, we found highly significant correlations of $EtCO_2$ with $PaCO_2$ and acidosis. $EtCO_2$ is generally used as a trend monitor and to guide ventilation in steering arterial CO_2[27,28]. Our simultaneous measurements of $EtCO_2$ and pH or $PaCO_2$, respectively, confirmed a robust correlation of these values. Measurements of high $EtCO_2$ with associated acidosis and hypercapnia are likely to reflect clinical circumstances, where the minute ventilation could not be increased further keeping the potential for ventilator induced lung injury low. However, in clinical application, $EtCO_2$ needs to be interpreted in conjunction with $PaCO_2$; a discrepancy or gap between these values suggests the presence of a ventilation-perfusion mismatch, which can be caused by the underlying pathophysiology of CDH, haemodynamic compromise or poor lung compliance exacerbated by iatrogenic pneumothorax. Once the discrepancy or gap between $EtCO_2$ and $PaCO_2$ is established and in the absence of major haemodynamic or respiratory changes, $EtCO_2$ remains a good trend monitor for $PaCO_2$.

The Carrico Index (PaO_2/FiO_2 ratio) can be used as an indicator of pulmonary oxygenation effectiveness and has been shown to be a useful predictor of outcome in neonates with CDH or with lung injury secondary to meconium aspiration[29,30]. Interestingly, we found the intraoperative Carrico Index to be highly correlated with hypercapnia and acidosis in OA/TOF patients only, whereas there was no correlation of these parameters in CDH patients. On one hand, these findings suggest that development of hypercapnia and acidosis in OA/TOF patients is related to the restrictive effect of the collapsed ipsilateral lung, which impedes CO_2-elimination as well as oxygenation of the alveolar blood. On the other hand, in CDH patients factors other than the compression of the hypoplastic ipsilateral lung may be more relevant for hypercapnia and acidosis during thoracoscopy. These factors could include pulmonary hypertension related shunting or ventilation/perfusion mismatch. These correlations taken together with the reduced hypercapnia and acidosis in CDH patients with lower insufflation pressures may propose CO_2 insufflation and absorption as the predominant driver for intraoperative acidosis and hypercapnia in CDH patients, whereas in OA/TOF patients, the necessary ipsilateral lung collapse with subsequent restriction of the oxygen exchange capacity could be the main reason for intraoperative rise in $PaCO_2$ and drop in pH.

Prematurity, low body weight at operation, gender and preoperative haemoglobin may confound the degree of intraoperative acidosis and hypercapnia in minimally invasive surgery. The latter can be adjusted prior to surgery and should always be accounted for when considering thoracoscopy. Our results suggest baseline Hb be inversely correlated with mean $EtCO_2$ and with end-operative $PaCO_2$. These observations might be correlated to the carbic anhydrase in erythrocytes and their CO_2-transport capacity, which amounts to about 75% of

CO_2 transport from body tissue to the alveolar capillaries, although increased cardiac output can to a certain extent compensate anaemia in normovolaemic conditions[31-33]. Since the inverse correlation of anaemia with hypercapnia was weak and is likely affected by several confounders, larger patient numbers or a more homogenous population is needed to further investigate this correlation. On the other hand, our finding corresponds to a report describing the need for blood transfusion to correct CO_2-regulated poor cerebral perfusion associated with anaemia, although a blood transfusion has several physiologic effects besides improvement of CO_2 elimination[17]. In clinical application, low Hb levels might contribute to ineffective CO_2 transport and therefore make patients more prone to hypercapnia during thoracoscopy; conversely, Hb levels physiologic for neonatal age are essential for cerebral oxygenation and in our study were associated with lower $EtCO_2$ and end-operative $PaCO_2$, which may support a more deliberate transfusion practice for these patients.

Reducing insufflation pressures did not prolong surgery duration. Furthermore, duration of the procedure was not correlated with hypercapnia or acidosis, suggesting that duration of thoracoscopy does not increase their risk. The latter is in keeping with earlier findings, where the amount of exhaled CO_2 originating from absorbed medical CO_2 plateaus after about one hour[15]. In addition, significant pulmonary hypertension treated with nitric oxide and/or high frequency oscillatory ventilation in CDH patients may also alter pulmonary capillary perfusion and alveolar ventilation and thus affect CO_2 elimination. However, these conditions were similar in HP and LP group.

