
Original Article***The Effects of Continuous Blood Gas Monitoring During Cardiopulmonary Bypass: A Prospective, Randomized Study—Part I***

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ABSTRACT

The use of continuous in-line blood gas management (CILBGM) is steeped in controversy concerning its potential utility and impact on patient outcomes. The purpose of this study was to determine whether the use of CILBGM results in improved quality of patient care.

Fifty-nine patients were enrolled in a Institutional Review Board-approved, prospective, randomized study. An in-line blood gas monitor (CDI 500) was placed into the arterial and venous lines for all patients. Blood gas monitoring in the control group was managed by intermittent sampling (every 20–30 min), while the treatment group was managed with continuous monitoring.

There were no differences between groups in preoperative, surgical, anesthetic, or perfusion variables. The accuracy of the in-line monitor was comparable to laboratory analysis for arterial blood gas parameters ($N = 160$; pH bias = 0.00; PaCO₂ bias = -1.1 mmHg; and PaO₂ bias = 0.7 mmHg). There was less deviation from target values (pH = 7.40, PaCO₂ = 40 mmHg, PaO₂ = 150–200 mmHg) when in-line monitoring was used versus intermittent sampling ($N = 784$; pH deviation = 0.05 ± 0.03 vs. 0.03 ± 0.01 , $p < 0.0001$; PaCO₂ deviation = 4.0 ± 2.9 mmHg vs. 2.0 ± 0.9 mmHg, $p < 0.0001$; and PaO₂ deviation = 22.7 ± 16.9 mmHg vs. 11.7 ± 8.3 mmHg, $p < 0.0001$).

In conclusion, the results of part I of this study demonstrate that the use of CILBGM results in more accurate blood gas management during CPB.

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INTRODUCTION

Continuous, in-line blood gas monitoring (CILBGM) has been purported to provide rapid information on patient acid-base and oxygenation status, such that it enables clinical decisions to be based on real-time events (1). Additional benefits include enhanced ability to track quality assurance, decreased blood loss to phlebotomy, and decreased clinician exposure to blood products.

The 1998 Perfusion Safety Survey, however, found that only 37% of perfusionists were using CILBGM technology (2), and many are discontinuing its use (3). When asked if the discontinuation was due to cost or perceived ineffectiveness, an alarming number reported cost (82%) as the primary determinant (3). Many of these decisions may have been guided by the inherent inaccuracy of previous instrumentation, which required perfusionists to rely on traditional laboratory analysis to finalize clinical decisions. However, data from Southworth et al. confirmed that accurate and reliable technology is available, refocusing the CILBGM controversy (4). Specifically, does the use of CILBGM result in better control of blood gas parameters, and can this control improve patient outcomes?

While CILBGM offers a tremendous advance in the perfusionist's ability to follow and track alterations in cardiopulmonary physiology, large-scale, in vivo human trials focusing on patient outcome have not been reported. The data available currently originate from relatively small research trials and examine only accuracy, precision, and complication rates (4–11). In the absence of well-designed prospective research on the utility of CILBGM, the potential benefits of the technology have not been pursued, and direct cost-reduction efforts guide the decision for utilization. The purpose of part I of this study was to determine whether the use of CILBGM results in more accurate blood gas control.

MATERIALS AND METHODS

After Institutional Review Board approval and informed consent were obtained, 59 patients participated in a prospective, randomized comparison of continuous blood gas monitoring versus intermittent blood gas analysis. All patients underwent either coronary artery bypass grafting (CABG), valvular surgery, or both. Patients were randomized into two groups, a control and a treatment group. Patients in the control group ($N = 29$) had an arterial CDI 500 shunt sensor^a placed in the circuit, but the monitor was covered, blinding the perfusionist conducting cardiopulmonary bypass (CPB). Blood gas control was performed via institutional protocol of intermittent sampling (20–30 min). Prior to the start of each case, an in vitro calibration was performed according to manufacturers instructions for use. In addition, an in vivo calibration was

performed immediately after the initiation of CPB. The same procedure was performed for the treatment group ($N = 30$), except the CDI 500 display was used to guide clinical decisions following the in vivo calibration.

All patients were operated on by one of five surgeons and received identical anesthetic and postoperative care. Aside from blinding the CDI monitor in the control group, the perfusion circuit was identical and consisted of a roller pump^b, oxygenator with an integral heat exchanger^c, integrated venous/cardiotomy reservoir^d, arterial line filter^e, and custom tubing pack^f. The prime solution consisted of approximately 1400 mL balanced electrolyte solution to which 100 mL 25% albumin, 100 mL 25% mannitol, and 10000 U of bovine lung heparin were added. During CPB, arterial pressures were maintained between 60–90 mmHg, with flow rates adjusted between 2.0 and 2.4 L/min/m². Mild hypothermia (32°C) was used, and blood gas management was maintained according to alpha-stat physiology. Both antegrade and retrograde cardioplegia were used, with potassium concentrations adjusted for arrest (16–25 mEq/L) and maintenance doses (4–5 mEq/L).

