CHAPTER 4 RESULTS

Data were reviewed according to acid-base reading of arterial blood samples obtained once before surgery (baseline), thrice during CPB and once after the surgery (post CPB). Cardiac index of 2.4 was used for the entire study group. Out of 120 procedures with cardiopulmonary bypass, only 21 patients underwent circulatory arrest. In our institution, pH-management (temperature corrected) method was used without carbogen. However for this study, pH-stat management with carbogen intervention was utilized as treatment groups for infants who were undergoing cardiac surgery. All data were analysed using SPSS statistics 17.0 for windows (SPSS Inc., Chicago, IL, USA). Data were reported as mean ± SD and percentages.

4.1 Statistical Analysis

Statistical comparisons were performed with Student's *t* tests by the SPSS statistical software PC package. Statistical process control charts were created using Microsoft Excel (Microsoft Corporation, Redmond, WA). All statistical comparisons were performed on the raw data set. Outcomes were reported as mean ± standard deviation unless otherwise noted. Repeated measurements were used for *p* value analysis according to statistics in plotted table. Since the measurement intervals were uneven, spatial exponential covariance structure was defined in repeated statements. Reported *p* values are as follows: p_{time} indicates change over time, $p_{\text{between groups}}$ indicates a level of difference between groups. The Mann-Whitney *U* test was used to assess the distribution of variables between groups. Pearson correlations were used to test correlations between the variables. The Fisher exact test was used to determine the significance of mortality rates between the groups. Outcome value of $p \leq 0.05$ was regarded as significant in this study.

4.2 Perfusion Data and Patient Demographic

Demographic data are summarized in Table 4.1. Basic patient demographic showed no significant differences within oxygenator groups in height, BSA, CPB duration, aortic cross-clamp time and weight (Minimax Plus) except for weight variable within group of Capiox RX05 oxygenator which shows significant *p* value of 0.006. Weight of Capiox RX05 patient (Crl: 3.4 ± 0.6 vs. Rx: 3.9 ± 0.7) are statistically significant because of uneven distribution of weight group, restricted by single-blind trial, carried throughout this study. A single-blind trial is defined as a study in which only research subjects are blinded to treatment assignment. Thus, the research subjects are kept unaware of whether they are receiving the active intervention or placebo, but investigators and outcome assessors know this information throughout the trial (Paul, 2005). Age variable of both oxygenators are independently significant but this is not the main control parameter to be evaluated and it's only shown as reference. There were no significant different between oxygenator groups, Capiox RX05 and Minimax Plus in all the demographic characteristics except for age (control versus control) group. As shown in this table, infants in the Medtronic Minimax Plus oxygenator group were older than those in the Capiox RX05 oxygenator group. Meanwhile, both control oxygenators groups were older than those in the treatment groups. Circulatory arrest time is total time spent without perfusion. Overall only 17.5% circulatory arrest procedure was performed and majority of those were performed under deep hypothermia. For both oxygenators, circulatory arrest was performed for various types of cases including Ventricular Septal Defect (VSD), Arterial Switch operation (ASO), Total Anomalous Pulmonary Venous Drainage (TAPVD), Truncus Arteriosus Repair and others. Other parameters such as number of patients (30 infants) for each groups and gender of the infants are almost evenly distributed according to the groups.

Table 4.1: Patient demographic data and results[a]

Parameter	Capiox RX05			Medtronic Minimax Plus			*p* value[c]	*p* value[c]
	Crl Group	**Rx Group**	***p* value[b]**	**Crl Group**	**Rx Group**	***p* value[b]**	Crl vs Crl	Rx vs Rx
Number of Patients (*n*)	30	30	-	30	30	-	-	-
Sex (M:F)	19:11	19:11	-	15:15	18:12	-	-	-
Circulatory Arrest (*n*)	8	7	0.770	2	4	0.398	0.038	0.325
Age (days)	391 ± 278	137 ± 151	<0.0001	502 ± 287	381 ± 160	0.049	0.136	<0.0001
Weight (kg)	3.4 ± 0.6	3.9 ± 0.7	0.006	4.3 ± 0.7	4.6 ± 0.6	0.091	<0.0001	<0.001
Height (cm)	54.7 ± 5.7	55.8 ± 7.3	0.514	61.9 ± 6.7	62.6 ± 5.4	0.625	<0.0001	<0.0001
BSA (m^2)	0.22 ± 0.03	0.24 ± 0.04	0.065	0.27 ± 0.04	0.28 ± 0.03	0.331	<0.0001	<0.0001
Duration of CPB (min)	176 ± 62	163 ± 73	0.474	116 ± 58	90 ± 50	0.069	<0.001	<0.0001
Cross-clamp time (min)	100 ± 50	97 ± 48	0.828	66 ± 40	49 ± 36	0.097	0.005	<0.0001
Temp. during CPB (%)								
Mild (33- 35˚C)	0	0	-	0	0	-	-	-
Moderate (25-32˚C)	63%	73%	-	80%	90%	-	-	-
Deep (15 - 20˚C)	37%	27%	-	20%	10%	-	-	-

Control group = Carbogen unused; Treatment group = Carbogen used; [a] Data are presented as mean ± standard deviation; [b] Student's *t* test performed within oxygenator group (Crl vs Rx). [c] Student's *t* test performed between oxygenator groups (Crl vs Crl; Rx vs Rx). Abbreviations: M, male; F, female; BSA, body surface area; CPB, duration of cardiopulmonary bypass; Temp., temperature.

Mild hypothermia cases were excluded from this study. Moderate hypothermia (77%) and deep hypothermia (23%) during CPB were investigated for this study. These hypothermic conditions are not evenly distributed and majority falls under category of moderate hypothermia for both oxygenators. However, Capiox RX05 have higher number of deep hypothermia (32%) compared to Minimax Plus which have only 15%.

Table 4.2 and Figure 4.1 showed the proportion of cases performed overall in this study according type of oxygenators; divided into control and treatment. Minimax Plus treatment group have the highest number of VSD case performed 53% (16 cases). Cases that were mostly performed for Minimax Plus control group are VSD Repair + Combine procedures 40% (12 cases). Where else, for Capiox RX05 control group, ASO were performed highest 30% (9 cases) and for Capiox RX05 treatment group 27% (8 cases) of ASO were performed. TAPVD, Truncus Arteriosus repair and ASO + VSD were least performed cases overall for both oxygenators. Compare to the Minimax Plus group, the Capiox RX05 group contained more ASO and Truncus Arteriosus repair on patients.

Figure 4.2 shows type of surgery distributed for overall (n=120) four groups. More than one quarter of the surgery for this study are dominated by combine procedure with VSD (30%) and one quarter more by VSD alone (26%). Since, this study have excluding factor that limits the CPB time and other factor in conjunction, many cases falls into category of case that showed in figure 4.2. 30% of the surgeries are VSD with combine procedure including cases such as VSD + Patent ductus arteriosus (PDA), VSD + Coarctation of the aorta, VSD + Atrial septal defect (ASD), VSD + Arch repair and etc. Arterial switch operation (ASO) is the third highest case done (16%) in this study. TAPVD case were performed 4% overall. 3% of this study occupied by two different surgeries namely Truncus Arteriosus Repair and ASO + VSD respectively. Other cases were performed at 18% including Anomalous left coronary artery from the

pulmonary artery (ALCAPA), Atrioventricular septal defect (AVSD), Atrioventricular canal canal defect (AVCD), Interrupted aortic arch (IAA) repair, Atrial septectomy, Right ventricle to pulmonary artery (RV to PA) conduit, Atrial septal defect (ASD) and combination of these surgeries.

Table 4.2: Type of surgery performed in two different type of oxygenator which further divided into control and treatment.

