CLINICAL STUDY

Impact of Different Sweep Gas Flow Rates on Respiratory Alkalosis and Cerebral Oxygenation during Cardiopulmonary Bypass

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Summary

There is no consensus on the ideal sweep gas flow volume for achieving targeted blood partial gas pressures during cardiopulmonary bypass (CPB). The sweep gas flow rate is one of the oxygenator's main gas exchange variables. High sweep gas flow rates can lead to respiratory and hypocapnic cerebral alkalosis, which can cause neurological complications.

This study included 84 patients aged > 18 years who were scheduled to undergo elective open-heart surgery with CPB. Before rewarming, the participants were randomly assigned to one of the three groups based on their sweep gas flow rates (Group 1, 1.35 L/m^2/minute; Group 2, 1.2 L/m^2/minute; and Group 3, 1 L/m^2/minute). During the surgery, arterial blood gases were sampled at six different time points, and regional cerebral oxygen saturation (rSO_2) levels were monitored bilaterally on the forehead.

The study found that all groups experienced a decrease in partial pressure of arterial carbon dioxide ($PaCO_2$) levels after the onset of hypothermia, which decreased to below the normal range at a moderate hypothermia level of 32°C. During both the baseline and hypothermic periods, the $PaCO_2$ were similar between the groups; however, after rewarming, Group 3 had significantly higher $PaCO_2$ than Groups 1 and 2 ($P < 0.001$). During the same period, Group 3 had significantly higher rSO_2 levels than Groups 1 and 2 ($P = 0.005$). For all patients, there was a significant correlation between delta-$PaCO_2$ and delta-rSO_2 levels after rewarming ($r = 0.45$, $P < 0.001$).

This study demonstrated that low sweep gas flow prevented alkalosis and preserved cerebral autoregulation.

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Key words: Optimal sweep gas flow rate, Open heart surgery, Cerebral autoregulation

Cardiopulmonary bypass (CPB) is an essential component of open-heart surgery. During this process, oxygenation helps with the circulation, ventilation, and gas exchange. The gas exchange efficiency in blood passing through an oxygenator depends on four variables: blood flow, gas solubility, temperature, and the partial gas pressure difference.[1)] However, the most critical variable is the partial gas pressure difference, which is mainly influenced by the sweep gas flow rate.

One of the gases that require careful monitoring in oxygenators is carbon dioxide (CO_2). An excessive exchange or accumulation of CO_2 can lead to severe consequences. Alkalemia is a common adverse effect of CPB. Hypocapnic cerebral alkalosis can result in reduced cerebral perfusion,[2)] which can cause neurological complications in patients with impaired cerebral autoregulation owing to CPB.[3)]

Although CPB surgery is well understood, there is no consensus on the ideal sweep gas flow rate required to achieve the desired blood partial gas pressures.[4)] Karabulut *et al*. researched various sweep gas flow rates, which were determined based on body surface area.[5)] However, even with the lowest sweep gas flow, it was not possible to prevent a decrease in partial pressure of arterial carbon dioxide ($PaCO_2$), resulting in alkalosis.

This study aimed to investigate the impact of various sweep gas flow rates during different phases of CPB. The primary objective of this study was to identify the optimal sweep gas flow rate that could achieve the best $PaCO_2$ based on clinical observations and previous research.

As a secondary objective, the study also explored whether preventing respiratory alkalemia would help preserve cerebral autoregulation and prevent a decrease in regional cerebral oxygen saturation (rSO_2) in patients monitored using near-infrared spectroscopy (NIRS).