Following heparinization (300 U/kg body weight), the activated clotting time (ACT) was maintained greater than 480 sec. At the end of the surgical repair and termination of CPB, heparin was reversed with protamine at a rate of 1 mg protamine for every 100 U of total heparin administered, with the adequacy of heparin reversal assessed via the return of the ACT to baseline pre-CPB values.

BLOOD GAS ANALYSIS

The patients in the treatment group were treated with the assistance of the in-line blood gas monitor. In addition, both the treatment and the control group had three arterial samples drawn for laboratory blood gas analysis. The first sample was drawn 5 min after the initiation of cooling, the second was drawn after 30 min on CPB, and the last sample was drawn 5 min after the initiation of rewarming. All samples were assayed for SaO₂, PaO₂, PaCO₂, pH, K⁺, and bicarbonate. The first sample was used to perform an in vivo calibration of the device. Agreement between the CDI 500 blood gas values and laboratory measured samples was analyzed using a method described by Bland and Altman (12). The method allows comparison between two methods of measurement in terms of accuracy (bias – the mean difference between values) and precision [expressed as limits of agreement – two times the standard deviation (SD) of the difference between values].

In addition to laboratory versus CDI 500 comparisons, the patients' blood gas status was evaluated every 7.5 min using the CDI 500 printing function. The deviation from target val-

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^b Sorin Biomedica, Stockert, Irvine, CA

^c Sorin Biomedica, Monolyth, Irvine, CA

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^e Cobe Laboratories, Arvada, CO

^f Cobe Laboratories, Arvada, CO

ues ($\text{pH} = 7.40$, $\text{PaCO}_2 = 40$, and $\text{PaO}_2 = 150\text{--}200$ mmHg) was calculated for each time point. The number of events which fell outside of normal range ($\text{pH} > 7.45$ or < 7.35 , $\text{PaCO}_2 > 45$ or < 35 , $\text{PaO}_2 > 250$ or < 150) were calculated as a percentage of total recorded events.

STATISTICS

Statistical analysis was performed by loading all data onto a personal computer in spreadsheet format. Parametric data was analyzed using a one-way analysis of variance (ANOVA). Additional multiple comparison tests (Fisher's least significant difference) were performed when significant differences ($p < 0.05$) were achieved. Nonparametric data were analyzed using chi-square analysis.

RESULTS

The CDI 500 values were compared to the laboratory analyzer values at 160 data points. The accuracy (bias) and precision (\pm limit of agreement) for the measured parameters were: $\text{pH} = 0.00 \pm 0.06$, $\text{PaCO}_2 = -1.1 \pm 7.0$ mmHg, $\text{PaO}_2 = 0.7 \pm 28.2$ mmHg, $\text{Hct} = 0.2 \pm 6.0\%$, and $\text{K}^+ = -0.3 \pm 1.8$ mEq (Figures 1–3).

The mean deviation from target values was calculated at 7.5-min intervals. In the treatment group ($N = 384$), the mean deviation in $\text{pH} = 0.03 \pm 0.01$, $\text{PaCO}_2 = 2.0 \pm 0.9$, and $\text{PaO}_2 = 11.7 \pm 8.3$. In the control group ($N = 400$), the mean deviation in $\text{pH} = 0.05 \pm 0.03$, $\text{PaCO}_2 = 4.0 \pm 2.9$, and $\text{PaO}_2 = 22.7 \pm 16.9$ (Figures 4–6). In all cases, the differences between the control group and the treatment group achieved statistical significance. In addition, the number of recorded events which fell outside of normal range were compared between the control group and the treatment group at all points. The results were as follows: $\text{pH} = 39 \pm 29\%$ vs. $16 \pm 21\%$, $p < 0.0001$; $\text{PaCO}_2 = 16 \pm 21\%$ vs. $3 \pm 7\%$, $p < 0.0001$; $\text{PaO}_2 = \text{PaO}_2 = 36 \pm 29\%$ vs. $14 \pm 20\%$, $p < 0.0001$.

DISCUSSION

When CILBGM technology first became available, wide-

spread utilization was impeded by the lack of accurate and precise instrumentation. As the technology evolved, these issues have been addressed, and devices that provide data comparable to traditional laboratory analysis have become available. This study confirms that the newest device, the CDI 500, agrees with the target values set forth by the Clinical Laboratory Improvement Act of 1988 for blood gas analyzers (4).