Type of Surgery	**Capiox (Crl)**	**Capiox (Rx)**	**Minimax (Crl)**	**Minimax (Rx)**
VSD Repair	3%	20%	27%	53%
Arterial Switch Operation	30%	27%	7%	0%
TAPVD	6%	3%	3%	3%
VSD Repair + Combine procedures	30%	23%	40%	27%
Truncus Arteriosus Repair	7%	7%	0%	0%
Arterial Switch Op + VSD Repair	7%	0%	3%	0%
Others	17%	20%	20%	17%
Total	100%	100%	100%	100%

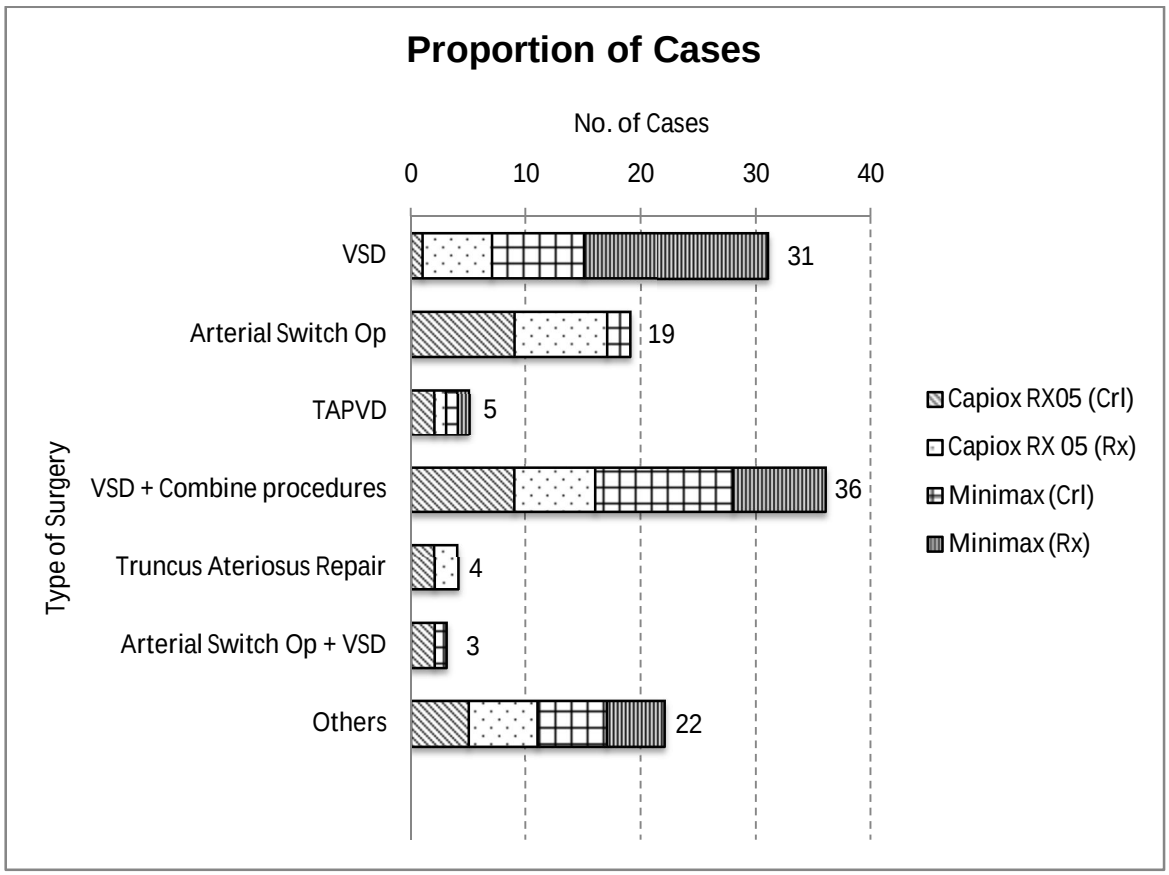


Figure 4.1: Proportion of cases according to oxygenators groups. Oxygenators that not stated in stacked bar are equal to zero according to type of surgery.

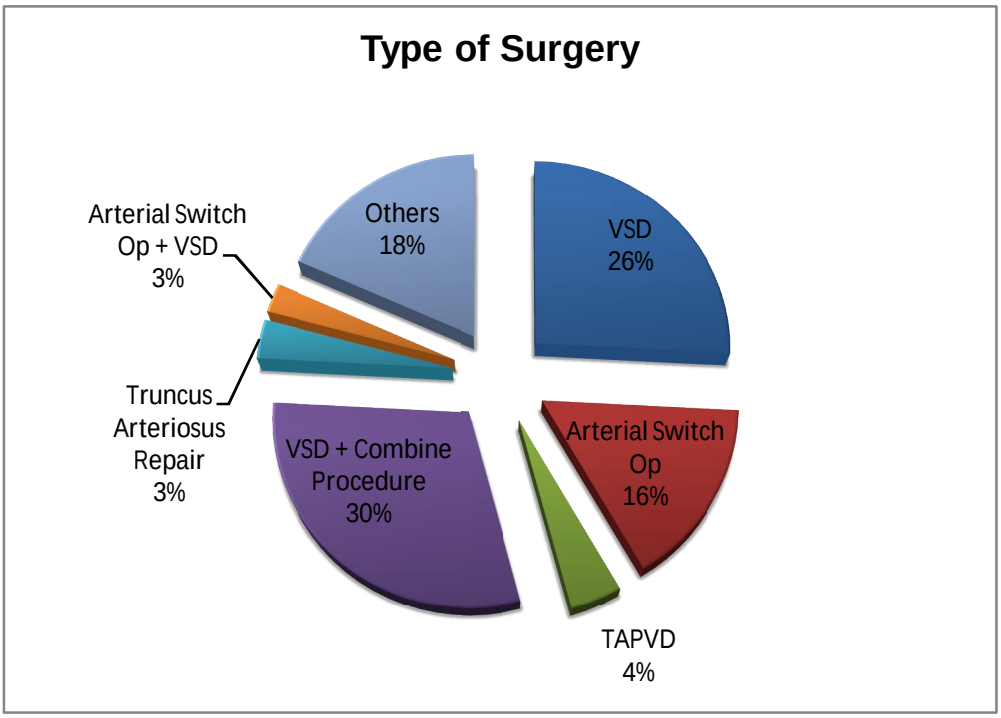


Figure 4.2: Pie-chart shows overall case distribution (*n* = 120). VSD, Ventricular Septal Defect; TAPVD, Total Anomalous Pulmonary Venous Drainage.

4.3 Comparison of the Study Groups

Hundred and twenty infants comprised both study groups (Capiox RX05 and Medtronic Minimax Plus), sixty for each oxygenators. These sixty infants for each oxygenator are further divided into control and treatment, thirty for each group. Table 4.3 (a) shows physiologic variables which describes variables within oxygenator (intra) namely Capiox RX05 (control versus treatment) and Minimax Plus (control versus treatment). Meanwhile, table 4.3 (b) shows physiologic variables describing between oxygenators (inter) namely Capiox RX05 and Minimax Plus (control versus control) and (treatment versus treatment). Five different study period (baseline, cooling, stable, rewarming and post CPB) values are evaluated, which were similar in baseline (within oxygenator) for nasopharyngeal temperature, arterial pH, $PaCO_2$, pump flow and haematocrit.

Each oxygenator (Capiox RX05 and Minimax Plus) contain control and treatment groups. This control group were compared among the treatment group shown in table 4.3 (a) describes statistical analysis using repetitive measurements to obtain *p* value within oxygenator group ($p_{\text{between groups}}$) and along five different study period (p_{time}). The *p* value within oxygenator group shows only partial pressure of carbon dioxide ($PaCO_2$) was statistically significant ($p_{\text{between groups}} = 0.008$) for Capiox RX05 (control versus treatment). The main contributing factor for $PaCO_2$ significant might be because of weight dissimilarity ($p = 0.006$) within Capiox RX05 (control versus treatment). This indirectly shows that Capiox RX05 needs carbogen intervention to maintain the pH-stat management for patient care with CPB. Lesser weight patients may need higher carbogen intervention to regulate the $PaCO_2$ which is also associated to the lowest temperature the patient were cool-down during CPB. Age group are varying among oxygenator groups but this might not be a contributing factor directly to $PaCO_2$ value.

