



Effect of different ventilation strategies during cardiopulmonary bypass on cardiac de-airing in congenital cardiac surgery: A trans-esophageal echocardiography comparative study

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ABSTRACT

Objectives: This study was conducted to evaluate the efficacy of using either low tidal ventilation or continuous positive pressure ventilation on the quality of de-airing procedure during cardiopulmonary bypass (CPB) surgery for correction of congenital heart diseases.

Patients and methods: This study was conducted on 48 children under the age of 6 years scheduled for elective correction of congenital heart diseases. Patients were randomly allocated into three groups. In the low tidal volume (LTV) group, ventilator was set to a respiratory rate of 5 breaths per minute with tidal volume of 2–3 ml/kg of ideal body weight and a positive end-expiratory pressure of 3–5 cmH₂O. In continuous positive airway pressure (CPAP) group, oxygen flow was maintained at 0.5 L/min during CPB, ventilator was shut off and the adjustable pressure-limiting valve (APL) was set at a pressure of 10 cmH₂O. In the no ventilation (NV) group, ventilator was shut off, fresh flow air was completely stopped and APL was adjusted on spontaneous position. The primary outcome was the total de-airing time using transesophageal echocardiography.

Results: The total de-airing time was significantly decreased in CPAP group, with the shortest duration of 246.88 ± 5.40 sec in comparison to both LTV group with 284.25 ± 6.52 sec and NV group with 452.12 ± 26.6 sec with *p*-value 0.001.

Conclusion: Use of CPAP 10 cmH₂O ventilation during CPB surgery for correction of congenital heart diseases could improve the process of de-airing by decreasing the total time needed to de-air heart chambers.

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1. Introduction

Congenital heart diseases (CHDs) are defined as structural abnormalities of the heart or great vessels existing from birth. [1] During embryological development, the heart is critically malformed, requiring immediate or urgent surgical correction. [2] In cardiac surgery, cardiopulmonary bypass (CPB) is a crucial procedure. It enables surgeons to operate in a bloodless environment while still maintaining blood flow and oxygenation. [3] Although it can result in postoperative atelectasis and pulmonary ischemia-reperfusion damage, apnea during CPB offers the best surgical vision [4]. One of the leading causes of mortality with open cardiac surgery was air embolism; the main source for these air emboli is the pulmonary veins. These residual emboli may lead to ventricular dysfunction, life-threatening arrhythmias, and transient or permanent neurologic deficits; therefore, several de-airing techniques were developed to address this problem, such as bleeding aortotomy, closure of left atrium, needle aspiration of cardiac chamber and posture change; however, evacuation of air through left ventricular vent with Trans-Esophageal Echocardiography (TEE) gained popularity

and devastating effects of air embolism became less common [5]. One of the most important non-invasive tools in cardiac practice is echocardiography. Using a transthoracic echocardiography probe during open heart surgery is challenging and so, by using 2D-mode TEE, it was possible to see pooled air which was primarily located in the pulmonary right upper vein, left atrium, and left ventricle (LV) [6,7]. In the majority of patients having CPB, the anesthesiologist can apply ventilation procedure such as positive end-expiratory pressure (PEEP), continuous positive airway pressure (CPAP), vital capacity maneuvers (VCMs) and low-volume ventilation without interfering the surgical process [8]. The ventilation/perfusion mismatch has improved with the use of CPAP at 10 cmH₂O, as evidenced by decreased pulmonary shunt values and improved gas exchange indices measured after CPB [9]. While the use of low tidal volume (LTV) could minimize inflammatory responses and some unfavorable immunological indicators like Interleukin-10 (IL10) and Tumour Necrotic Factor- α (TNF- α), it could also decrease the incidence of CPB-related lung injury [10]. Comparing the effects of various breathing techniques

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during CPB in congenital heart surgery in children was the aim of the current study as regard total de-airing time. The authors hypothesized that use of either LTV or CPAP during CPB could decrease the total de-airing time as a primary outcome. The secondary outcome measures were pre-ejection de-airing time, post-ejection de-airing time, cross-clamp time, incidence of postoperative complications (pneumonia and atelectasis) and the length of Intensive Care Unit (ICU) and hospital stays.