Methods

Following the approval of the Ethics Committee (Acibadem University and Acibadem Healthcare Institu-

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Table I. Patient and Operational Characteristics

	Total (n = 84)	Group 1 (n = 28)	Group 2 (n = 28)	Group 3 (n = 28)	P
Age, years	64 (56–69)	62 (51–69)	66 (58–71)	61 (53–68)	0.224
Males, n (%)	67 (79.8)	22 (78.6)	22 (78.6)	23 (82.1)	0.929
BMI kg/m^2	28.4 ± 3.9	28.2 ± 3.6	28.0 ± 4.0	29.0 ± 4.3	0.417
BSA, m^2	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.2	0.358
Hct (admission), %	38.2 ± 4.6	38.6 ± 4.6	37.5 ± 5.3	38.6 ± 4.0	0.553
Comorbidities, n (%)					
Smoking	14 (16.7)	5 (17.9)	5 (17.9)	4 (14.3)	0.788
Hypertension	59 (70.2)	20 (71.4)	19 (67.9)	20 (71.4)	0.711
Dyslipidemia	50 (59.5)	17 (60.7)	18 (64.3)	15 (53.6)	0.649
Diabetes	17 (20.2)	5 (17.9)	7 (25.0)	5 (17.9)	0.483
Renal failure	0	0	0	0	
Cardiac failure	0	0	0	0	
Pulmonary disease	5 (6.0)	2 (7.1)	1 (3.6)	2 (7.1)	0.188
Type of surgery, n (%)					0.106
CABG	60 (71.4)	16 (57.1)	22 (78.6)	22 (78.6)	
AAG	8 (9.5)	5 (17.9)	2 (7.1)	1 (3.6)	
AVR	5 (6.0)	3 (10.7)	2 (7.1)	-	
MVR	5 (6.0)	3 (10.7)	1 (3.6)	1 (3.6)	
CABG + AAG	3 (3.6)	-	-	3 (10.7)	
Others	3 (3.6)	1 (3.6)	1 (3.6)	1 (3.6)	
Duration of CPB (minutes)	87 (70–104)	79 ± 21	76 ± 16	87 ± 24	0.134
Duration of CC (minutes)	49 (39–62)	52 (38–65)	45 (39–55)	50 (42–62)	0.321
Extubation time (hours)	7.6 ± 3.2	7.3 ± 2.8	7.8 ± 2.6	7.1 ± 3.3	0.649
Length of ICU stay (hours)	21 ± 4	21 ± 6	22 ± 4	21 ± 5	0.702
Length of hospital stay (days)	7 ± 4	7 ± 3	7 ± 4	8 ± 2	0.685
EuroScore	2.9 ± 1.5	2.9 ± 1.4	2.7 ± 1.7	3.1 ± 1.6	0.613

Hct indicates hematocrit; AAG, ascendant aortic graft; AVR, aortic valve replacement; BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; CC, cross-clamping; MVR, mitral valve replacement; and ICU, intensive care unit.

tions Medical Research Ethics Committee - ATADEK 2019-19/21), a randomized study was conducted at Acibadem Altunizade Hospital between August-November 2023. The study was registered with clinical trials ID number NCT06013189.

This study included 84 patients aged > 18 years who were scheduled for elective open-heart surgery with CPB. All patients were informed about the study and provided informed consent. Patients who had previously undergone minimally invasive and robotic cardiac surgery, deep hypothermia, total circulatory arrest, or could not reach the target sweep gas flow owing to high fraction of inspired oxygen (FiO_2) requirements were excluded from the study.

After administering midazolam premedication (0.30-0.35 mg/kg i.v.), inserting a radial arterial catheter, and performing routine monitoring, anesthesia induction was achieved using propofol (1.5-2.0 mg/kg i.v.), fentanyl (2 μg/kg i.v.), and rocuronium (0.6-1 mg/kg i.v.). After the completion of endotracheal intubation, anesthesia was maintained with sevoflurane inhalation. The same type of heart-lung machine (Terumo Cardiovascular Group, Ann Arbor, Michigan, USA) was used for the CPB system in all patients. Following the installation of the CPB system, a prime solution was used to fill the pump circuits; this solution included 1150 mL of Ringer's solution, 150 mL of 20% mannitol, and 2 mL of heparin (10000 IU).