Table 4.3 (a): Physiologic variables describing within oxygenator Capiox RX05 or Minimax Plus (Control versus Treatment) during five study period.

Variables	**Oxygenator**	**Prebypass (Baseline)**	**Cardiopulmonary Bypass**			**Post CPB**	***p* Value Between Groups**	***p* Time**
		I	**II**	**III**	**IV**	**V**		
Nasopharyngeal Temperature (˚C)	Capiox (Crl)	36.2 ± 0.45	27.6 ± 3.56	24.7 ± 4.16	33.2 ± 2.53	35.5 ± 0.30	0.144	<0.0001
	Capiox (Rx)	35.7 ± 1.01	29.3 ± 3.62	26.9 ± 4.19	33.1 ± 2.07	35.3 ± 0.57		
	Minimax (Crl)	36.3 ± 0.39	30.7 ± 3.82	28.2 ± 4.59	33.5 ± 2.05	35.7 ± 0.31	0.180	<0.0001
	Minimax (Rx)	36.1 ± 0.58	32.4 ± 2.19	29.1 ± 3.56	33.7 ± 1.03	35.4 ± 0.41		
Arterial pH	Capiox (Crl)	7.40 ± 0.11	7.50 ± 0.12	7.48 ± 0.12	7.42 ± 0.11	7.34 ± 0.10	0.083	<0.0001
	Capiox (Rx)	7.37 ± 0.14	7.46 ± 0.10	7.43 ± 0.08	7.43 ± 0.08	7.34 ± 0.10		
	Minimax (Crl)	7.40 ± 0.11	7.46 ± 0.15	7.43 ± 0.12	7.38 ± 0.10	7.33 ± 0.11	0.791	<0.0001
	Minimax (Rx)	7.40 ± 0.11	7.44 ± 0.08	7.40 ± 0.09	7.41 ± 0.07	7.36 ± 0.07		
$PaCO_2$ (mmHg)	Capiox (Crl)	41.0 ± 11.61	26.7 ± 9.27	22.4 ± 7.77	32.3 ± 10.38	43.6 ± 10.67	0.008	<0.0001
	Capiox (Rx)	46.1 ± 18.92	30.7 ± 7.99	32.1 ± 6.86	33.1 ± 5.04	43.4 ± 11.19		

	Minimax (Crl) Minimax (Rx)	40.6 ± 15.83 43.4 ± 20.32	26.3 ± 7.47 30.4 ± 8.25	29.5 ± 10.20 33.1 ± 8.74	34.4 ± 7.85 35.9 ± 7.54	47.8 ± 15.71 43.1 ± 7.71	0.354	<0.0001
Pump flow (L/min)	Capiox (Crl) Capiox (Rx)	No flow No flow	0.62 ± 0.15 0.60 ± 0.16	0.54 ± 0.13 0.57 ± 0.15	0.58 ± 0.14 0.64 ± 0.13	No flow No flow	0.474	<0.001
	Minimax (Crl) Minimax (Rx)	No flow No flow	0.78 ± 0.16 0.80 ± 0.15	0.73 ± 0.14 0.81 ± 0.14	0.82 ± 0.15 0.83 ± 0.14	No flow No flow	0.245	0.002
Hematocrit (%)	Capiox (Crl) Capiox (Rx)	39.1 ± 6.14 37.9 ± 4.99	29.7 ± 4.59 29.3 ± 4.15	28.8 ± 4.59 30.4 ± 5.04	34.1 ± 5.06 32.8 ± 5.16	36.3 ± 6.01 34.0 ± 4.77	0.306	<0.0001
	Minimax (Crl) Minimax (Rx)	34.8 ± 5.41 37.2 ± 5.33	25.7 ± 4.04 26.7 ± 4.25	26.3 ± 4.78 27.4 ± 4.94	31.8 ± 6.01 29.6 ± 4.66	35.6 ± 6.19 34.1 ± 5.07	0.833	<0.0001

All values are shown as mean ± standard deviation. Abbreviations: $PaCO_2$, arterial CO_2 partial pressure; Crl, control; Rx, treatment; CPB, Cardiopulmonary bypass. I = baseline; II = cooling; III = stable; IV = warming; V = post CPB.

p_{time} = change over time; $p_{between\ groups}$ = level of difference between groups.

Other variables such as nasopharyngeal temperature, arterial pH, pump flow and haematocrit shows no significant difference within oxygenator group. However, for five study period namely pre-bypass (baseline), cooling, stable, rewarming and post CPB the repetitive measurement ($p_{\text{time/change over time}}$) was significantly different. This shows that the study period follows a different stage of variable management during each period. Each period requires careful hemodynamic or physiologic titration to maintain pH-stat management.

Table 4.3 (b) shows the same variables as discussed above compared between inter-oxygenators (Capiox RX05 and Minimax Plus) for control versus control and treatment versus treatment. Significant data values are achieved for *p* value between oxygenators ($p_{\text{between groups}}$) for variables such as nasal temperature (Crl vs. Crl) *p* value of <0.001 and (Rx vs. Rx) *p* value of <0.0001. For arterial pH only (Crl vs. Crl) shows a *p* value of 0.032 which is statistically significant. Pump flow shows a significant *p* value of <0.0001 for both (Crl vs. Crl) and (Rx vs. Rx). Haematocrit variable shows (Crl vs. Crl) group achieve *p* value of <0.0001 and (Rx vs. Rx) group of $p = 0.021$. $PaCO_2$ comparison between oxygenators does not show a statistically significant different (Crl vs. Crl) $p = 0.066$ and (Rx vs. Rx) $p= 0.066$. Nevertheless, the p_{time} value during five study period shows statistically significant value $p<0.0001$ for all the variables. Comparison between oxygenators might not be relevant in this study since the statistically significant value in demographic data between Capiox 05 and Minimax Plus.

Table 4.3 (b): Physiologic variables describing between oxygenator Capiox RX05 and Minimax Plus (Control versus Control) and (Treatment versus Treatment) during five study period.

Variables	**Oxygenator**	**Prebypass (Baseline)**	**Cardiopulmonary Bypass**			**Post CPB**	***p* Value Between Groups**	***p* Time**
		I	**II**	**III**	**IV**	**V**		
Nasopharyngeal Temperature (˚C)	Capiox (Crl)	36.2 ± 0.45	27.6 ± 3.56	24.7 ± 4.16	33.2 ± 2.53	35.5 ± 0.30	<0.001	<0.0001
	Minimax (Crl)	36.3 ± 0.39	30.7 ± 3.82	28.2 ± 4.59	33.5 ± 2.05	35.7 ± 0.31		
	Capiox (Rx)	35.7 ± 1.01	29.3 ± 3.62	26.9 ± 4.19	33.1 ± 2.07	35.3 ± 0.57	<0.0001	<0.0001
	Minimax (Rx)	36.1 ± 0.58	32.4 ± 2.19	29.1 ± 3.56	33.7 ± 1.03	35.4 ± 0.41		
Arterial pH	Capiox (Crl)	7.40 ± 0.11	7.50 ± 0.12	7.48 ± 0.12	7.42 ± 0.11	7.34 ± 0.10	0.032	<0.0001
	Minimax (Crl)	7.40 ± 0.11	7.46 ± 0.15	7.43 ± 0.12	7.38 ± 0.10	7.33 ± 0.11		
	Capiox (Rx)	7.37 ± 0.14	7.46 ± 0.10	7.43 ± 0.08	7.43 ± 0.08	7.34 ± 0.10	0.770	<0.0001
	Minimax (Rx)	7.40 ± 0.11	7.44 ± 0.08	7.40 ± 0.09	7.41 ± 0.07	7.36 ± 0.07		
$PaCO_2$ (mmHg)	Capiox (Crl)	41.0 ± 11.61	26.7 ± 9.27	22.4 ± 7.77	32.3 ± 10.38	43.6 ± 10.67	0.066	<0.0001
	Minimax (Crl)	40.6 ± 15.83	26.3 ± 7.47	29.5 ± 10.20	34.4 ± 7.85	47.8 ± 15.71		