During the intervening period, however, there has been a dramatic shift in the economic environment of medicine. According to the 1998 Perfusion Safety Survey, accurate and precise technology alone was not justification for using CILBGM to 63% of practicing perfusionists (3). The utility of continuous, accurate information concerning the physiological status needed to be shown.

The first part of this study, while reconfirming the capabilities of modern CILBGM technology, demonstrated that blood gas variables can be more precisely controlled with in-line utilization. The impact of closely regulating blood gas status during CPB has not been examined previously, although the negative consequences of their deviation has been well demonstrated on an individual basis (14–30).

The importance of blood gas status becomes apparent when one examines anesthesia-related investigative work. Tinker and associates (13) performed a closed-claims study to determine whether identified "mishaps" could have been avoided by the appropriate use of additional monitoring devices, and if so, which devices could have afforded prevention (14). In all, 1,175 closed-claim files were evaluated by a panel of at least 11 independent case reviewers. The reviewers concluded that 93% of the serious mishaps could have been prevented by a combination of pulse oximetry and capnography. Adverse respiratory events were the largest class of injuries, 85% of which led to death or brain damage. Also of interest, the cost of cases judged to be preventable by improved monitoring was 11 times greater than the cases that were not preventable. The authors concluded that continuous monitoring of oxygenation and ventilation provides earlier diagnosis and treatment of developing physiological aberrations, thus avoiding patient injury.

ACCURACY AND PRECISION

Although the accuracy of the technology used in this experiment has been established previously, the monitor was used for

Table 1: Accuracy and precision by sample

	pH (units)	PCO₂ (mmHg)	PO₂ (mmHg)	K⁺ (mEq/mL)	n
Sample 1	0.01 ± 0.06	0.9 ± 7.0	-3.3 ± 14.9	N/A	62
Sample 2	0.00 ± 0.04	-1.6 ± 5.9	3.6 ± 26.0	-0.3 ± 0.8	61
Sample 3	0.00 ± 0.06	-3.3 ± 7.0	2.5 ± 28.2	0.2 ± 0.5	37
CLIA '88 Target	± 0.04	± 5.0	± 3 standard deviation	± 0.5	N/A

Accuracy (bias, mean difference between CDI and laboratory measurements) and precision (limits of agreement, ± 2 SD of the difference between methods) by sample. Sample one was before an in vivo calibration had been performed, and samples two and three are subsequent to the in vivo calibration.

Table 2: Accuracy and precision by perfusionist

Perfusionist	pH	PCO ₂	PO ₂	n
A	0.00 ± 0.04	-0.4 ± 6.6	5.1 ± 36.4	25
B	0.00 ± 0.04	-1.1 ± 5.7	1.8 ± 21.3	18
C	0.00 ± 0.04	-1.9 ± 6.7	-3.7 ± 21.4	29
D	0.01 ± 0.05	-0.6 ± 7.8	1.7 ± 32.2	31
E	0.01 ± 0.05	-0.9 ± 7.3	1.4 ± 21.6	34
F	0.02 ± 0.05	-1.9 ± 8.3	-5.9 ± 21.6	16

Accuracy (bias, mean difference between CDI, and laboratory measurements) and precision (limits of agreement, ± 2 SD of the difference between methods) by individual perfusionist (A–F).

a portion of the data collection and the accuracy of the device needed to be shown to validate the methods. In addition, the importance of in vivo calibration, sensor drift, and individual perfusionist performance on the accuracy and precision of the device has not been examined. It must be emphasized that the results from the device sufficiently agree with the results obtained from laboratory analyzers, such that clinical decisions may be made from the in-line monitor.

In vivo calibration and the effect of drift: The in-line monitor values were compared to simultaneous laboratory analyses at three distinct points (Table 1). The first point was after an in vitro calibration was performed, but before an in vivo calibration was performed, providing information concerning the importance of performing an initial in vivo calibration. The second sample was taken, on average, 30 min after the in vivo calibration, and may represent the accuracy potential of the device on CPB. The third sample was taken after the initiation of rewarming, and may serve as an indicator of sensor drift.