During hypothermic CPB, the blood pump flow was maintained at 2.2-2.4 L/m^2/minute, while FiO_2 was maintained at 0.6. The hematocrit levels were maintained within the range of 25%-30% to ensure adequate tissue perfusion throughout the extracorporeal circulation. Various measurements were taken periodically to monitor tissue perfusion adequacy, including blood lactate levels, veno-arterial CO_2 difference ($Pv\text{-}aCO_2$), urine output rate, and arterial base deficit. In addition, cerebral perfusion was monitored using NIRS, which was used to measure the bilateral frontal rSO_2. Body temperature was also monitored using a heat probe placed in the nasopharynx, with a target hypothermia level of 32°C.

All patients were ventilated in volume control ventilation mode with 6 mL/kg tidal volume, Ppeep 5-10 cmH_2O, 4.5-6 lt/minute volume, and Ppeak max 25 cmH_2O after endotracheal intubation. Lung ventilation was not performed during CPB. Both lungs were deflated to ensure that all CO_2 elimination was via the oxygenator; they were ventilated again 1-2 minutes after CPB ended.

The study randomly assigned participants to one of three groups using a computer program. Group 1 had a constant sweep gas flow rate of 1.35 L/m^2/minute during the CPB. Group 2 started with a sweep gas flow rate of 1.35 L/m^2/minute at the beginning of the CPB but was lowered to 1.2 L/m^2/minute before rewarming. Group 3 also started with a sweep gas flow rate of 1.35 L/m^2/minute at the start of the CPB but gradually decreased to 1 L/m^2/minute before rewarming.

Arterial blood gases were sampled at six different

Table II. Comparisons of Blood Gas Parameters in the T0, T2, T3 (32°C), T4 (36°C), and T5

	Group 1 (n = 28)	Group 2 (n = 28)	Group 3 (n = 28)	P
At T0				
pH	7.42 (7.39–7.46)	7.44 (7.42–7.47)	7.44 (7.42–7.45)	0.781
PaO_2 (mmHg)	89 (73–132)	82 (75–104)	93 (78–132)	0.712
$PaCO_2$ (mmHg)	37.1 ± 4.0	38.6 ± 4.6	37.5 ± 4.4	0.422
HCO_3 (mmol/L)	23.4 ± 2.5	24.3 ± 2.3	24.0 ± 2.0	0.344
SBE (mmol/L)	−0.9 ± 1.9	−0.1 ± 2.5	−0.1 ± 2.1	0.562
Hct (%)	38.6 ± 4.6	37.5 ± 5.3	38.6 ± 4.0	0.553
rSO_2 (%)	67 ± 8	66 ± 8	65 ± 6	0.458
At T2				
pH	7.38 ± 0.04	7.39 ± 0.04	7.39 ± 0.03	0.324
PaO_2 (mmHg)	157 ± 34	167 ± 27	161 ± 30	0.681
$PaCO_2$ (mmHg)	36.0 ± 4.6	35.9 ± 2.4	35.7 ± 2.9	0.730
HCO_3 (mmol/L)	21.0 ± 2.0	21.7 ± 1.6	21.4 ± 1.7	0.466
SBE (mmol/L)	−4.0 (−5.1, −2.7)	−2.4 (−4.2, −2.0)	−3.4 (−4.6, −2.1)	0.153
Hct (%)	27.9 ± 4.4	25.4 ± 4.7	26.9 ± 3.7	0.325
rSO_2 (%)	65 ± 8	61 ± 8	63 ± 7	0.375
At T3				
pH	7.40 ± 0.04	7.42 ± 0.04	7.42 ± 0.04	0.381
PaO_2 (mmHg)	149 (128–160)	158 (120–173)	149 (132–172)	0.596
$PaCO_2$ (mmHg)	33.7 (30.6–36.5)	32.6 (29.1–35.3)	33.3 (30.8–34.7)	0.483
HCO_3 (mmol/L)	20.7 ± 2.6	21.0 ± 1.9	21.0 ± 1.8	0.889
SBE (mmol/L)	−3.7 ± 2.7	−3.3 ± 1.9	−3.3 ± 2.2	0.801
Hct (%)	28.5 ± 4.3	25.8 ± 4.7	27.4 ± 3.6	0.063
rSO_2 (%)	59 (56–64)	57 (54–62)	59 (54–63)	0.254
At T4				
pH	7.43 (7.40–7.49)	7.41 (7.38–7.44)	7.35 (7.33–7.39) ***,###	< 0.001
PaO_2 (mmHg)	203 ± 52	205 ± 50	180 ± 47	0.120
$PaCO_2$ (mmHg)	32.4 ± 2.5	33.8 ± 3.4	38.3 ± 3.3***,###	< 0.001
HCO_3 (mmol/L)	20.2 ± 2.0	21.0 ± 2.2	20.9 ± 1.6	0.305
SBE (mmol/L)	−3.7 ± 2.2	−3.5 ± 2.6	−4.2 ± 1.9	0.478
Hct (%)	28.9 ± 3.8	26.9 ± 4.5	28.1 ± 3.7	0.198
rSO_2 (%)	59 ± 4	59 ± 8	65 ± 8**,##	0.005
At T5				
pH	7.38 ± 0.05	7.37 ± 0.05	7.35 ± 0.05	0.154
PaO_2 (mmHg)	154 (122–199)	131 (108–191)	115 (98–152)	0.067
$PaCO_2$ (mmHg)	36.0 ± 4.6	36.3 ± 3.6	38.6 ± 3.9*,#	0.034
HCO_3 (mmol/L)	20.8 (18.5–22.5)	20.9 (19.8–21.5)	20.8 (20.2–22.4)	0.794
SBE (mmol/L)	−4.1 ± 2.4	−3.9 ± 1.9	−4.0 ± 2.0	0.931
Hct (%)	31.0 (27.3–32.0)	27.5 (26.0–31.8)	30.0 (29.0–32.0)	0.345
rSO_2 (%)	64 (60–71)	64 (60–67)	65 (62–70)	0.413