In the greater picture, our findings add important information to the ongoing controversy comparing minimally invasive surgery for OA/TOF or CDH to the traditional open approach via thoracotomy. On one hand, the largest multi-institutional retrospective study describing OA with TOF repair by the thoracoscopic approach in 104 patients found that the minimally invasive approach avoided the musculoskeletal complications associated with thoracotomy[34]. Furthermore, a PRISMA-compliant - Preferred Reporting Items for Systematic Reviews and Meta-Analyses[35] - systematic review covering 452 patients reported that thoracotomy and thoracoscopic repair of OA with TOF had similar stricture rate and occurrence of leaks; however, patients operated minimally invasively had a shorter time to extubation, benefitted from earlier enteral feeds and had a shorter hospital stay(8). On the other hand concerns about minimally invasive surgery (thoracoscopy and laparoscopy) for OA/TOF or CDH are based on CO_2 insufflation associated undesired side effects, which include haemodynamic instability, systemic CO_2 absorption[17], restriction of lung capacity and reduction of pulmonary oxygen and carbon dioxide exchange capacity, all of which can lead to acidosis and hypercapnia [12,14,15]. Subsequently, CO_2 insufflation can lead to decreased regional cerebral oxygenation (rcO_2), which in one study has been demonstrated in 17% of patients undergoing thoracoscopic surgery for OA/TOF or CDH[13]; alterations in cerebral oxygenation have been observed to last for up to 24 hours postoperatively. Whether hypercapnia and acidosis leading to decreased cerebral oxygenation have long term effects on the infant's developing brain is still unknown; however, a significant recent study showed no structural, neurodevelopmental or behavioural alterations in rat pups after exposure to thoracic CO_2 insufflation[36].

In patients undergoing minimally invasive CDH repair, the main additional concern besides insufflation related effects is that thoracoscopic CDH repair appears to be associated with a higher recurrence rate[8,37,38]. Some attribute the higher recurrence rate to technical demands or the learning curve[8,39]. However, benefits of MIS were a shorter time to extubation, enteral feeds, hospital stay and less postoperative need of opioids.

This retrospective study has significant limitations. Preoperative blood gas results were only available in a minority of patients in the historical cohort, which precluded a meaningful comparison of the 2 groups regarding preoperative pH and $PaCO_2$. However, these values typically only show small variations among preoperatively stable infants[14,20]. Also, the timing of intraoperative arterial BGA was not standardized or at regular intervals; samples were taken at the discretion of the anaesthetist, and simultaneous $EtCO_2$ was not always recorded. Additionally, there was no measurement of cerebral oxygen saturation and there was no systematic follow up to assess neurologic outcome. Also, since intraoperative cardiovascular parameters were recorded in an analogous fashion, we did not consider them reliable enough to include them in our data analysis. Furthermore, the retrospective nature of our study did not allow to gather reliable data about the ventilatory strategies utilised. While some information about the initial ventilation mode and settings was recorded, we were unable to determine exact changes in ventilatory parameters made during the anaesthetic in order to restore normocapnia or minimise hypercapnia; it thus remains unclear what changes were made to increase alveolar minute ventilation and how they affected our endpoints. Also, ventilation strategies might have changed over the observation period. Current strategies in neonatal ventilation include maintenance of an 'open lung' with avoidance of excessive tidal volumes and excessive oxygen administration[40]. A recent survey provided some evidence that practices are changing, albeit slowly[41]. On one hand, analysing parameters of hypercapnia and acidosis of our CDH and OA + TOF patients during their open repair showed absolutely no difference when comparing historical to more recent patients (time frames corresponding to “historical” or “low pressure” period, respectively). On the other hand, FiO_2 in our LP CDH group was lower than in the HP cohort; this finding could reflect the increased awareness of the possible harm caused by hyperoxia, yet it could also be the result of decreased need of high FiO_2 in associated with lower insufflation pressures. Additionally, we found that CDH patch repair was more common in the LP group than the HP group, which did not prolong procedures in the LP group. Although larger diaphragmatic defect size might have prompted the greater use of patches, the clinically significant increase in numbers is more likely reflecting the institutional practice of the recent years to obtain a dome-shaped, tension free repair, which in our experience appears to reduce the cumbersome high recurrence rate reported earlier[12]. Furthermore, we recognise the limitations of the sample size, especially for the OA-TOF group. A power calculation suggests that to determine whether the apparent difference in peak PaCO2 (2.3 kPa) between the historical group and the low pressure group is significant would require 57 patients in each arm, which we think is unrealistic for a single centre study (alpha=0.05, power = 80%).