	Capiox (Rx) Minimax (Rx)	46.1 ± 18.92 43.4 ± 20.32	30.7 ± 7.99 30.4 ± 8.25	32.1 ± 6.86 33.1 ± 8.74	33.1 ± 5.04 35.9 ± 7.54	43.4 ± 11.19 43.1 ± 7.71	0.941	<0.0001
Pump flow (L/min)	Capiox (Crl) Minimax (Crl)	No flow No flow	0.62 ± 0.15 0.78 ± 0.16	0.54 ± 0.13 0.73 ± 0.14	0.58 ± 0.14 0.82 ± 0.15	No flow No flow	<0.0001	<0.0001
	Capiox (Rx) Minimax (Rx)	No flow No flow	0.60 ± 0.16 0.80 ± 0.15	0.57 ± 0.15 0.81 ± 0.14	0.64 ± 0.13 0.83 ± 0.14	No flow No flow	<0.0001	0.006
Hematocrit (%)	Capiox (Crl) Minimax (Crl)	39.1 ± 6.14 34.8 ± 5.41	29.7 ± 4.59 25.7 ± 4.04	28.8 ± 4.59 26.3 ± 4.78	34.1 ± 5.06 31.8 ± 6.01	36.3 ± 6.01 35.6 ± 6.19	<0.0001	<0.0001
	Capiox (Rx) Minimax (Rx)	37.9 ± 4.99 37.2 ± 5.33	29.3 ± 4.15 26.7 ± 4.25	30.4 ± 5.04 27.4 ± 4.94	32.8 ± 5.16 29.6 ± 4.66	34.0 ± 4.77 34.1 ± 5.07	0.021	<0.0001

All values are shown as mean ± standard deviation. Abbreviations: $PaCO_2$, arterial CO_2 partial pressure; Crl, control; Rx, treatment; CPB, Cardiopulmonary bypass. I = baseline; II = cooling; III = stable; IV = warming; V = post CPB.

p_{time}= change over time; $p_{\text{between groups}}$ = level of difference between groups.

4.4 Multivariate Analysis

Multivariate analysis involves observation and analysis of more than one statistical variable at a time. In design and analysis, the techniques are used to perform studies across multiple dimensions while taking into account the effects of all variable on the responses of interest. Regression can be extended to non-linear relationships and to more than two variables. In this study more than two variables approach is utilised. Regression was a method of estimating a numerical relationship. Regression was both descriptive and predictive. Regression also provides a means of prediction of the value of variable *x* and calculation of the associated confidence interval. The square of the correlation (r^2), or the 'coefficient of determination', represents the proportion of the variability which was explained by the regression model. It's a measure of the goodness of fit of a particular model (Alan, 1999). There are a linear relationship between $PaCO_2$ and temperature gradients which are shown in straight line through the points are used to summarize the data. Simple linear regression formula $y = a + bx$ used in for this model, where *a* were the intercept (value for *y* when $x = 0$) and b is the slope or regression coefficient (amount by which *y* increases for unit increase in *x*). On regression of these data, $PaCO_2$ showed a weak correlation with the change in temperature in general [Figure 4.3 (a) & (b)]. The formula derived from Capiox RX05 (control) are $PaCO_2 = 0.72x + 7.0$ (where *x* were temperature in ˚C). The correlation coefficient for Capiox RX05 control group is 0.17 that were 2.9% of the variability was explained by the model. The linear regression analysis graph shows statistically significant *p* value of 0.00006 without carbogen treatment because pCO_2 levels are hard to be maintain along the normal range. The formula derived from Capiox RX05 (treatment) are $PaCO_2 = 0.25x + 24.6$. The correlation coefficient for Capiox RX05 treatment group is 0.04 that is 0.2% of the variability is explained by the model.

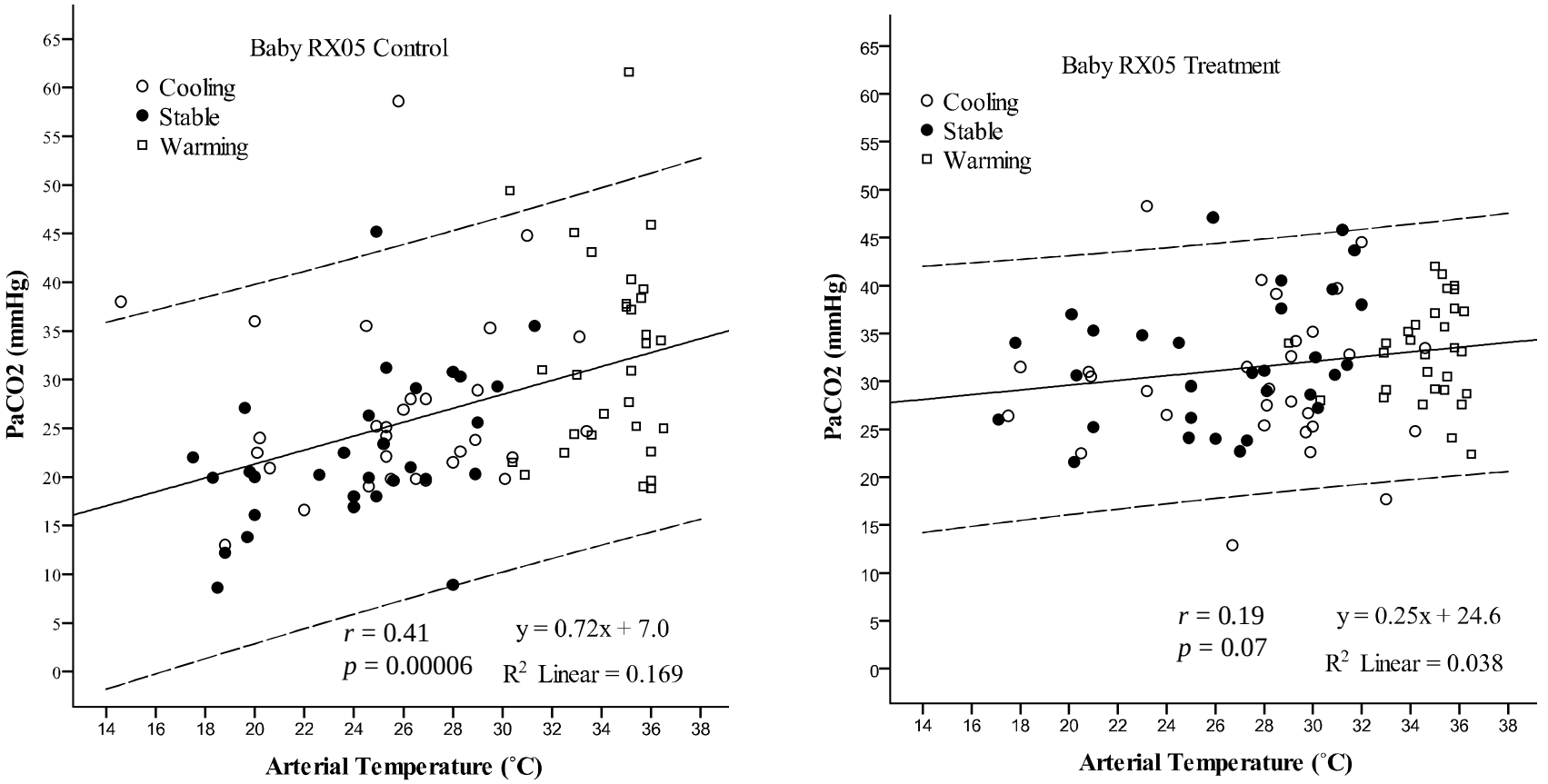


Figure 4.3 (a): Linear regression analysis of temperature and the $PaCO_2$ in infant (n = 30; repeated measurements = 3 times) undergoing temperature changes during CPB using Capiox RX05. Shown are individual data points with the best fitted line (solid line) to $y = a + bx$ along with 95% confidence intervals (dashed lines). The legend depicts that status of temperature management during CPB when the data point was observed.