2. Materials & methods

This prospective randomized study was conducted at Mansoura University Children Hospital from July 2021 to May 2022. The study was approved by the local Mansoura University Institutional Review Board, with code number MD.20.01.266, and it was registered at Pan African Clinical Trial Registry ID PACTR202107745714528. Before surgery, each patient's legal guardians provided written consent that was free from misinformation. The authors recruited 48 children of either sex under the age of 6 years and weighed between 8 and 25 kg and were enrolled for elective correction of CHDs using CPB. Children with contraindication to use TEE (previous esophageal surgery, esophageal fistula, severe coagulopathy, cervical spine disease and mediastinal radiation) were excluded.

2.1. Anesthetic management

Preoperative evaluation of each patient included clinical evaluation, radiographic evaluation and laboratory workup. Transthoracic echocardiography and chest X-ray were done. All were revised during the preoperative visit. On arrival to preoperative room and 15 min before induction, all patients received intramuscular 5 mg/kg ketamine and 0.02 mg/kg atropine sulphate. In the operating room, standard monitoring began with electrocardiogram, non-invasive blood pressure monitoring and oxygen saturation. After induction of anesthesia capnography, invasive intra-arterial pressure, central venous pressure and oral temperature monitoring were connected. Anesthesia was induced with sevoflurane 2 MAC in 50% oxygen. Once the patient lost the consciousness, intravenous line was inserted. Muscle relaxation was achieved by rocuronium 0.9 mg/kg. Then, an oral endotracheal tube of appropriate size was inserted and mechanical ventilation was started before and after CPB in a pressure-controlled mode with pressure that gave tidal volume equaling 6–8 ml/kg of the patient body weight and respiratory rate according to age which maintain end-tidal CO₂ at 35–40 mmHg, and the inspiratory-to-expiratory (I:E) ratio was adjusted at 1:2. An arterial line and central venous catheter was inserted. The oropharynx was then lubricated and an orogastric

tube was inserted to ensure empty stomach then removed. The TEE probe GE Vivid S5 (General Electric VingMed Systems, Horten, Norway) was inserted. Examination was performed by an anesthesiologist who was trained in the intraoperative TEE, and echocardiographic examinations were performed in accordance with the criteria of the Society of Cardiovascular Anesthesiologist [11]. Before skin incision, fentanyl 5 µg/kg was given, maintaining anesthesia with a combination of sevoflurane at MAC 2, ketamine infusion 1 mg/kg/h and muscle relaxant (rocuronium). Heart rate and blood pressure were maintained within 80% of their baseline values. Patients received continuous fentanyl infusion 1 µg/kg/hour. After sternotomy, for all children of all ages and weight, heparin was given in a dose of 300–400 IU/kg through the central venous catheter in order to increase the activated clotting time (ACT) above 480 sec before starting CPB. If the ACT did not reach 480 sec, additional doses of heparin (100 IU/kg) were given to increase the ACT above 480 before instituting CPB. If there was heparin resistance, fresh frozen plasma was given, and then cannulation of ascending aorta and both vena cava was done and patients were ready to go on CPB machine. During the study, patients of all groups received the same cardioplegic solution (Bretschneider HTK solution) at a dose of 50 ml/kg once only (50 ml/kg) for all ages and weight, and this single dose provides myocardial protection for long time up to 3 hours on the CPB machine.

2.2. Randomization

Patients were randomly allocated into three groups during CPB. In the LTV group, the ventilator (Drager, Fabius) was set to a respiratory rate of 5 breaths per minute with a tidal volume of 2–3 ml/kg of ideal body weight and PEEP of 3–5 cmH₂O, while in the CPAP group, the ventilator was shut off, oxygen flow was maintained at 0.5 L/min during CPB and the adjustable pressure limiting valve (APL) was set at a pressure of 10 cmH₂O. In the no ventilation (NV) group, the ventilator was shut off, the fresh gas flow was completely stopped and APL was adjusted on a spontaneous position. The results of randomization were kept in sealed opaque envelopes that were opened by an anesthesiologist who was not involved in the study, while the attending anesthesiologists and surgeons were aware about the allocation.