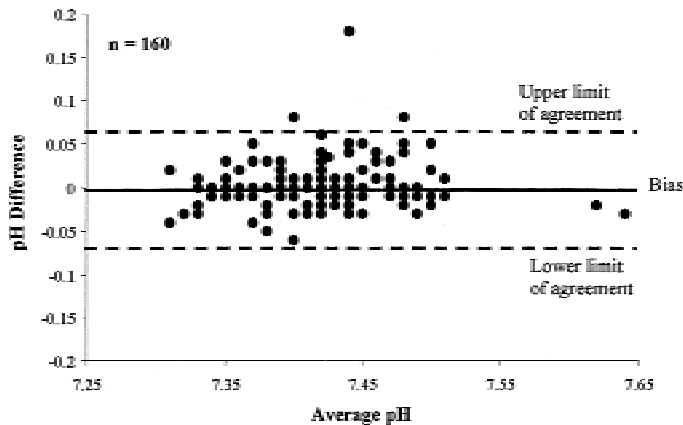


Figure 1: Agreement between CDI 500 and laboratory pH. Accuracy is represented by the solid bias line. Precision is represented by the dashed limits of agreement lines. Bias is a measure of accuracy used when comparing two independent measurement methods and is equivalent to the mean difference between the two measurement methods. The limits of agreement are measures of precision when comparing two independent measurement methods and is equivalent to 2 SD of the mean difference.

Aside from calibrating the potassium sensor, the importance of performing an in vivo calibration early in the case is questionable. The device demonstrated similar accuracy before and after the in vivo calibration for pH, PaCO₂, and PO₂. There was a limited degree of accuracy drift associated with the sensor, especially with respect to PaCO₂. If accurate K⁺ values (which require an in vivo calibration) can wait, the in vivo calibration may be more effective if it is performed later in the case.

The individual perfusionist: The set-up and calibration of the in-line monitor adds steps to the perfusion routine, and the possibility for error and different levels of competency exist. It would be expected that larger differences of device performance between individual perfusionists would reflect the level of difficulty in operation. Therefore, the accuracy and precision of the in-line monitor was examined versus the individual perfusionists involved in the study.

Although the use of the CDI 500 is not associated with complex or cognitive tasks, there was a degree of variability in

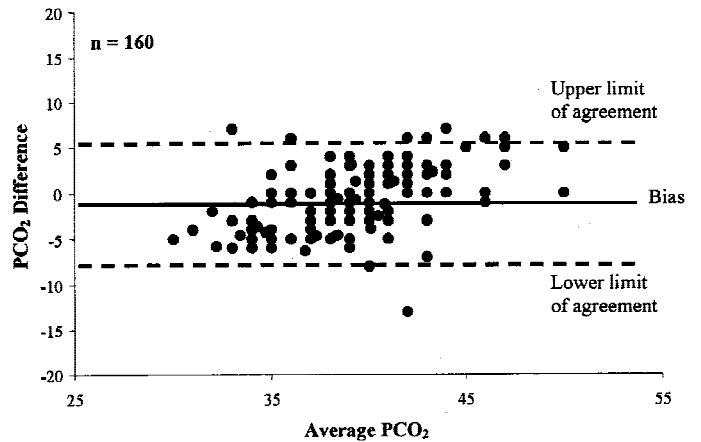


Figure 2: Agreement between CDI 500 and laboratory PCO₂. For details, see legend to Figure 1.

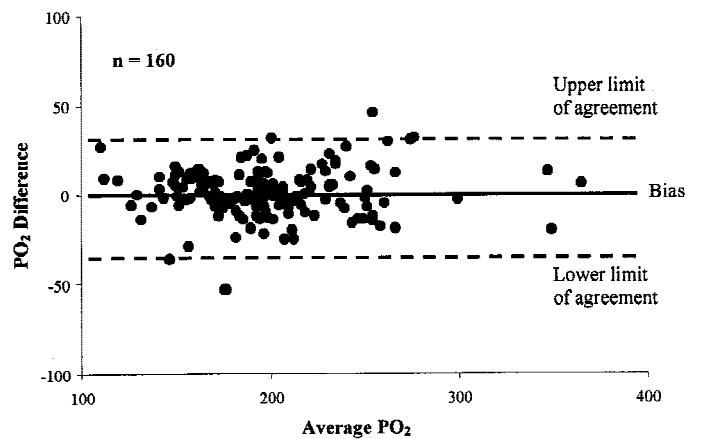


Figure 3: Agreement between CDI 500 and laboratory PO₂. For details, see legend to Figure 1.

accuracy between perfusionists (Table 2). If the device is to be used, it may be advisable to institute individual competency and quality control reviews similar to those performed for other measurement devices.

The perfusionists involved in this study averaged over 8 years of experience, and ranged from 4 years to nearly 20 years. The range of experience raised the question: do some perfusionists benefit more from using CILBGM?

When examining PO_2 management in terms of how frequently it falls out of range, it is clear that some individuals benefited more than others from the use of CILBGM (Figure 7). Perfusionist B had PO_2 values, which fell outside of range nearly 60% of the time, regardless of CILBGM utilization. In contrast, perfusionist C was able to maintain normal PO_2 values 39% more often when using CILBGM, and the other individuals followed a similar pattern. It is interesting to note that neither perfusionist B or C was the most senior or junior member of the study.