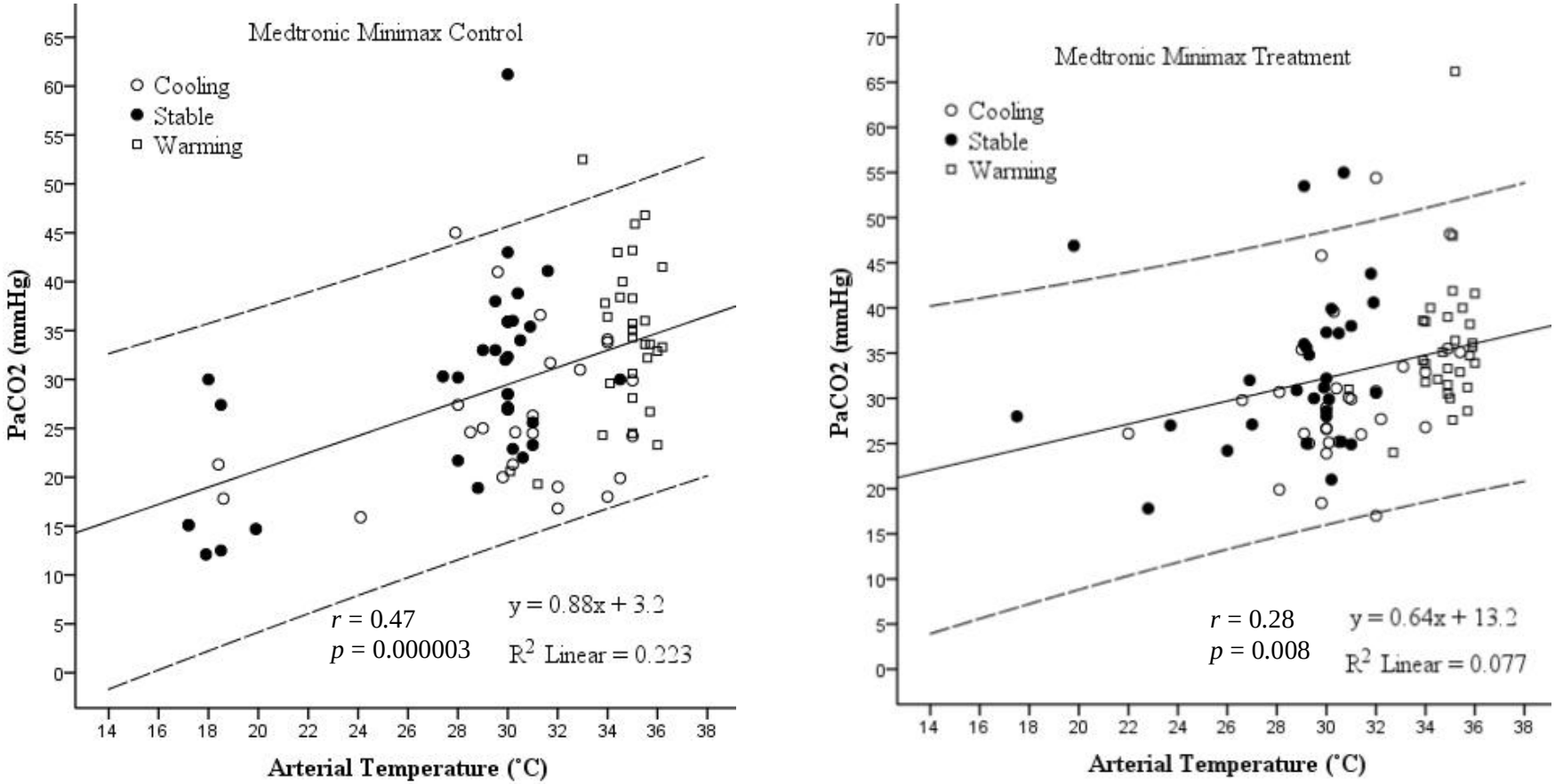


Figure 4.3 (b): Linear regression analysis of temperature and the $PaCO_2$ in infant (n = 30; repeated measurements = 3 times) undergoing temperature changes during CPB using Minimax Plus. Shown are individual data points with the best fitted line (solid line) to $y = a + bx$ along with 95% confidence intervals (dashed lines). The legend depicts that status of temperature management during CPB when the data point was observed.

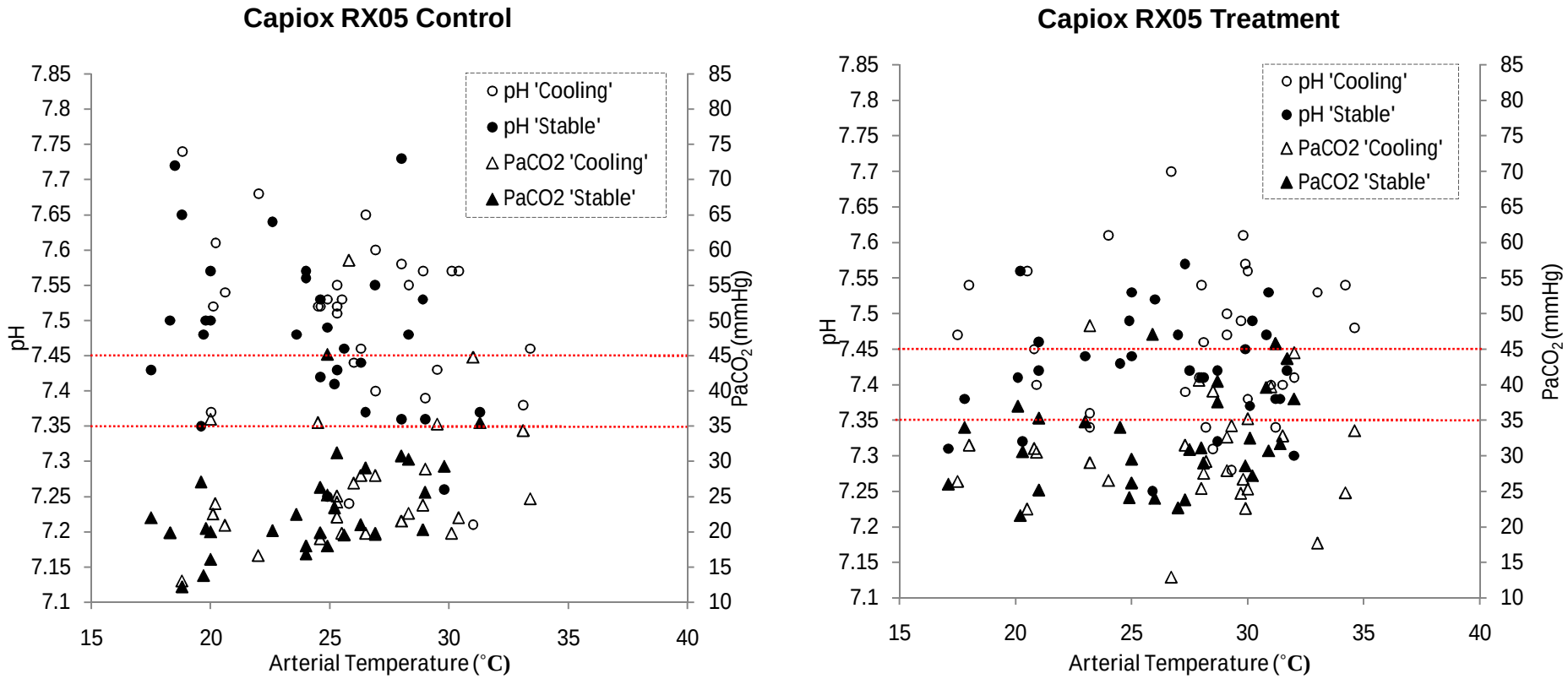
The linear regression analysis graph shows statistically not significant *p* value of 0.07 with carbogen treatment because pCO_2 levels are maintain along the normal range.