2.3. De-airing process

After surgical procedure, the de-airing process and weaning from CPB were commenced guided with TEE; if the serum potassium level (K⁺) was less than 6 mmol/dl, a normal body temperature had been established and the ABG was normal and no cardiac

arrhythmia was detected. The lungs were ventilated and de-airing of the LV apex and aortic root was carried out continuously using the vent catheter that was inserted in these locations, and then the aortic cross-clamp was released. The patient was positioned head down, and the surgeon gradually decreased the CPB venous return with gradually filling the heart chambers and de-airing continued while the patient was checked with TEE. De-airing process was carried out until no air emboli were noticed in the left atrium and the heart was allowed to start ejection (pre-ejection de-airing time in seconds before removal of aortic cross clamp). After hemodynamic stability and weaning patient from CPB, TEE monitoring continued till it showed that there were no air emboli in the left side of the heart and the LV vent was stopped (post-ejection de-airing time in seconds). Heparin was reversed with protamine sulphate at a ratio of 1:1.5 to the heparin initial dose to achieve ACT baseline levels. In all patients, hemoglobin was maintained at around 10 gm% postoperatively. Following their transfer to ICU under monitoring, the patients had their chest X-rays taken once every day until their ICU discharge.

2.4. Outcome measures

During the study, the total de-airing time in seconds (pre-ejection de-airing time + post-ejection de-airing time) was recorded as primary outcome while the pre-ejection de-airing time in seconds, post-ejection de-airing time in seconds, CPB time in minutes, the duration of surgery in hours and time needed to extubate patients after surgery in hours were recorded. The criteria of extubation were adequate level of consciousness, hemodynamic stability on minimal inotropic support, absence of hypothermia (core temperature 36°C), minimal bleeding, adequate spontaneous breathing with tidal volume of 5–7 ml/kg and normal arterial blood gases and serum electrolytes. Incidence of postoperative pneumonia and postoperative atelectasis, and length of ICU stays in days were recorded, and criteria of ICU discharge were full consciousness, oral feeding, normal hemodynamics and breathing without support and no need for invasive monitoring. Also, hospital stay in days was recorded, and the criteria for hospital discharge were full consciousness, normal hemodynamic and breathing, removal of mediastinal drainage tubes and good wound healing. All data were collected by anesthesiologists not included in the study protocol.

2.5. Sample size calculation

PASS software of the version 15.0.5 for Windows (2017) was used to determine sample size using data from a pilot study with the total de-airing time as the

primary outcome. To reach 80% power ($1-\beta$), a sample size of 42 patients were required. The total number of patients was increased to 50 patients to compensate for dropout. Data were analyzed using the Statistical Package of Social Science program for Windows (standard version 26). The normality of data was first tested with one-sample Kolmogorov–Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using a chi-square test, while Monte Carlo test was used when expected cell count was less than 5. Continuous variables were presented as mean \pm standard deviation for normally distributed data. The three groups were compared using ANOVA test. The threshold of significance is fixed at 5% level (p -value). The results were considered statistically significant if $p \leq 0.05$.

3. Results

In this study, patients enrollment, randomization, allocation, follow-up and analysis are shown in the flow chart. Fifty children of either sex who had elective cardiac surgery with CPB for correction of CHDs were enrolled and evaluated for eligibility, and 48 patients completed the study after exclusion of two patients who did not meet the inclusion criteria with body weight more than 25 kg (Figure 1). Regarding demographic and anthropometric data among the three studied groups, statistical analysis revealed no significant differences (Table 1). Regarding the type of lesion, statistical analysis revealed no significant differences (Table 2). However, as regard total de-airing time measured with TEE, it showed significant differences among the three examined groups, with more prolonged time of 452.12 ± 26.6 sec in NV group in comparison to both LTV group 284.25 ± 6.52 sec and CPAP group 246.88 ± 5.40 sec which had the shortest time with $p \leq 0.001$ (Table 3). The pre-ejection de-airing time measured with TEE showed significant prolongation of time in the NV group 110.88 ± 8.9 sec in comparison to both LTV group 73.68 ± 3.91 sec and CPAP group 61.75 ± 3.51 sec which had the shortest time with $p \leq 0.001$ (Table 3). Similarly, there were statistically significant differences among the examined groups as regard post-ejection de-airing time measured with TEE, with more prolonged time in NV group 341.25 ± 23.9 sec in comparison to both LTV group 210.56 ± 3.68 sec and CPAP group 185.12 ± 3.09 sec which had the shortest time with $p \leq 0.001$ (Table 3). With regard to the duration of CPB time measured in minutes, cross-clamp time measured in minutes, the duration of surgery measured in hours and time needed to extubate patients after surgery measured in hours, there were no statistically significant differences among the studied groups (Table 4). The frequency of postoperative pneumonia was