Hct indicates hematocrit; and SBE, standard base-excess. *P = 0.05–0.01, **P = 0.01–0.001, ***P < 0.001 comparison between GI-GIII. #P = 0.05–0.01, ##P = 0.01–0.001, ###P < 0.001 comparison between GII-GIII.

time points during the procedure: T0 (before anesthesia induction), T1 (after the start of CPB but before cross-clamping [CC]), T2 (after CC at moderate hypothermia of 32°C), T3 (before warming at moderate hypothermia of 32°C), T4 (rewarming to 36°C), and T5 (immediately after CPB was terminated).

This study presents descriptive data as mean ± SD, median (quartiles), and percentage. The Shapiro-Wilcox test was used to assess normality. Kruskal-Wallis and analysis of variance (ANOVA) tests were used to compare the three groups, whereas Student's t, Mann-Whitney U, and chi-square (Fisher's exact) tests were used to compare each group. For the comparison of time points within each group, paired Student's t-test and Wilcoxon rank test were used. The Pearson correlation coefficient was used to detect the correlation between $PaCO_2$ and rSO_2. The total sample size for the three groups was determined as 84 (28 for each group) for a 10% increase in rSO_2 in Group 3 at T4 (F test, ANOVA one way, groups ratio 1:1:1, partial n^2:0.11 effect size 0.35, power 0.80, G-Power 3.1.9.4). All statistical analyses were conducted using SPSS version 29, and a P-value of < 0.05 was considered significant.