In conclusion, to the best of our knowledge, this is the first study to compare higher vs lower intraoperative thoracic insufflation pressures regarding concomitant acidosis and hypercapnia. We found that lowering insufflation pressures results in significant improvement of hypercapnia and acidosis in CDH and it results in decreased $EtCO_2$ in OA/TOF patients while total procedure time remained similar. Furthermore, $EtCO_2$ confirms to be a useful surrogate reflecting pH and $PaCO_2$ and anaemia should be corrected before minimally invasive repair of CDH or OA/TOF.

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Figure Legends

Figure 1: Median nadir pH in patients with congenital diaphragmatic hernia was significantly higher in the low pressure group compared to the historic pressure group (7.20 or 7.03, respectively; #p=0.01).

Figure 2: Lower insufflation pressures in CDH patients were associated with decrease in peak intraoperative $PaCO_2$ and end-operative $PaCO_2$ (Median of 15.7 kPa and 9.6 kPa vs 9.3 kPa and 7.6 kPa, #p=0.002 and §p=0.02, respectively). Peak intraoperative $PaCO_2$ and end-operative $PaCO_2$ in patients with OA/TOF were similar in the historical pressure group compared to the low pressure group. “o” marks an outlier.

Figure 3: In CDH patients lower insufflation pressures did not affect peak end-tidal CO_2 ($EtCO_2$) levels. In patients with OA/TOF median peak $EtCO_2$ in the low pressure group was significantly lower by 29 % compared to the historical pressure group (8.2 kPa vs 5.7 kPa, #p=0.04).

Figure 4: Increased end-tidal CO_2 ($EtCO_2$) levels correlated very well with simultaneously measured acidosis and hypercapnia in CDH patients but not in OA/TOF patients. **A+B)** Intraoperative $EtCO_2$ was inversely correlated with intraoperative pH (p<0.001) in CDH patients but not in OA/TOF patients. **C+D)** Intraoperative $EtCO_2$ was positively correlated with arterial partial pressure of CO_2 ($PaCO_2$; p<0.001) in CDH patients but not in OA/TOF patients.

Figure 5: Poor intraoperative Carrico Index was correlated with acidosis and anaemia was weakly associated with increased end-tidal CO_2 ($EtCO_2$) levels. **A+B)** In OA/TOF patients, the first intraoperative Carrico index was correlated with nadir intraoperative pH (p<0.001) while no correlation was found in CDH patients. **C)** Mean $EtCO_2$ showed a weak yet highly significant inverse correlation with preoperative haemoglobin (Hb; p<0.001).

Table 1: Patient characteristics and perioperative factors (* Data are reported as median and range