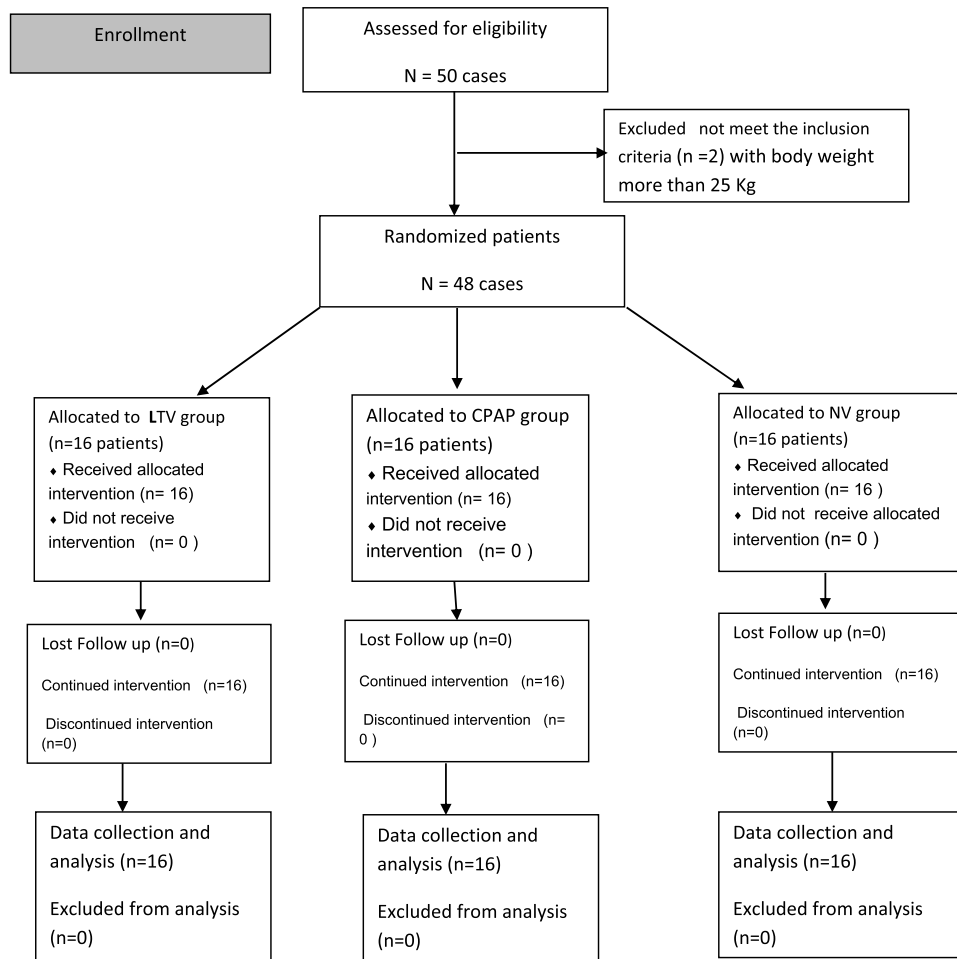


Figure 1. Consort flow diagram.

Table 1. Patient's demographic data and anthropometric measurements.

Variables	LTV group (n = 16)	CPAP group (n = 16)	NV group (n = 16)	Test of significance	P value
Age (month)	25.62 ± 17.49	23.62 ± 17.15	22.18 ± 14.9	F = 0.173	0.841
Gender				$\chi^2 = 0.671$	0.715
Male	10 (62.5%)	8 (50%)	8 (50%)		
Female	6 (37.5%)	8 (50%)	8 (50%)		
Weight (kg)	11.72 ± 2.17	11.06 ± 1.69	11.75 ± 2.31	F = 0.558	0.576
Height (cm)	84.37 ± 9.91	79.37 ± 9.44	82.18 ± 11.1	F = 0.972	0.386
BSA (m ²)	0.524 ± 0.07	0.494 ± 0.06	0.517 ± 0.08	F = 0.665	0.519

Data are expressed as mean ± standard deviation, percentage (%) and numbers (n). Significant $p \leq 0.05$

BSA: body surface area

χ^2 : Chi-square test, F: ANOVA test

Table 2. Type of lesion among the studied groups.

Operations	LTV group (n = 16)	CPAP group (n = 16)	NV group (n = 16)	P value
Tetralogy of Fallot (TOF)	6 (37.5%)	6 (37.5%)	5 (31.2%)	0.74
Ventricular septal defect (VSD)	2 (12.5%)	3 (18.8%)	4 (25.0%)	
Atrial septal defect (ASD)	2 (12.5%)	3 (18.8%)	4 (25.0%)	
Double outlet right ventricle (DORV)	4 (25.0%)	4 (25.0%)	3 (18.8%)	
Ventricular septal defect with mitral stenosis (VSD, MS)	2 (12.5%)	0 (0%)	0 (0%)	

Data are expressed as percentage (%) and number (n).