The other measured parameters follow a similar trend, with

some individuals benefiting slightly more than others from the use of CILBGM (Figures 8 and 9). However, none were as dramatically demonstrated and in nearly every other case, each perfusionist was able to control the parameter better when CILBGM was used. The exception to this was perfusionist F's pH management in the control group (Figure 8). The average number of events falling outside of range was higher in the treatment group. Only two treatment patients were cared for by perfusionist F, however, and one entered the operating room with a marked metabolic alkalosis.

THE UTILITY OF CILBGM

PO_2 management: The use of in-line monitoring resulted in more consistent control of PO_2 (Figure 6). The treatment group had normal PO_2 values (150–250 mmHg) more than 2.5 times as often than the control group, and there was 30% less variability between sample points. Of the 46 hypoxic events in this study, 78% of them occurred in the control group, suggesting that venous oximetry alone may not be sufficient to avoid this

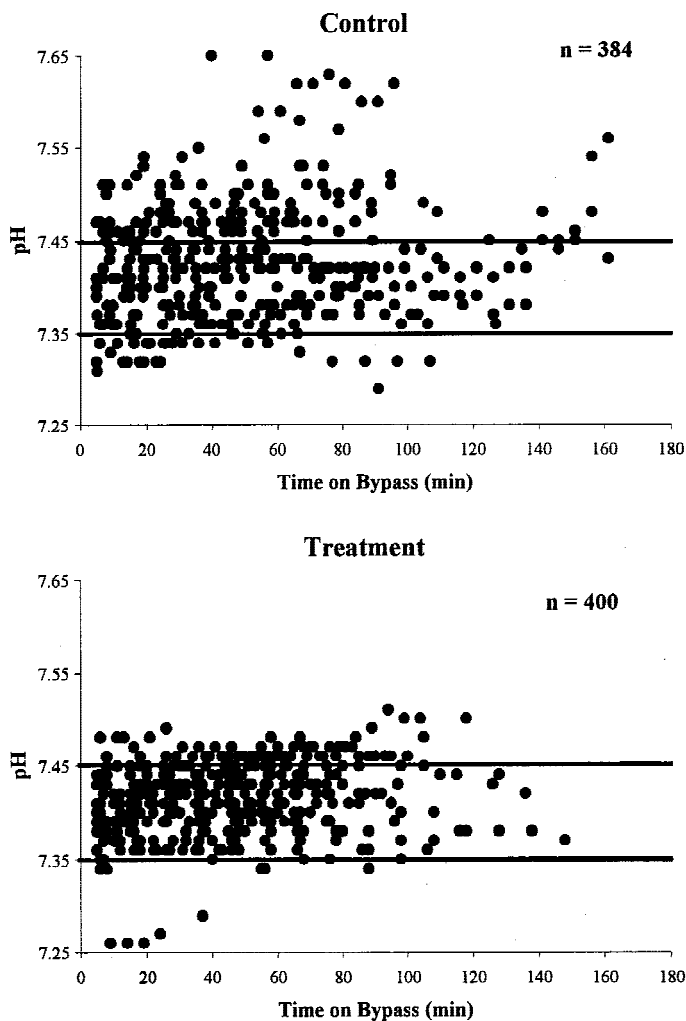


Figure 4: pH control in the treatment and experimental groups.