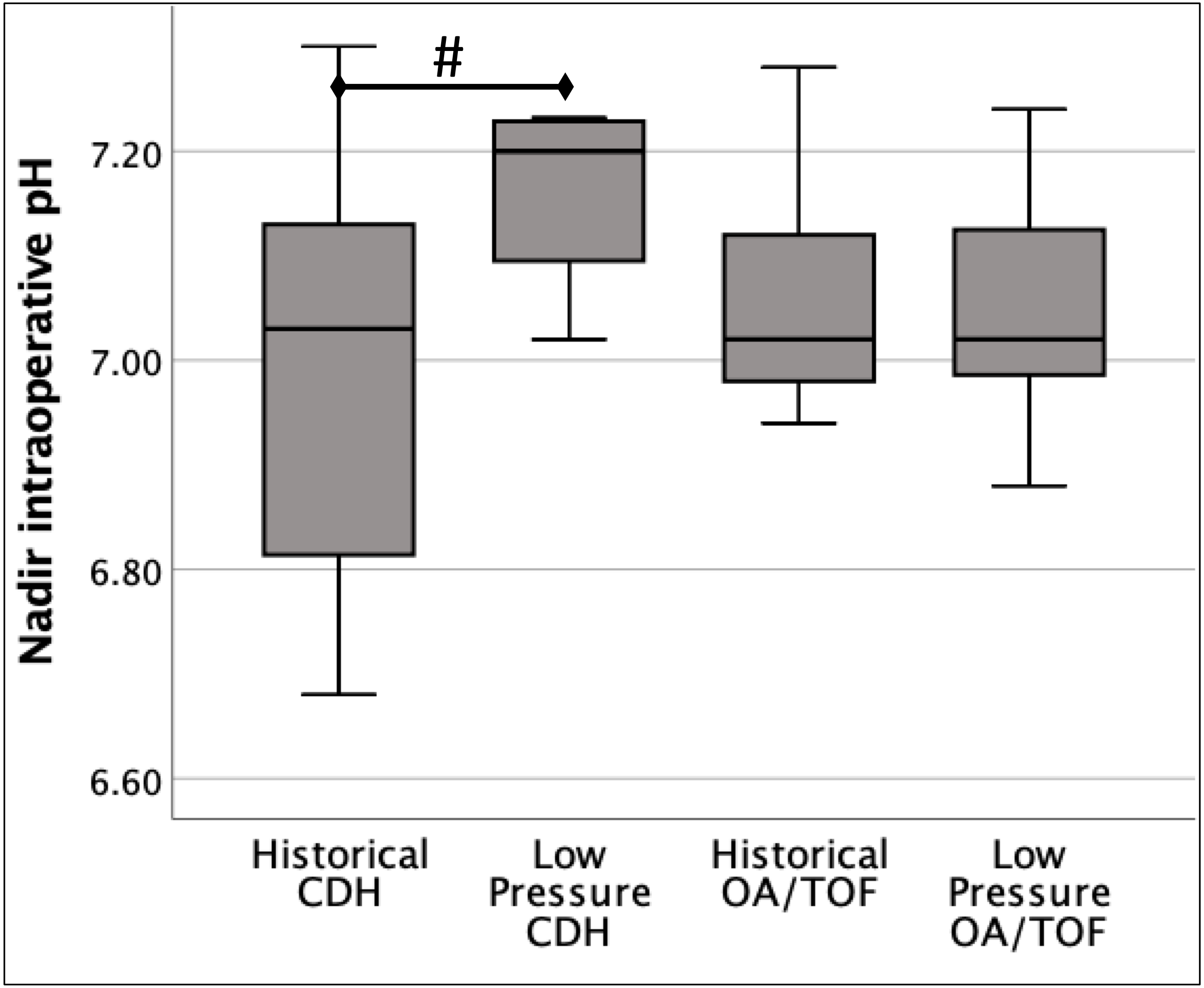
	CDH repair			OA/TOF repair		
	Historical pressure n=15	Low Pressure n=15	p-Value	Historical pressure n=15	Low Pressure n=9	p-Value
Corrected gestational age (weeks+days)*	39+1 (38+1 – 44+2)	39+2 (34+0 – 43+0)	0.82	38+1 (35+5 – 40+4)	39+2 (36+6 – 42+2)	0.13
Weight (kg)*	3.5 (2.4 – 4.2)	3.2 (1.9 – 4.0)	0.16	2.9 (1.8 – 4.2)	3.1 (2.4 – 3.6)	0.80
Preoperative Haemoglobin (g/L)*	139 (92 – 190)	139 (103 – 201)	0.84	165 (138 – 193)	165 (147 – 192)	0.86
Duration of surgery (min)*	128 (50 – 265)	137 (61 -220)	0.81	217 (110 – 260)	285 (148 – 379)	0.10
Insufflation pressure (mmHg)*	8.5 (8 – 9)	6 (5 – 8)	0.06	8 (8 – 10)	6.5 (6 – 7)	0.08
Male to female ratio	10:5	9:6	>0.99	5:10	2:7	>0.99
HFOV	5	2	0.39	0	0	>0.99
Nitric Oxide and HFOV	2	2	>0.99	0	0	>0.99
Use of patch	4	11	0.03	n/a	n/a	n/a

Table 2: Studies addressing intraoperative hypercapnia and acidosis in minimally invasive CDH or OA/TOF repair.