Results

All groups had similar patient characteristics, preoperative hematocrit levels, and CPB and CC durations (P > 0.05, Table I). There were no significant differences between the groups in the demographic characteristics and comorbid diseases of the patients (e.g., diabetes mellitus, hypertension, and renal failure) (P > 0.05, Table I). Arterial blood gas parameters and rSO_2 levels were compara-

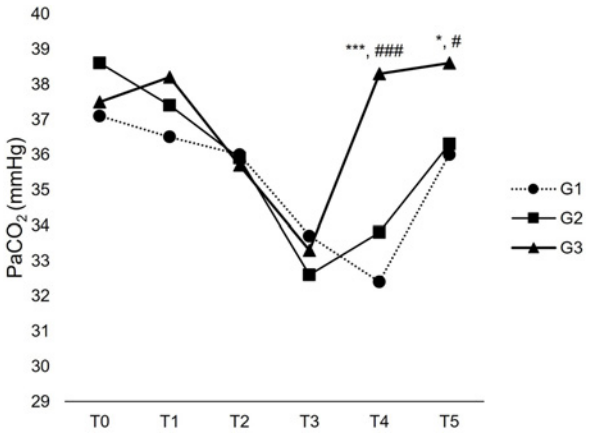

Figure 1. Comparisons of $PaCO_2$ of all groups. $^{*}P$ = 0.05–010, $^{***}P < 0.001$ comparison between G1–G3. $^{\#}P$ = 0.05–0.01, $^{\#\#}P$ = 0.01–0.001, $^{\#\#\#}P < 0.001$ comparison between G2–G3.

ble between all groups at T0 ($P > 0.05$, Table II). At T0, T3, and T5, the arterial pH levels of Groups 1, 2, and 3 were similar. However, at T4, the arterial pH levels for Group 3 (7.43 [7.40-7.49]) were significantly higher compared with Group 1 (7.41 [7.38-7.44]) and Group 2 (7.35 [7.33-7.39]) ($P < 0.001$, $P < 0.001$, respectively, Table II).

$PaCO_2$ were comparable between all groups at T0, T1, T2, and T3 (Figure 1). However, at T4 and T5, Group 3 exhibited significantly higher levels of $PaCO_2$ (38.3 ± 3.3 and 38.6 ± 3.9) than Group 1 (32.4 ± 2.5 and 36.0 ± 4.6) and Group 2 (33.8 ± 3.4 and 36.3 ± 3.6) ($P < 0.001$ and $P = 0.034$, respectively, Figure 1 and Table II).

At T4, the rSO_2 level was significantly higher in Group 3 than in Groups 1 and 2 ($P = 0.005$, Table II). Between T3 and T5 in each group, there was a significant increase in rSO_2 and $PaCO_2$, and vice versa (Figure 2). At T4, there was a significant correlation between delta-$PaCO_2$ and delta-rSO_2 for all patients, where delta values were calculated by subtracting T3 values from T4 (r = 0.45, $P < 0.001$, Figure 3). No significant clinical differences or neurological complications were observed among the patients. During the postoperative follow-up period, no patient exhibited signs of cerebral hypoxia or hypoperfusion. There were no complaints of headache, dizziness, numbness, or tingling sensations in the hands or feet; muscle cramps; or peripheral neuropathy, unilateral or bilateral. Additionally, no patient developed delirium, agitation, confusion, or seizures.

Discussion

In all groups, $PaCO_2$ level gradually decreased after the onset of hypothermia. At T3, the decrease in $PaCO_2$ was below the normal physiological limits in all groups. However, in Group 1, where the sweep gas flow rate remained constant, $PaCO_2$ did not increase as expected after rewarming at T4 but continued to decrease. This decrease can be attributed to the unnecessarily high flow rate of the sweep gas, which created an excessive CO_2 gradient in the oxygenator and removed CO_2 from the blood at a level that causes respiratory alkalosis. In Group 2, there was no significant decrease in $PaCO_2$ as observed in Group 1; however, it remained below the standard physiological limit. Finally, Group 3 experienced the expected 4.6% increase in $PaCO_2$, which returned to the normal physiological limits after the reduction of the sweep gas flow ($P < 0.001$ and $P = 0.034$, respectively; Figure 1 and Table II). A significant difference in $PaCO_2$ between Groups 1 and 3 persisted even after the rewarming period when CPB was terminated at the T5 time point.