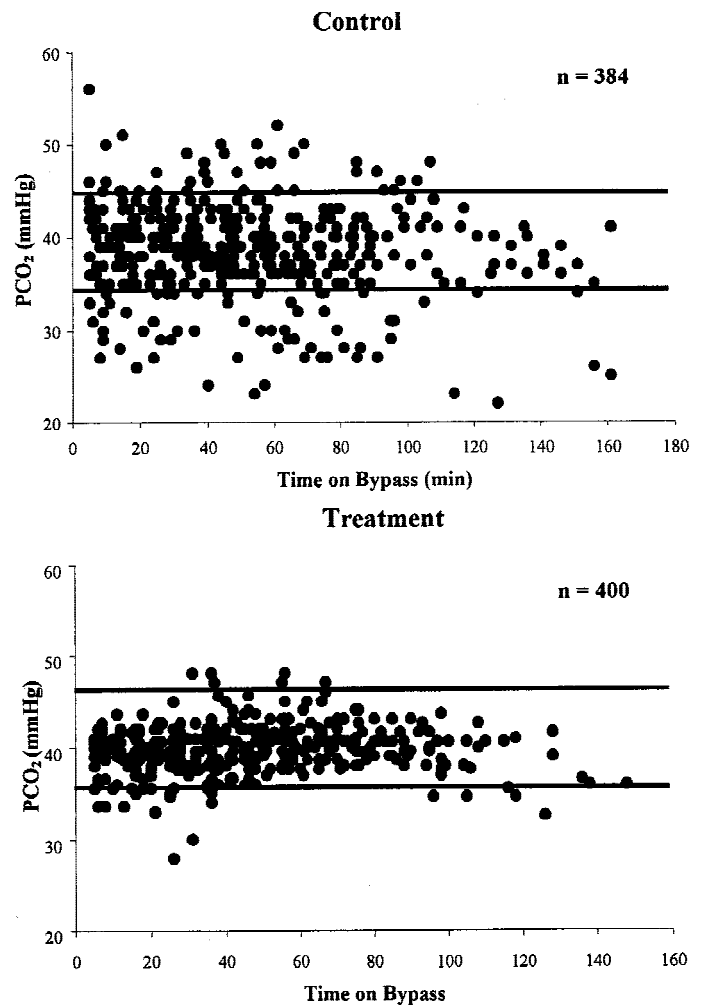


Figure 5: PCO_2 control in the treatment and experimental groups.

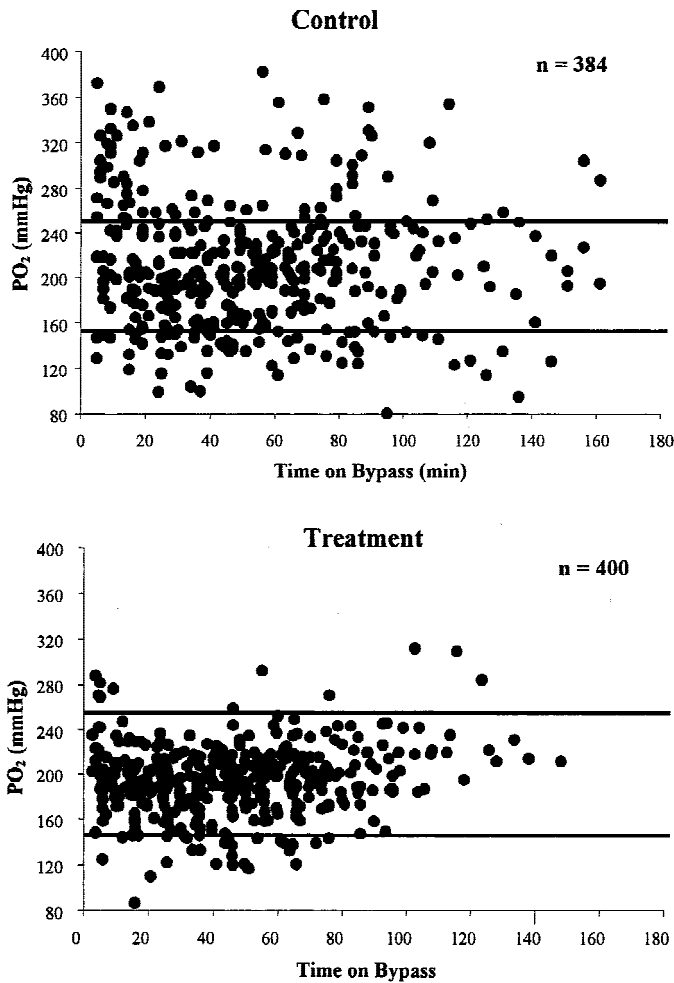


Figure 6: PO₂ control in the treatment and experimental groups.

condition. CILBGM was slightly less effective in avoiding hyperoxia, with 34% of the 116 events occurring in the treatment group. Due to the relative risks of hyperoxia vs. hypoxia (Table 3), clinicians often error on the high side of PaO₂. One of the major benefits of CILBGM may be the avoidance of hyperoxia, as the individual can successfully reduce PaO₂ while still avoiding dangerously low levels.

Acid-base management: Deviations in acid-base status, either respiratory, metabolic, or both, can have adverse consequences (Table 3). Better control of pH was provided by the use of in-line monitoring than with intermittent sampling (Figure 4). The pH fell outside of range 39% of the time in the control group, more than 2.4 times as often as the treatment group. Of the 175 recorded alkalotic events, 66% of them occurred in the control group. Perhaps more significant, in light of the relative severity of both conditions, 78% of the 46 acidotic events occurred in the control group.

In addition to the contribution to acid-base physiology, carbon dioxide is a potent component in the autoregulation of several vascular beds, including the brain, heart, and lungs.