Reference	Year	Study type	Diagnosis	N	Pressure (mmHg)	Findings
Bliss et al (21)	2009	Retrospective	CDH	31	3	No clinically evident compromise from elevated $EtCO_2$ and $PaCO_2$.
McHoney et al (12)	2010	Prospective	CDH	13	5-8	Compared to open repair, thoracoscopic repair had significantly higher peak $EtCO_2$.
Fishman et al (26)	2011	Ambispective	CDH	8	4-10	Discontinuation of insufflation after visceral reduction resulted in similar pH when compared to open repair.
Bishay et al (13)	2011	Prospective	CDH OA/TOF	6 2	5-10	Drop in rcO_2 up to 24 hours after thoracoscopic repair.
Mortellaro et al (25)	2011	Retrospective	CDH OA/TOF	5 12	Not described	Intraoperative HFOV improved CO_2 elimination.
Bishay et al (15)	2013	Randomised control trial	CDH OA/TOF	5 5	5-10	Thoracoscopic repair of CDH was associated with a lower pH compared to open repair.
Tytgat et al (16)	2015	Retrospective	OA/TOF	15	5	The rcO_2 was higher only at induction but normalized and remained normal during and after the operation.
Inoue et al (24)	2016	Retrospective	CDH	8	4	Intrapulmonary percussive ventilation avoided hypercapnia.
Zani et al (14)	2017	Retrospective	CDH OA/TOF	23 14	Not described	More pronounced acidosis thoracoscopic compared to open repair.
Okazaki et al (22)	2017	Retrospective	CDH	23	Not described	Intraoperative HFOV improved CO_2-elimination.
This study	2018	Retrospective	CDH OA/TOF	28 11	2 groups: 5-10 or 4-7, respectively	Decrease in insufflation pressures can reduce $EtCO_2$, $PaCO_2$ and acidosis.

CDH: Congenital diaphragmatic hernia. CO_2: Carbon dioxide. $EtCO_2$: end tidal CO_2. $PaCO_2$: arterial partial pressure of carbon dioxide. OA/TOF: Oesophageal atresia with tracheo-oeosophageal fistula. N: Number of patients. rcO_2: regional cerebral oxygenation. HFOV: High frequency oscillatory ventilation.

Figure 1



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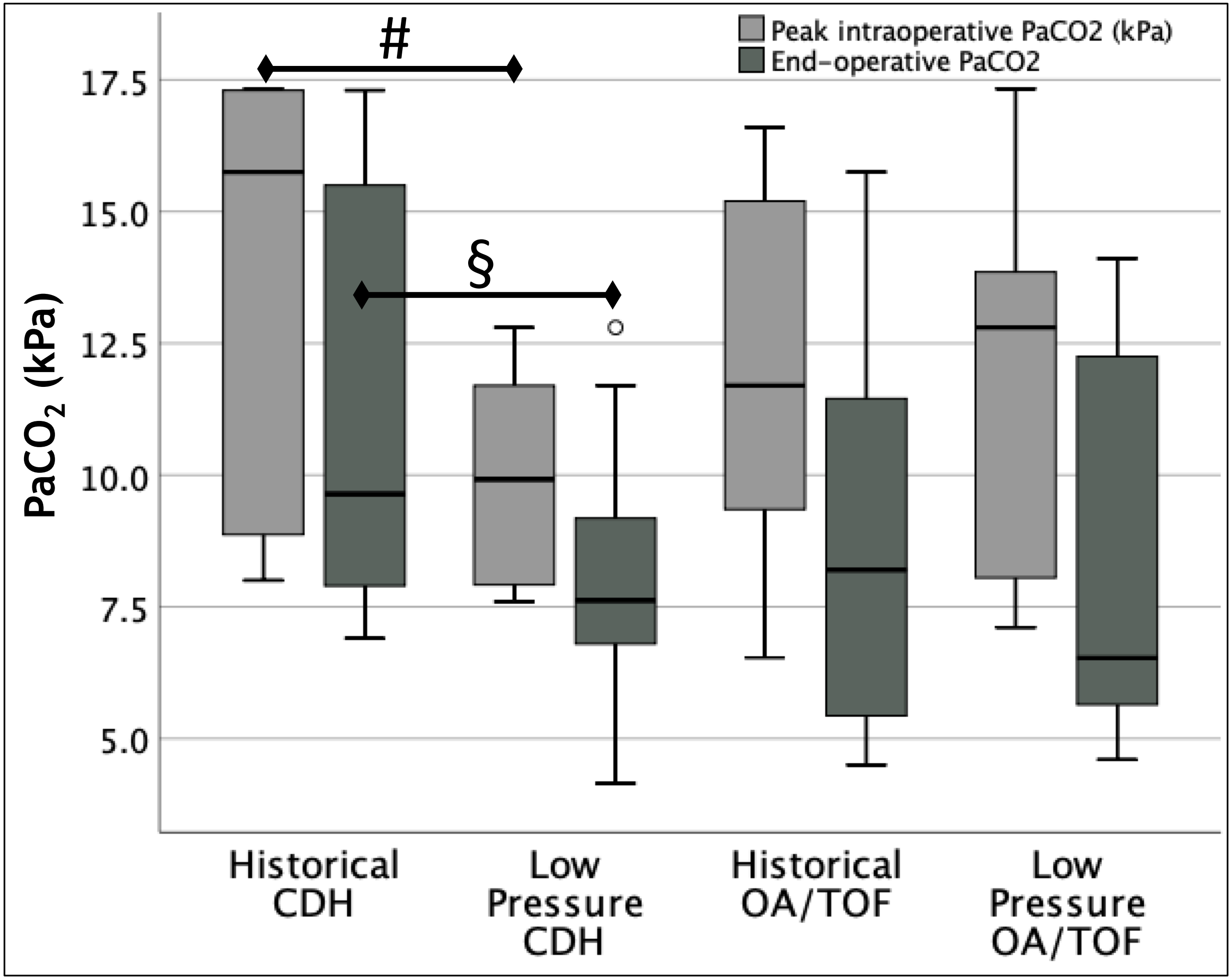