Meanwhile, formula derived from Minimax Plus (control) are $PaCO_2 = 0.88x + 3.2$. The correlation coefficient for Minimax Plus control group is 0.22 that is 4.8% of the variability is explained by the model. The linear regression analysis graph shows statistically significant *p* value of 0.000003 without carbogen treatment because pCO_2 levels are hard to be maintain along the normal range. The formula derived from Minimax Plus (treatment) are $PaCO_2 = 0.64x + 13.2$. The correlation coefficient for Minimax Plus treatment group is 0.08 that is 0.6% of the variability is explained by the model. The linear regression analysis graph shows statistically significant *p* value of 0.008 with carbogen treatment because pCO_2 levels are hard to be maintain along the normal range. This result shows that Minimax Plus hard to be maintain the PCO_2 level but this might be bias according to temperature that favours along moderate hypothermia that deep hypothermia. When numbers are small, the sampling variation for a correlation coefficient is surprisingly large and the confidence interval (CI) correspondingly wide. In this study all CI are calculated according to 95%. The numbers for all four groups are small suggesting parameters of a regression equation may be highly influenced by the inclusion of an outlier, which then qualifies as an 'influential point'. This regression model used only for part of data that excludes an influential outlier.

4.5 Analysis of the range of pH and $PaCO_2$

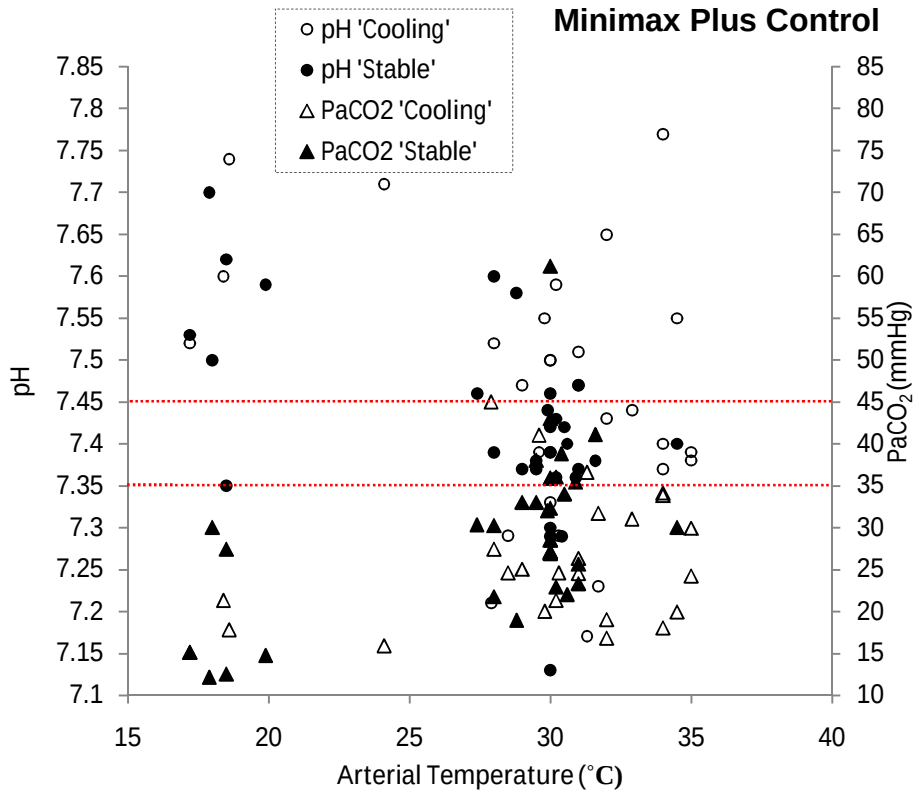
This study establishes the direct relationship between $PaCO_2$ partial pressure and temperature gradient during CPB without the effects of mechanical ventilation and patient's pulmonary vasculature. With the continuous measurement of arterial blood gas with two different monitoring devises namely CDI 500 and capnography (CPB oxygenator expired CO_2 monitoring device), it was possible to continuously predict $PaCO_2$ in the cooling, stable and rewarming phases of CPB. Figure 4.4 (a) shows the difference between control and treatment groups of Capiox RX05 oxygenator exploring relationship within temperature, pH and $PaCO_2$ in infant (n = 30; repeated measurements = 2 times) undergoing temperature changes during two stages namely cooling and stable period. All relationship was cross-referred with reference range and percentage was counted. There is significant difference between control and treatment group in Capiox RX05 oxygenator within two variable $PaCO_2$ (p<0.0001) and pH (p = 0.0147). When going onto CPB, cooling and stable phrase were investigated for $PaCO_2$ level between control group (reference range: 7%; *outré*: 93%) and treatment group (reference range: 18%; *outré*: 82%). On the other hand, pH level between control group (reference range: 27%; *outré*: 73%) and treatment group (reference range: 40%; *outré*: 60%). This shows that treatment of carbogen does improve percentage within reference range in Capiox RX05 oxygenator.

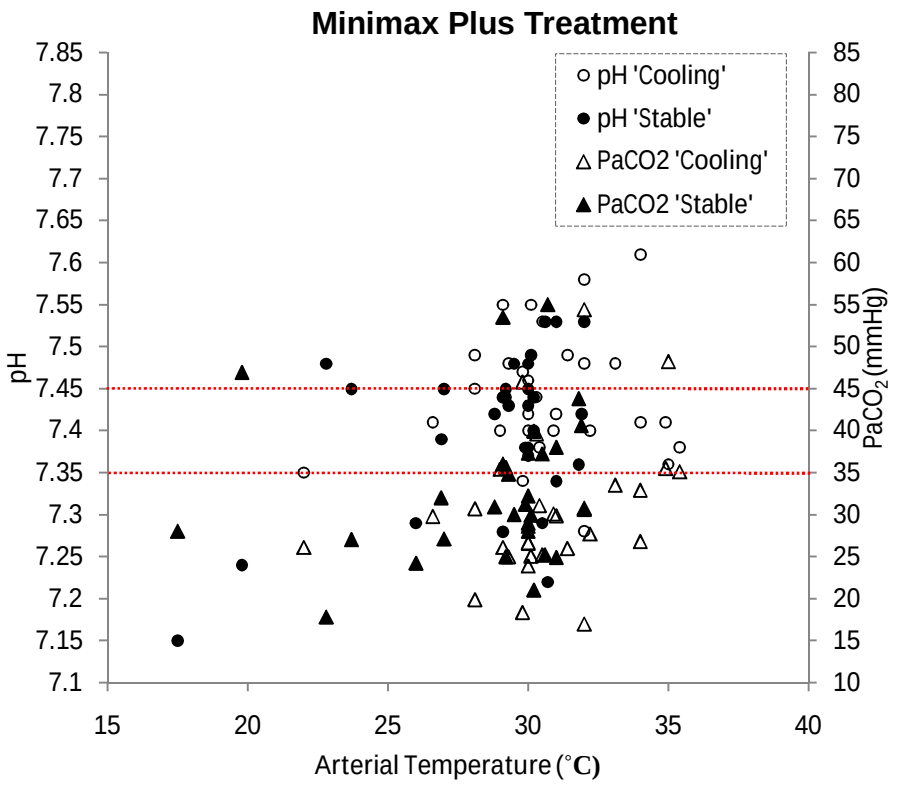
Figure 4.4 (b) shows difference between control and treatment groups of Minimax Plus oxygenator exploring relationship within temperature, pH and $PaCO_2$ in infant (n = 30; repeated measurements = 2 times) undergoing temperature changes during two stages namely cooling and stable period. There is significant difference between control and treatment group in Minimax Plus oxygenator for $PaCO_2$ (p<0.0191), however pH level shows no significant difference (p = 0.3138).



