
Oxygen Content: Measured versus Calculated Values in Hypothermic Cardiopulmonary Bypass

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Abstract

Various formulae and methods have been utilized to arrive at blood oxygen content values, often disregarding effects of p50 shifts due to temperature and other factors on the oxyhemoglobin dissociation curve. This study seeks to compare direct oxygen content measurements utilizing a galvanic fuel cell with traditional methods of blood gas analysis and co-oximetry. Several standard formulae and methods were applied to arrive at oxygen content and consumption which were compared with the values obtained by direct measurement. Several indirect methods appeared to approximate the oxygen content values as directly measured. When applied to oxygen consumption calculations, the data points became widely scattered. Sources of error appear to lie in the application of temperature corrected blood gas data to a 37°C oxyhemoglobin dissociation curve.

Introduction

During extracorporeal circulation a major goal of the perfusionist is to deliver adequate amounts of

oxygen to the tissues. The degree of success is measured by arterial-venous oxygen (A-V O₂) content difference and oxygen (O₂) consumption. In the clinical situation oxygen content and consumption are not measured directly but are computed from other measured parameters. Usually the oxygen partial pressure (pO₂) of a blood sample is the measured parameter from which percent oxygen saturation and oxygen content value are computed.¹ Because temperature affects the partial pressure of oxygen, and temperature, pCO₂, and pH affect the slope of the oxyhemoglobin dissociation curve,^{2,3,4} several methods for temperature correcting these values have come into use.⁵⁻¹⁴

In using a single set of values for pO₂, pCO₂, and pH as a reference, different temperature correcting equations result in significantly different calculated oxygen content values and even more variance in oxygen consumption calculations. It is the purpose of this paper to determine which temperature correction method yields the most accurate oxygen content during various degrees of hypothermia, pO₂ levels, and hemodilution.

Methods and Materials

The total oxygen content of blood was measured directly using the Lex O₂ Con* in which oxygen in solution and bound to hemoglobin are displaced from the

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Article submitted at AmSECT's 19 Int'l. Conference, San Francisco, CA, March 1981.

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sample by a carrier gas and detected by a fuel cell. An electric current is generated in proportion to the number of oxygen molecules released. Oxygen content in volumes percent (vol %) is displayed digitally. This technique has been found to correlate very closely to the standard Van Slyke technique¹⁵⁻¹⁹ and eliminates the need for correction formulae.

The Lex O₂ Con is easily calibrated with the content of 20 μL sample of room air corrected for temperature and barometric pressure.²⁰ For three successive calibration samples, ±.1 vol% is used to determine adequate calibration. Calibration was checked periodically. All 20 μL injections were introduced through a 50 μL Hamilton Syringe, insuring that the volumes were identical.

Dual sets of three milliliter arterial and venous blood samples were drawn, simultaneously, from each patient during patient cooling on cardiopulmonary bypass. Esophageal temperatures were used in temperature correction. The samples were drawn in disposable, polypropylene syringes. Air was removed from the capped syringe to maintain an anaerobic environment. One set of samples was immediately sent to the lab for priority analysis in the IL 813 blood gas analyzer and IL 282 co-oximeter.* Both temperature-uncorrected and IL 813 temperature-corrected blood gas values were recorded. A direct measurement of hemoglobin (Hgb) was taken by the Coulter Counter technique.

Lex O₂ Con samples were labeled and iced to inhibit metabolism. Oxygen content was measured from homogeneous samples and an average of two trials was recorded for each arterial and venous sample. The two trials agreed within ±.2 vol%.

The uncorrected blood gas data were applied to several of the temperature correction formulae and content was calculated according to the formula:

$$O_2 \text{ content (vol\%)} = \frac{\% O_2 \text{ sat.}}{100} (\text{Hgb}) \frac{(1.34 \text{ ml } O_2)}{(\text{Hgb})} + \alpha \frac{(pO_2)}{(760)} (100)$$

where α is the solubility coefficient of oxygen in whole blood and is dependent upon blood temperature and hemoglobin mass.^{2,21} O₂ content is a measure of all oxygen present in the blood; that which is bound to hemoglobin and also that dissolved in plasma. Content also refers to the quantity of oxygen which is potentially

TABLE 1
Group Definition

Group	pO ₂	pH	O ₂ Saturation
1	IL 813 BGA, UNC.	IL 813 BGA, UNC.	IL SLIDE RULE
2 ^{1,3}	IL 813 BGA, TEMP. CORR. O ₂ Sat ≤ 95%, pO ₂ (PT) = pO ₂ (37) × 10 ^[.031(PT-37)] O ₂ Sat > 95% pO ₂ (PT) = pO ₂ (37) × 10 ^{[.032-.0268e(.35-30)](PT-37)} e = 2.71 S = % HbO ₂	IL 813 BGA, TEMP. CORR. pH(PT) = pH ₍₃₇₎ - .0146(PT - 37)	IL SLIDE RULE
3 ^{1,3}	IL 813 BGA, TEMP. CORR. Identical formula as Group 2	N/A	CO-OXIMETRY
4 ⁵	KELMAN COMPUTER SUBROUTINE pO ₂ (PT) = pO ₂ (37) × 10 ^[.024(37-T)-.4(pH-7.4)+.06(log40-logpCO₂)]	IL 813 BGA, UNC.	KELMAN COMPUTER SUBROUTINE SO ₂ = 100 $\frac{a_1 + a_2x^2 + a_3x^3 + x^4}{a_4 + a_5x + a_6x^2 + a_7x^3 + x^4}$ x = O ₂ tension; a ₁ ...a ₇ = constants
5 ^{8,9}	SEVERINGHAUS Described by correction factors in Appendix A.	ROSENTHAL For every degree Celsius decrease, pH increases by .0147 units	IL SLIDE RULE