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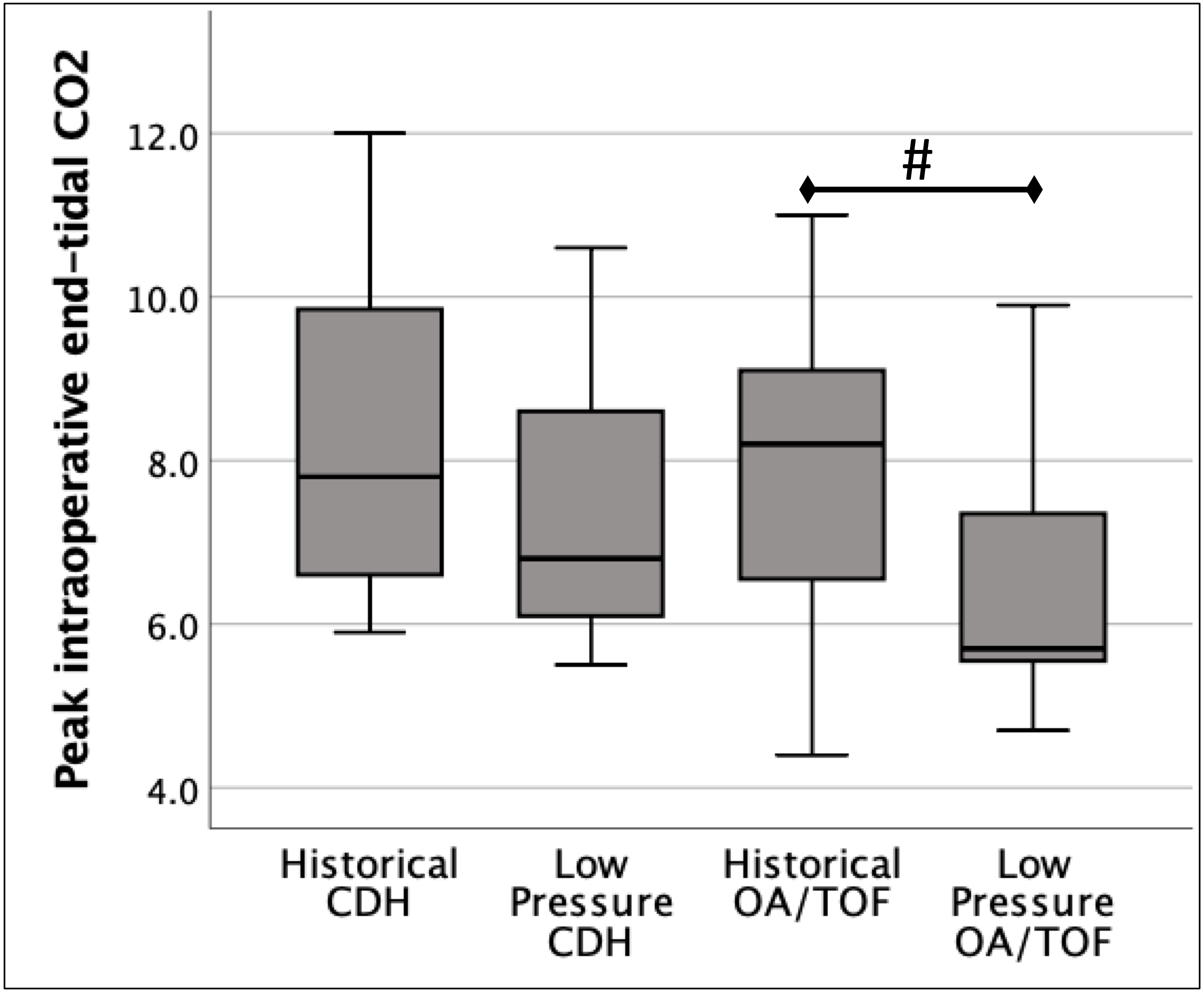