	$PaCO_2$ (Crl)	$PaCO_2$ (Rx)	*p* value	pH (Crl)	pH (Rx)	*p* value
Reference range	7%	18%	0.0001	27%	40%	0.0147
outré	93%	82%		73%	60%	

Figure 4.4 (a): Difference between control and treatment groups of Capiox RX05 oxygenator exploring relationship within temperature, pH and $PaCO_2$ in infant (*n* = 30; repeated measurements = 2 times) undergoing temperature changes during two stages namely cooling and stable period. Shown are plots for Capiox RX05 (control versus treatment) with reference line marked (round dot) along the reference range.





	$PaCO_2$ (Crl)	$PaCO_2$ (Rx)	*p* value	pH (Crl)	pH (Rx)	*p* value
Reference range	17%	20%	0.0191	42%	53%	0.3138
outré	83%	48%		58%	47%	

Figure 4.4 (b): Difference between control and treatment groups of Minimax Plus oxygenator exploring relationship within temperature, pH and $PaCO_2$ in infant (*n* = 30; repeated measurements = 2 times) undergoing temperature changes during two stages namely cooling and stable period. Shown are plots for Minimax Plus (control versus treatment) with reference line marked (round dot) along the reference range.

When going onto CPB, cooling and stable phrase were investigated for $PaCO_2$ level between control group (reference range: 17%; *outré*: 83%) and treatment group (reference range: 20%; *outré*: 48%). On the other hand, pH level between control group (reference range: 42%; *outré*: 58%) and treatment group (reference range: 58%; *outré*: 47%). This shows that treatment of carbogen does improve percentage within reference range of $PaCO_2$ in Minimax Plus oxygenator but not much vary in pH percentage.

Although there are statistically significant difference between control and treatment group but there are room for improvement to elevated $PaCO_2$ and pH within reference range. Furthermore, the percentage difference between reference range and *outré* are quiet highly vary. These percentage differences have to be favouring to reference range compare to *outré*. There is, however, difficult to maintain blood gases during cooling period because insufficient time to regulate $PaCO_2$ or pH. This might influence the outcome of the result that we have produce.

Physical laws determine that the solubility of the gas within a liquid decreases when lowering the temperature. During hypothermia, arterial PCO_2 decreases and pH increases compared with 37˚C when measurements are made at the actual body temperature. In healthy subjects with a body temperature of 37˚C, pH and pCO_2 should approach 7.4 and 5.3 kPa (40 mm/Hg), respectively. During hypothermia (33˚C), pH will rise to 7.5 and pCO_2 will decrease to 4.5 kPa (34 mm/Hg) (Groenendaal *et al*., 2009).

4.6 Analysis of the carbogen intervention

Table 4.4 and Figure 4.5 shows carbogen usage comparing between Capiox RX05 and Medtronic Minimax Plus oxygenator group in cooling and stable phase during CPB. There are statistically significant difference between cooling and stable period for Minimax Plus (p = 0.04) but it is not significant for Capiox RX05 oxygenator group (p = 0.50). All oxygenator groups consist of 30 infant but two repetitive measurements were taken during cooling and stable period. Significant in statistical term means the extent to which a result deviates from a hypothesis such that the difference is due to more than errors in sampling. These means Capiox RX05 oxygenator in this study have less difference between cooling and stable period in comparison with Minimax Plus.

For Capiox RX05 oxygenator carbogen were used more during cooling 0.38 ± 0.35 L/min and stable period 0.44 ± 0.33 L/min in comparison with Minimax Plus, which needs less during cooling only 0.13 ± 0.13 L/min were used meanwhile during stable period 0.21 ± 0.16 L/min carbogen were used. These means carbogen usage in Minimax Plus are lower compared to Capiox RX05. But are several reasons why this phenomenon happens in this study. Primarily, temperature management for Capiox RX05 are more favouring on deep hypothermia in comparison with Minimax Plus which majority temperature falls under moderate hypothermic CPB. Moreover, the weight group of both oxygenators are differing and can’t be taken into consideration for comparison for this study.

Table 4.4: Carbogen usage comparison between Capiox RX05 and Medtronic Minimax Plus groups in cooling and stable phase of temperature were investigated during CPB.

Oxygenators	Carbogen (L/min)				
	Cooling		Stable		
	Mean ± SD	Median	Mean ± SD	Median	*p* value[a]
Capiox RX05	0.38 ± 0.35	0.25	0.44 ± 0.33	0.38	0.50
Minimax Plus	0.13 ± 0.13	0.1	0.21 ± 0.16	0.2	0.04

[a] Student's *t* test performed between two phase.

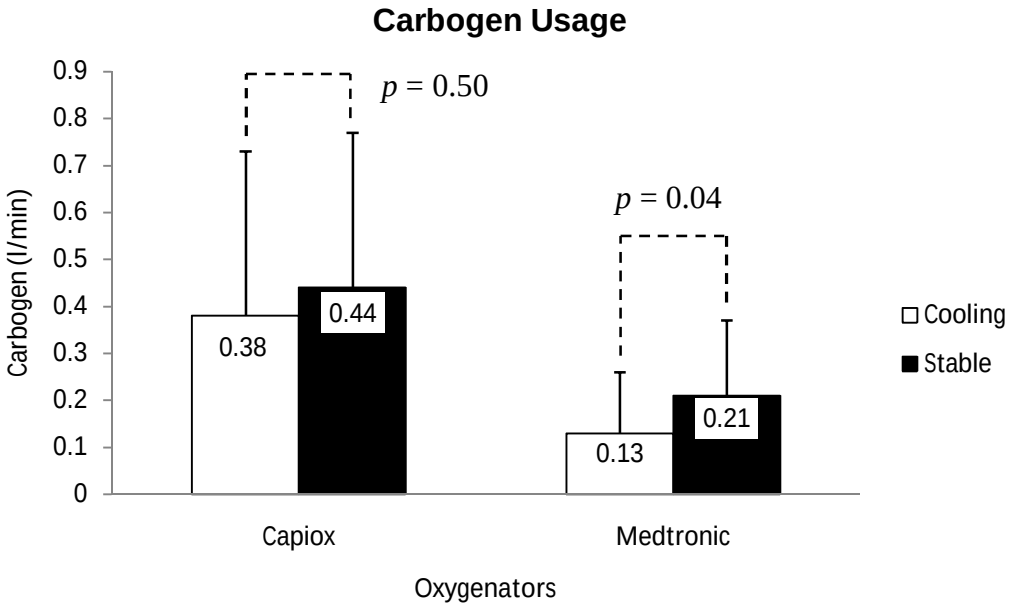


Figure 4.5: Carbogen usage between Capiox RX05 and Medtronic Minimax Plus (treatment groups) were measured during cooling and stable hypothermic phase of CPB. In both groups, significant differences were found between carbogen usages during the cooling phase. Each group consist of 30 subjects.

4.7 Analysis of the relationship between arterial temperature and carbogen

Surgical repair of complex intracardiac congenital heart lesions has required the use of cardiopulmonary bypass (CPB), and the symbiotic relationship between the two is exemplified in their parallel development. Figure 4.6 (a) shows relationship between arterial temperature and carbogen usage for infant undergoing hypothermic CPB on Capiox RX05 oxygenator. There were significant differences of carbogen usage measured during the stable phase (p = 0.004) for Capiox RX05. Meanwhile, carbogen usage measured during cooling phase are not significant (p = 0.15).