Significant $p \leq 0.05$

statistically insignificant, although the number of patients who developed pneumonia in CPAP group was 3 (18.8%) and in LTV group, it was 5 (31.2%) compared to 9 (56.2%) in NV group with the p value of 0.078 (Table 5). Similarly, the frequency of post-operative atelectasis was statistically insignificant,

although the number of patients who developed atelectasis in CPAP group was 2 (12.5%) and in LTV group, it was 2 (12.5%) compared to 7 (43.8%) in NV group with the p value of 0.073 (Table 5). With regard to ICU stay time measured in days, no statistical significant difference was noticed among the studied

Table 3. Total de-airing time, pre-ejection de-airing time and post-ejection de-airing time.

Variables	LTV group (n = 16)	CPAP group (n = 16)	NV group (n = 16)	Test of significance	P value
Total de-airing time in sec	284.25 ± 6.52 ♣	246.88 ± 5.40 ¥♣	452.12 ± 26.6	F = 737	≤0.001*
Pre-ejection de-airing time in sec	73.68 ± 3.91♣	61.75 ± 3.51 ¥♣	110.88 ± 8.9	F = 300	≤0.001*
Post-ejection de-airing time in sec	210.56 ± 3.68 ♣	185.12 ± 3.09 ¥♣	341.25 ± 23.9	F = 563	≤0.001*

Data are expressed as mean ± standard deviation. F: ANOVA test, ♣ significant difference compared to NV group, ¥: significant difference compared to LTV group by post hoc LSD test

*Significant $p \leq 0.05$

Table 4. Duration of surgery by hours, time needed to extubate patients after surgery, cross-clamp time and CPB time.

Variables	LTV group (n = 16)	CPAP group (n = 16)	NV group (n = 16)	Test of significance	P value
Duration of surgery (hour)	4.81 ± 0.98	4.50 ± 0.89	4.37 ± 0.62	F = 1.13	0.33
Total extubation time (hour)	18.60 ± 6.02	15.00 ± 5.15	17.56 ± 6.98	F = 1.44	0.247
Cross-clamp time (min)	87.25 ± 30.01	87.18 ± 32.29	86.56 ± 27.8	F = 0.003	0.997
CPB time (min)	115.62 ± 33.6	113.12 ± 33.2	110.94 ± 28.7	F = 0.086	0.917

Data are expressed as mean ± standard deviation. F: ANOVA

Significant $p \leq 0.05$

groups, while hospital stay showed statistically significant decrease in LTV group (6.40 ± 0.91 days) and CPAP group (6.75 ± 0.93 days) compared to 8.25 ± 2.41 days in NV group with the p value of 0.005 (Table 5).

4. Discussion

In the current study, the use of either CPAP or LTV during CPB significantly decreased the total de-airing time in children undergoing elective correction of CHD in comparison to NV group. However, CPAP group had the shortest total de-airing time with better de-airing process and the pre-ejection de-airing time and post-ejection de-airing time were significantly decreased in comparison to LTV and NV groups. Anesthesia for pediatric patients undergoing cardiac surgery involves anesthetizing very small children with CHD for major surgical procedure that requires CPB [12]. Despite advancements in surgical and CPB procedures, systemic air embolism, as detected on TEE, still happens often during open heart surgery. The pulmonary veins are the primary source of these air emboli. After weaning from CPB, these air emboli can still be seen on TEE for up to 28 min [13]. The air trapped in pulmonary vein and heart chambers is expelled to prevent air emboli [14]. Cardiac arrhythmias, cerebral complications and renal and pulmonary failure can result from air emboli [15]. De-airing techniques include venting the heart chambers and the ascending aorta, placing