Table 3: Adverse effects of blood gas parameter deviation

Hypoxia ¹⁴
Metabolic disruption
Death
Hyperoxia ¹⁵⁻¹⁶
Maldistributed capillary flow
Decreased organ performance
Increased red cell damage
Oxygen free radicals
Higher frequency of arrhythmias
Acidosis ¹⁷⁻²⁷
Decreased cardiac output
Decreased arterial blood pressure
Decreased hepatic and renal blood flow
Centralization of blood
Reentrant arrhythmias
Reduction in the threshold for ventricular fibrillation
Hyperkalemia
Alkalemia ²⁸⁻³⁰
Neurological abnormalities (including headache, tetany, seizures, lethargy, delirium, and stupor)
Reduces the anginal threshold
Refractory supraventricular and ventricular arrhythmias
Depressed respiration
Hypokalemia

Compared to PaO₂, PaCO₂ is more dependent upon patient-related variables such as metabolic rate and substrate utilization. Further, PaCO₂ levels are completely under the perfusionists control, and it is not surprising that the greatest difference in blood gas control between experimental groups occurred here. The control group fell outside of range more than 5 times as often as the treatment group (Figure 5). These events were predominantly hypocarbic (61 events < 35 mmHg,

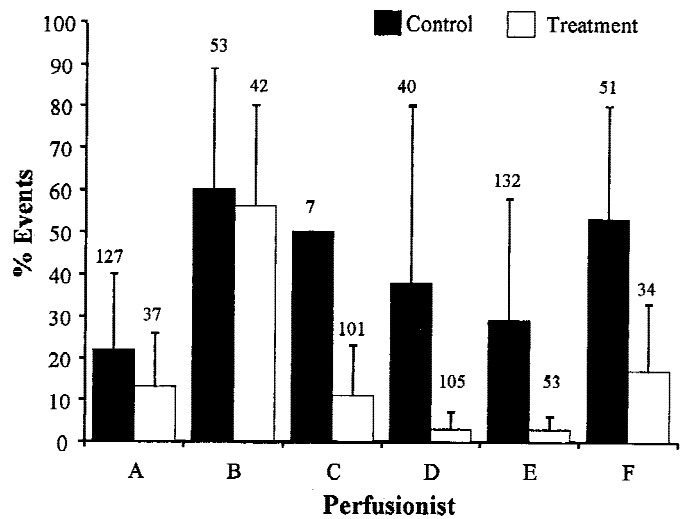


Figure 7: Percent recorded PO₂ events outside of normal range by perfusionist.

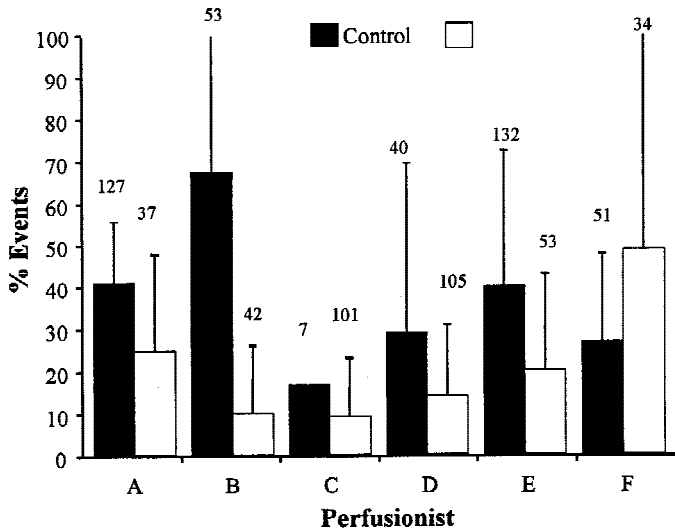


Figure 8: Percent recorded pH events outside of normal range by perfusionist.

28 events >45 mmHg), suggesting an overestimation of required gas flow rates when CILBGM is not used.

Operative variables: Different operative procedures, such as deep hypothermic circulatory arrest, demand alternative blood gas management strategies. Although this study was limited to CABG and valvular operations, some procedures were conducted under a CO₂ atmosphere. The effects of a CO₂ blower proximal to variable flow pump suction on blood gas management is not quantifiable, and may be a circumstance when CILBGM is most useful. Figure 10 shows blood gas regulation according to experimental group, blood gas parameter, and the use of a CO₂ blower. When a CO₂ atmosphere was used in the control group, PaCO₂ values fell outside of range more frequently