Figure 4.6 (b) shows relationship between arterial temperature and carbogen usage for infant undergoing hypothermic CPB on Minimax Plus oxygenator. There were significant differences of carbogen usage measured during the stable phase (p = 0.000001). Meanwhile, carbogen usage measured during cooling phase are not significant (p = 0.54).

Carbogen usage during cooling phase for both oxygenators shows significant value because it is hard to titrate carbogen within the short period of time of cooling. Even with the aid of CDI 500 it is quite tricky to adjust all the parameters of arterial blood gases together with controlling vital sign that are priorities such as ABP, ECG, sedation and temperature control during early stage of initiating CPB (during cooling). However, by stable phase the hemodynamic of blood gases are fairly stabilised which can be shown by the none significant value for both oxygenators. Deep hypothermia for Capiox RX05 shows higher percentage (32%) in comparison with Minimax Plus (15%). In the other hand, moderate hypothermia for Capiox RX05 shows lower percentage (68%) in comparison with Minimax Plus (85%). This uneven ratio of hypothermia condition might influence the outcome of carbogen usage which may need more intervention usage during deep compare to moderate hypothermia.

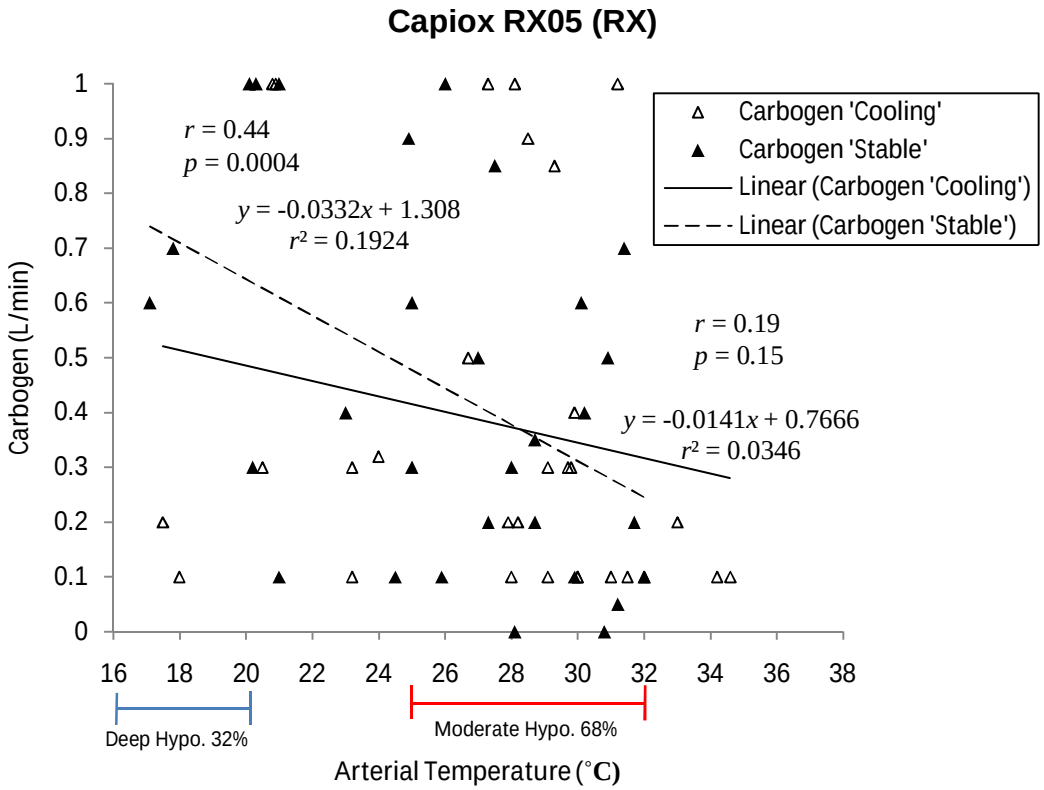


Figure 4.6 (a): Relationship between arterial temperature and carbogen usage was illustrated for infant undergoing hypothermic CPB on Capiox RX05 oxygenator.

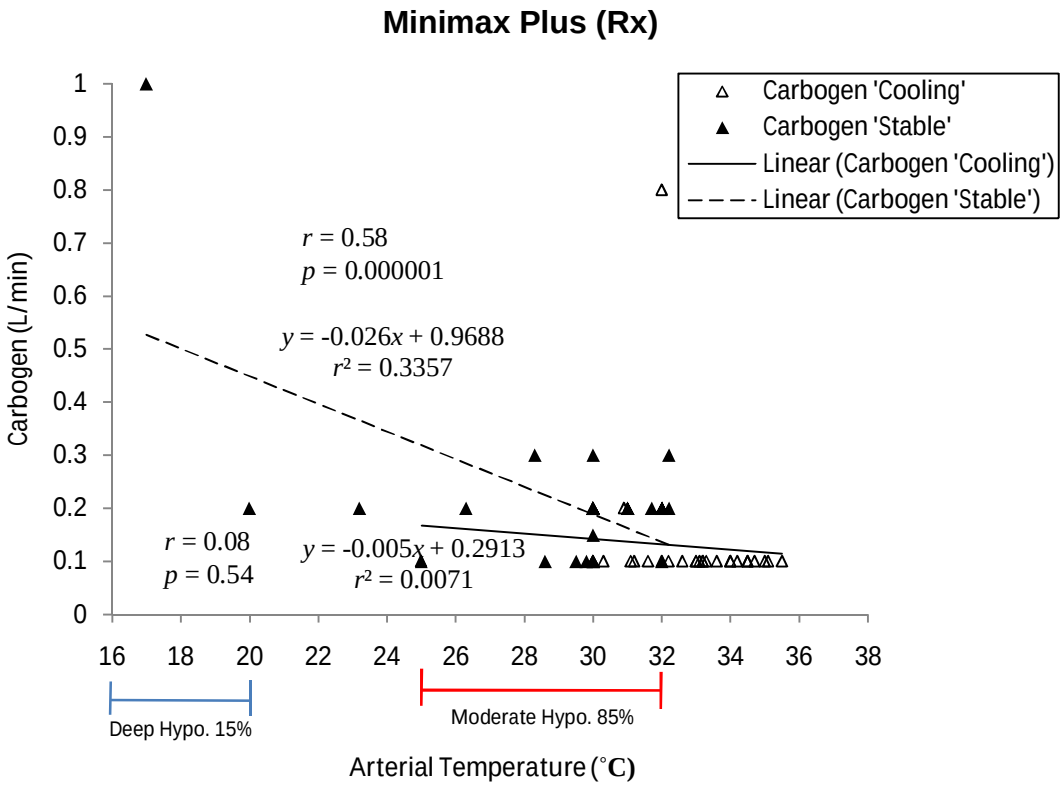


Figure 4.6 (b): Relationship between arterial temperature and carbogen usage was illustrated for infant undergoing hypothermic CPB on Minimax Plus oxygenator.

4.8 In-hospital mortality

Overall mortality percentage in this study was 3% (4 patients). At postoperative day 2 patients (2%) in the Capiox RX05 treatment group and Minimax Plus group died respectively (p = 0.4915). Causes of death for patients in the Capiox RX05 treatment group (each) are attributed to congenital abnormality of heart [original case: septectomy + Blalock-Taussig (BT) shunt] and Acute respiratory distress syndrome (ARDS) accompanied by myocardiac failure [original case: Arterial Switch Operation for Transposition of the Great Arteries (TGA) + IVS]. Cause of death for patients in the Medtronic Minimax Plus control group (each) are attributed to left ventricle failure (original case: arterial switch) and heart failure (original case: closure of VSD + RV-PA conduit). All deceased patients underwent moderate hypothermia except for one of the Medtronic Minimax Plus (control group) patient who died because of left ventricle failure (original case: arterial switch undergone deep hypothermia). All mortality occurred postoperatively in paediatric intensive care unit and the survivors' rate (97%) prevails over mortality (3%).