the patients in the head-down position and at the end of surgery, the patient is rapidly shaken by the surgeon [15]. The complications brought on by air embolism decreased with the use of TEE-guided de-airing techniques [5]. Using LTV during CPB is a cheap and simple method used to prevent prolonged deflation in the lung in patients having cardiac surgery [16]. There have been conflicting experimental and clinical findings about the potential advantages of using CPAP or intermittent ventilation during CPB [17]. Therefore, this study aimed at improving TEE-guided cardiac de-airing procedure after CPB in children with the use of either LTV or CPAP. Although its benefits are still debatable in adults, mechanical ventilation during CPB could be safe according to meta-analysis on 17 trials with 1162 adult patients. [18] In the pediatric surgery, very few studies have been reported. Sasson et al. [19] compared five different forms of mechanical ventilation in 50 children who underwent CPB and no significant clinical improvement was noticed in ventilated patients. In a study by Padalino and colleagues, a total of 140 children below the age of 5 years who had undergone open cardiac surgery due to multiple CHD were included. They used assist-control ventilation with tidal volume of 4 ml/kg, 10 breaths per minute, PEEP of 5 cmH₂O and FiO₂ (0.21) and concluded that continuous low-tidal/low-frequency ventilation used for CPB was safe and easy to use with no harm to pediatric patients. [20] In the current study,

Table 5. Frequency of pneumonia, atelectasis, ICU stay and hospital stay.

Variables	LTV group (n = 16)	CPAP group (n = 16)	NV group (n = 16)	Test of significance	P value
Pneumonia					
Yes	5 (31.2%)	3 (18.8%)	9 (56.2%)	$\chi^2 = 5.1$	0.078
No	11 (68.8%)	13 (81.2%)	7 (43.8%)		
Atelectasis					
Yes	2 (12.5%)	2 (12.5%)	7 (43.8%)	$\chi^2 = 5.89$	0.073
No	14 (87.5%)	14 (87.5%)	9 (56.2%)		
ICU stay (day)	3.47 ± 0.64	3.44 ± 0.63	4.00 ± 1.03	F = 2.52	0.091
Hospital stay (day)	6.40 ± 0.91♣	6.75 ± 0.93♣	8.25 ± 2.41	F = 5.98	0.005*

Data are expressed as mean ± standard deviation or percentage (%) and numbers (n).

ICU: intensive care unit. χ^2 : Chi-square test, F: ANOVA test, ♣ significant difference compared to NV group by post hoc LSD test.

*Significant $p \leq 0.05$.

the total de-airing time, and pre- and post-ejection de-airing times were significantly reduced in CPAP group, with the shortest de-airing time compared to LTV group and lastly NV group which had the prolonged de-airing time. In a study by Mansour et al. [21,22], they conducted randomized, double-blind, prospective clinical trial on 40 patients during CPB and in the control group, ventilator was turned off and APL valve was adjusted at spontaneous mode, while in CPAP group during CPB, after shutting the ventilator off, the oxygen flow was maintained at 0.5 L/min and APL valve was placed at 20 cmH₂O. They found that the mean de-airing time in CPAP group was statistically significantly shorter than in the control group. Interestingly, in our study, we observed that the number of patients who developed pneumonia and atelectasis after surgery was greater in NV group compared to LTV group and CPAP group, although they were statistically insignificant. Zhang et al. [22] evaluated 413 adult patients who underwent elective CPB cardiac surgery. The patients were divided into three groups, NV (no ventilation) group, LOV (LTV and FiO₂ 30%) group and HOV (LTV and FiO₂ 80%) group, and they found no statistical significant differences between the three groups as regard the overall frequency of post-operative pulmonary complications, although the number of patients who developed atelectasis in HOV group was greater than in LOV group and NV group. In our study, we noticed that hospital stay/day significantly decreased in LTV group. Davoudi et al. [23] in their study on the effect of low tidal ventilation during CPB on 100 patient showed that there were no statistically significant differences between LTV and NV, although there was a decrease in the stay time in ICU and total duration of hospitalization and relative costs. The variability of the results in different studies and the current study could be explained by using different measured mechanical ventilation parameters, different anesthetic management, pulmonary function assessment and different included patients.

5. Limitations and recommendations

Limitations of the current study were that the calculated sample size based on total de-airing time was relatively small, it was a single-center study and, finally, the study was done on different congenital heart lesions. So, we recommended that another studies be done in multiple centers with increased number of researched patients to find higher statistical significances with selection of lesion.

6. Conclusion

Use of CPAP at pressure 10 cmH₂O during CPB could improve the process of de-airing by decreasing time needed to de-air heart chambers in children

undergoing elective correction of CHD in comparison to LTV and NV groups.

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Author contribution

Study design, patients recruitment, data collection and analysis were done by Salwa M.S. Hayes, Mohamed Magdy, Ghada A. El Rahamawy and Naglaa A. Elnegeery. Surgical procedure was done by Mohamed A. Elgamal.

Disclosure statement

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