The secondary aim of this study was to investigate the effect of alkalosis prevention on cerebral autoregulation and rSO_2. rSO_2 never decreased by more than 20% from baseline during surgery in any patient. It has been demonstrated that $PaCO_2$ and rSO_2 affect each other and that their variations occur in the same direction (Figure 2). More importantly, delta-$PaCO_2$ and delta-rSO_2 were correlated with T4 in all groups (Figure 3). We believe that rSO_2 is correlated with $PaCO_2$ within the physiological limits. This is because cerebral autoregulation is better preserved in these patients than in others who develop alkalosis. Previous studies have shown that hypocapnic cerebral alkalosis impairs cerebral perfusion, and rSO_2 monitoring is sensitive to $PaCO_2$.[6,7] Therefore, multimodal neuromonitoring is recommended to improve patient outcomes.

When the pH level of arterial blood rises above 7.45, it is called alkalemia;[8] this condition can lead to various complications, including a shift in the oxygen-hemoglobin dissociation curve to the left and an increase in hemoglobin's oxygen affinity. Alkalemia is often associated with hypokalemia and hypocalcemia, leading to an increase in systemic vascular resistance, which can cause coronary vasospasm.[9-11]

In addition, respiratory alkalosis can cause hypocapnic cerebral alkalosis, which can decrease cerebral perfusion and lead to neurological complications.[3,12] Studies have shown that in patients with impaired cerebral autoregulation owing to extracorporeal circulation, $PaCO_2$ is an independent factor determining cerebral perfusion;[2,6,13] therefore, considering all these factors, it is crucial to maintain $PaCO_2$ within the physiological limits.

Sweep gas is the most critical factor for determining $PaCO_2$. Previous studies on membranous gas exchange devices have shown that increasing the sweep gas flow rate has little effect on the partial arterial oxygen gas pressure but significantly affects PCO_2.[14,15] Three different sweep gas flows were studied in an experimental simulation study that modeled the exchange of $PaCO_2$ in a membranous oxygenator. It was found that increasing the sweep gas flow rate in a constant blood flow resulted in a linear and significant increase in $PaCO_2$ removal.[16] Conversely, reducing the sweep gas flow rate allowed CO_2 to accumulate in the fiber lumens, increasing the partial gas pressure of CO_2 in the fiber lumen and decreasing the concentration gradient required for gas exchange.[17-19]

During the rewarming period and extracorporeal circulation termination, two factors can affect $PaCO_2$. The first factor is the increase in CO_2 production owing to the increase in the metabolic rate. The second factor is the decrease in CO_2 solubility resulting from an increase in body temperature. According to physiological studies,