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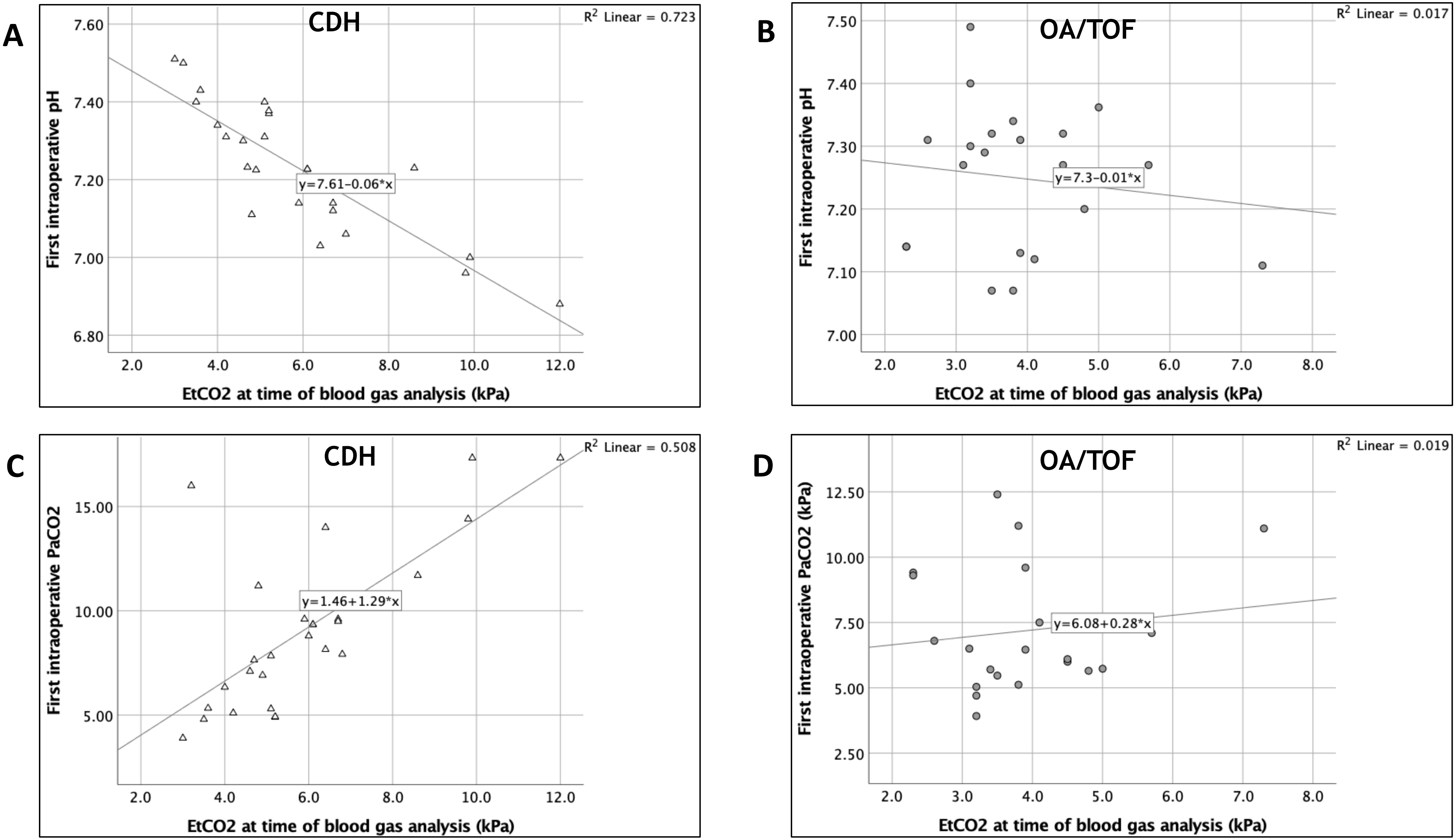