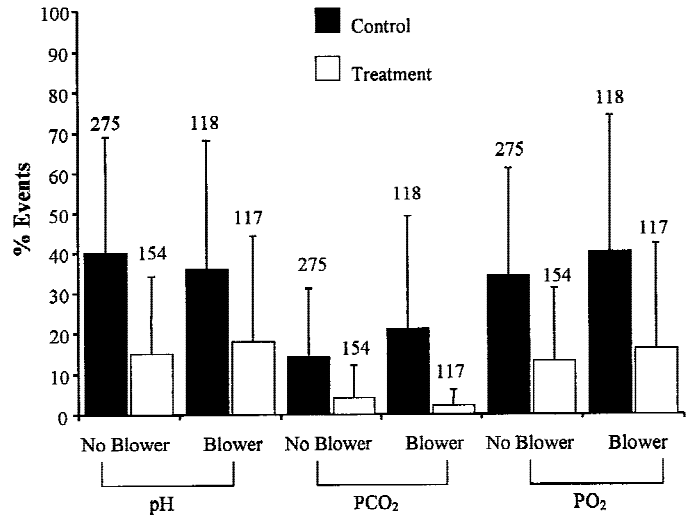


Figure 10: Percent recorded events outside of normal range by experimental group, use of CO₂ blower, and blood gas parameter.

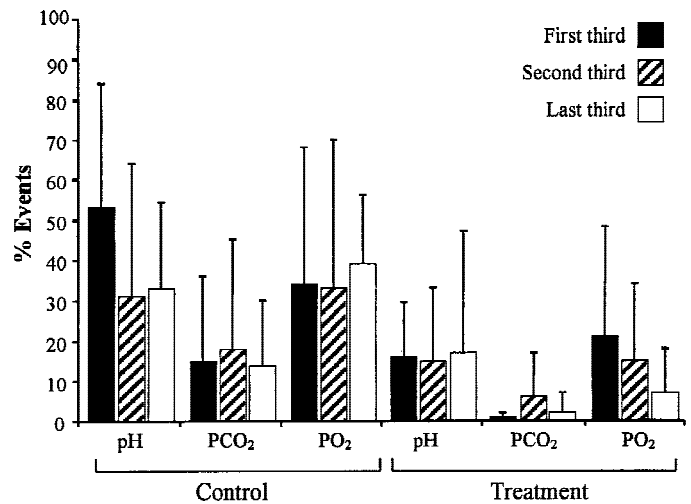


Figure 11: Percent recorded events outside of normal range by experimental group, stage of experiment, and blood gas parameter.

quently than when it wasn't used (21% vs. 14%). In contrast, PaCO₂ values fell within range more frequently when a CO₂ blower was utilized in the treatment group (2% vs. 4%). While a CO₂ atmosphere may not affect blood gas management to the extent commonly believed, the use of CILBGM eliminated the difference.

Developing competency: A learning curve?: Most new additions to the operating room are associated with a human learning curve (1). As the operators gain experience, the full potential of the new device or technology is realized. It was therefore of interest to examine the management of blood gas parameters as the experiment progressed and the individuals gained experience with the device. Figure 11 displays each

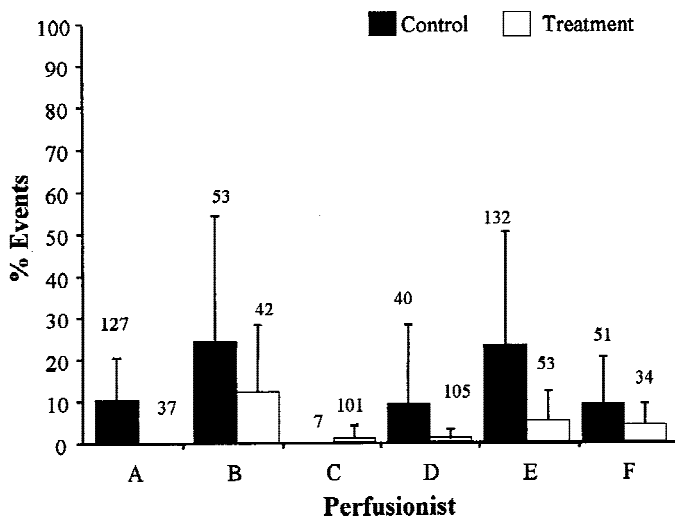


Figure 9: Percent recorded PCO₂ events outside of normal range by perfusionist.

parameter in both experimental groups plotted by the first third, second third, and last third of subjects. As the experiment progressed, PO₂ management in the treatment group grew tighter, suggesting that the individual perfusionist gained more confidence in the device and used it more rigorously to control the patients PO₂. Another point of interest is the pH management in the control group, which also trended towards tighter regulation as the experiment progressed. Perhaps the individual perfusionists learned to manipulate this parameter due to their experience with CILBGM in the treatment group.

CONCLUSION

The debate concerning the use or exclusion of continuous in-line blood gas monitoring is no longer centered on the utility of current technology. According to the data collected in this study and others, the technology currently available provides a level of accuracy comparable to laboratory analysis. In addition, the use of in-line monitoring results in more consistent management of arterial pH, PO₂, and PCO₂.

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