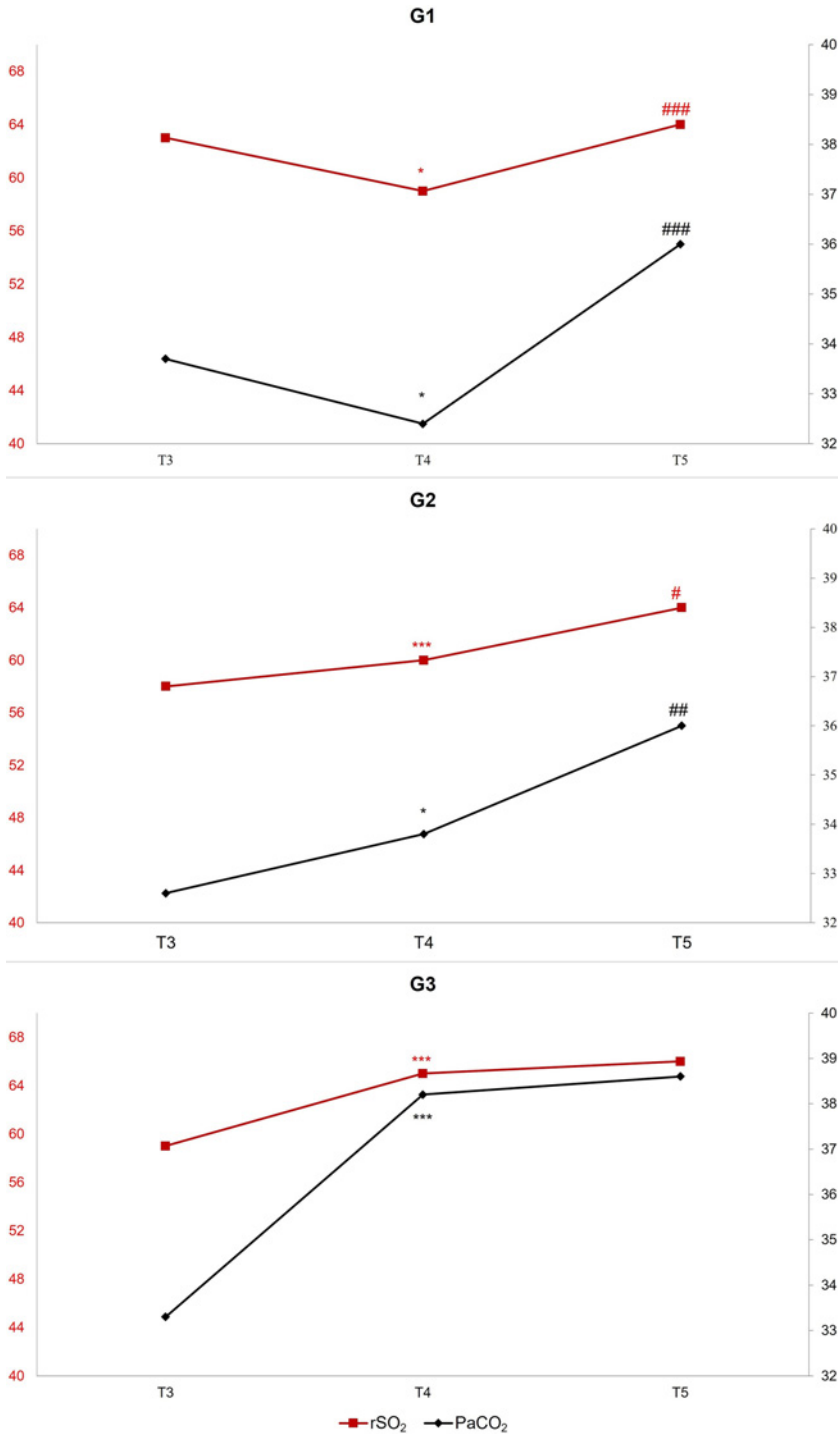

Figure 2. Progress of rSO_2 and $PaCO_2$ at k points in Groups 1, 2, and 3. $^{*}P = 0.05–0.01$, $^{***}P < 0.001$ comparison between T3 and T4. $^{\#}P = 0.05–0.01$, $^{\#\#}P = 0.01–0.001$, $^{\#\#\#}P < 0.001$ comparison between T4 and T5.

$PaCO_2$ can increase by 4.6% (SD 0.8%) for every 1°C warming.[20] However, some clinical observations and previous studies have shown that even though the patient's rewarming period is slowed and their metabolic rate increases, the expected rise in $PaCO_2$ is not always achieved.[5] In some cases, there may be a decrease in $PaCO_2$, and metabolic alkalosis may develop.