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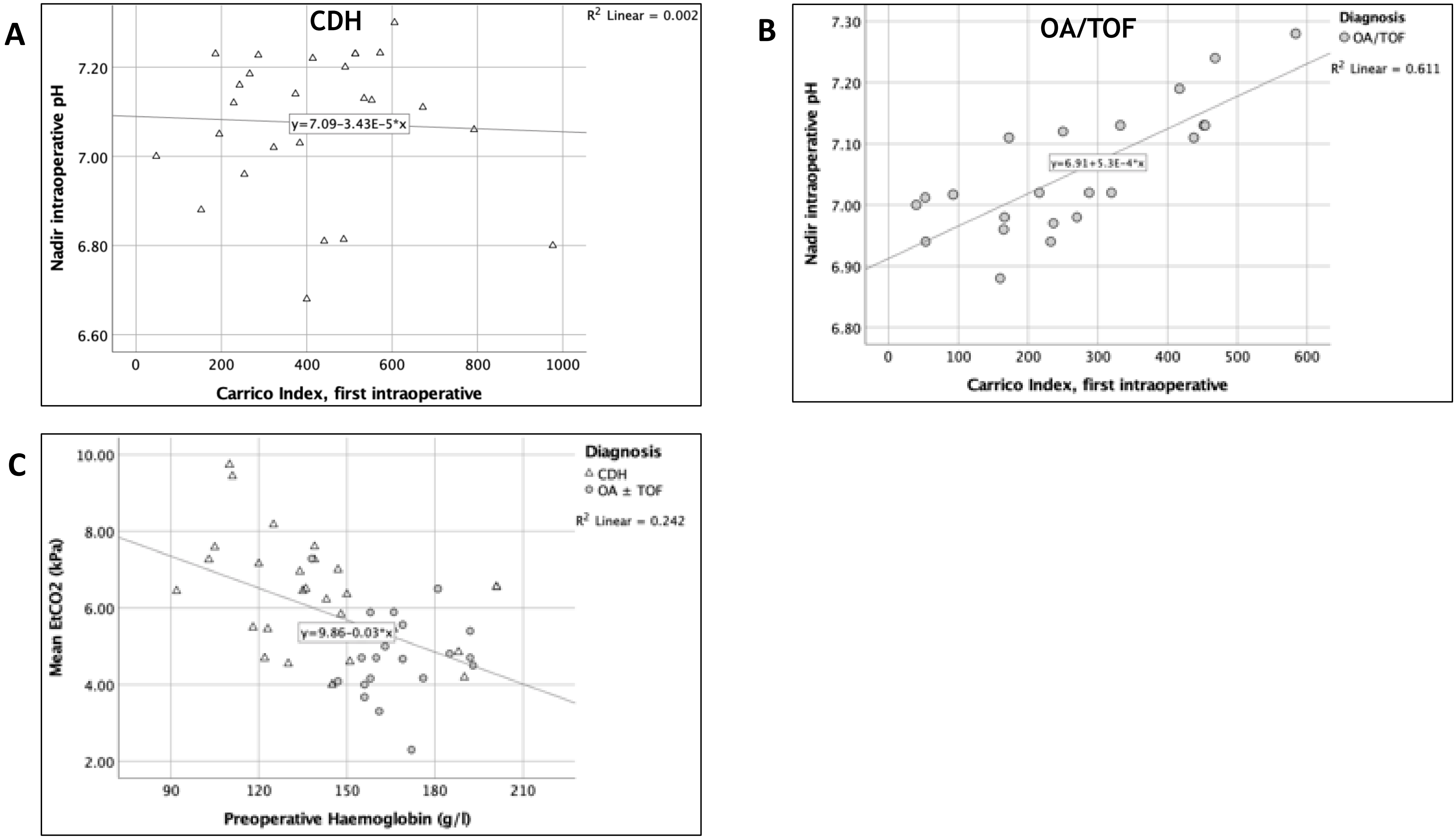

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