Adjusting the sweep gas flow rate according to the CPB stage is advisable to prevent respiratory alkalosis and hypocapnia. This study examined the impact of reducing

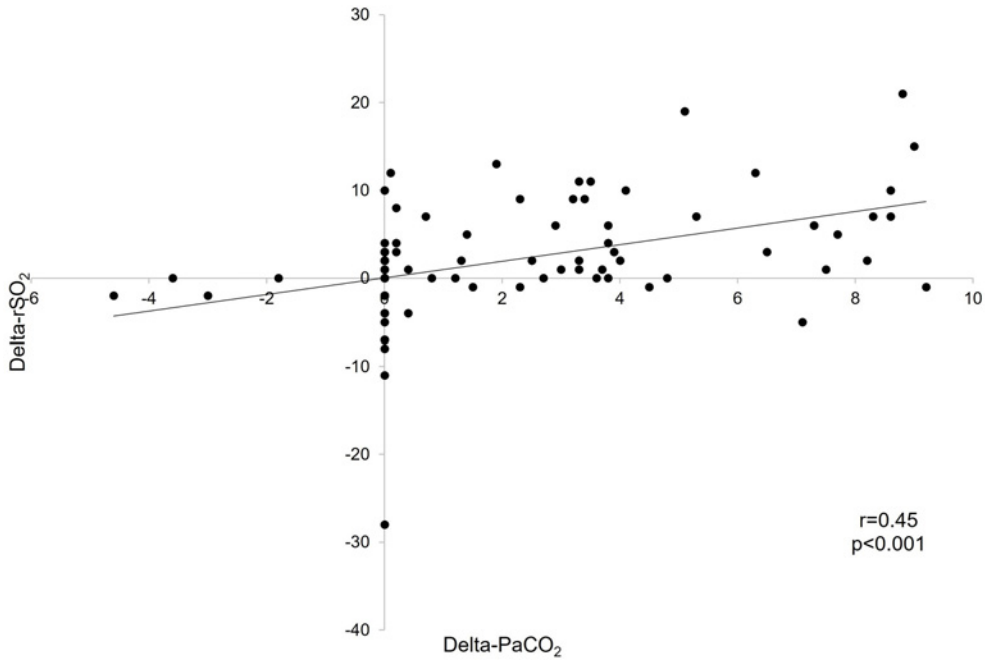

Figure 3. Correlation between delta-$PaCO_2$ and delta-rSO_2 at T4 in all groups. The delta values were calculated by subtracting the T3 values from the T4 values.

the sweep gas flow rate dat various levels during the rewarming phase while maintaining a standard dose based on body mass index during CPB induction and maintenance.

This study showed that using alternative sweep gas rates in different phases of the CPB is more effective than keeping the sweep gas flow at a constant rate throughout the process; this helps maintain $PaCO_2$ within physiological limits.

Furthermore, this study also found that rSO_2 was better preserved when $PaCO_2$ was maintained within physiological limits. We believe that avoiding alkalosis while monitoring neurological function is beneficial in patients at risk of cerebral autoregulation.

This study has two limitations. First, and most importantly, no guiding study exists on how much scavenging gas flow can be reduced. Second, the cerebral effects of alkalosis can only be assessed with frontal rSO2 monitoring, and the device has limitations (e.g., only the frontal area is evaluated; it is affected by skin thickness and hypothermia).

Conclusion

Keeping the sweep gas flow constant during rewarming and adjusting it only after the blood gas analysis results are obtained after rewarming may cause some undesirable values (PCO_2 < 30 mmHg, pH > 7.50) and related undesirable outcomes, such as a decrease in cerebral blood flow secondary to respiratory alkalosis and neurological changes on a wide scale ranging from stroke to neurocognitive changes. We believe that these undesirable effects can be avoided by adjusting the sweep gas flow rate before rewarming.

Disclosure

Conflicts of interest: The authors declare that the research was conducted without any commercial or financial relationships that could create a conflict of interest.

Data availability: The corresponding author will share the data relating to this study upon reasonable request.

Author contributions: MT: Writing of original draft, reviewing, and editing. BD: Writing, reviewing, and editing. BG: Writing, reviewing, and editing. FT: Writing, reviewing, and editing.

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