* Instrumentation Laboratory, Inc., Lexington, MA.

available to the tissues. Perfusionists must also concern themselves with total body oxygen consumption, calculated by the formula:

$$\text{O}_2 \text{ consumption (ml/min)} = (\text{arterial content vol\%} - \text{venous content vol\%}) (\text{Cardiac Output L/min}) (10)$$

Five techniques of temperature correction were reviewed by the authors to determine a method which best approximates the value obtained by direct measurement. Referring to Table I, Group I used uncorrected pO₂ and pH as recorded by the IL 813 blood gas analyzer at 37°C. Saturations in this experiment, unless otherwise indicated, were determined from the IL slide rule. These values were pH dependent, representing a normal dissociation curve at 37°C. Group 2 used pO₂ and pH corrected using the formula programmed into the IL 813 blood gas analyzer.¹³ Group 3 was a combination of corrected pO₂ and pH from the IL 813 blood gas analyzer but, unlike Group 2, used co-oximetry for hemoglobin saturation. Group 4 involved Kelman's computer correction formula⁵ programmed for pO₂ and O₂ saturation on the Texas Instrument Calculator, Model 59, to obtain corrected pO₂ and hemoglobin saturation. Variables in the Kelman pO₂ formula are the uncorrected values from the IL 813 blood gas analyzer at a bath of 37°C. Group 5 employed an early Severinghaus technique which generated a corrected pO₂ by multiplying the blood gas analyzer values by the correction factors⁸ presented in Appendix A. A linear increase in pH by .0147 units occurs for each degree of Celsius change.⁹

Samples of arterial and venous blood were collected from 13 male and 6 female patients undergoing hypothermic cardiopulmonary bypass surgery at Harper-Grace Hospital in Detroit, Michigan. All patients were adults ranging from 24 to 70 years of age with a mean age of 54.7 years. Seventeen patients were diagnosed as having coronary artery disease, and two patients had diagnosed valvular disease. The total number of samples drawn from 19 cases was 141, averaging 7.4 samples per case. This included 15 arterial prebypass samples, 63 arterial and 63 venous samples. Thirty-five samples were greater than 32°C, 66 samples 28 to 32°C, and 40 samples less than 28°C.

The Pearson correlation coefficient determination²² was included in the statistical analysis of the data. It presents the degree of linear relationship between the direct content measurement on the y-axis and the calculated content on the x-axis; that is, the closeness of the points around the line defined by the specific slope

TABLE 2
Statistical Results of Oxygen Content and Consumption for All Groups and All Samples

Conditions	Groups				
	1	2	3	4	5
O ₂ Content, All Samples n = 141					
Pearson Correlation Coefficient (r)	.97	.93	.96	.94	.95
Slope	.98	.83	.97	.84	.86
Y Intercept	.53	2.97	.73	3.01	2.82
Standard deviation about regression (Sy·x)	.68	1.07	.80	.97	.91
O ₂ Consumption, All Samples n = 63					
Pearson Correlation Coefficient (r)	.95	.66	.84	.71	.72
Slope	1.03	.37	.85	.43	.47
Y Intercept	8.86	46.08	33.42	39.73	35.89
Standard deviation about regression (Sy·x)	13.38	31.82	22.82	29.93	29.36

and y intercept. The Pearson correlation coefficient in this study has a range from 0 to +1, where +1 is the highest correlation. The slope and y intercept shown in Table 2 and 3 were also determined from linear regression. (See Figures 1-12.) An ideal relationship would be represented by a line with a slope of one and y intercept of zero. The solid black line on all graphs presented in this paper is representative of the ideal.

Results and Discussion

The linear regression data of all groups for oxygen content are illustrated in Figure 1. The differences between the groups are evidence that the correction formulae that were tested are notably different. Note also that most groups deviate from ideal in the lower content values. The clinical implication of these differences is impressive when we consider the same data in terms of oxygen consumption in Figure 2. The lines generated by consumption data in all samples of different groups clearly show the magnitude of potential error.

Considering the possibility that these formulae may be accurate only under certain conditions, the content data were examined for pre-bypass samples only, arterial samples, venous samples, and then over different temperature ranges. Graphic and/or tabular results from two widely diverse groups were examined under all these conditions and compared. Group 4 by Kel-

TABLE 3
Statistical Results of Oxygen Content and Consumption in Groups 4 and 1 for All Categories

Category	Group 1			Group 4		
O ₂ Content	<i>Linear Regression</i>	<i>R</i>	<i>Sy-x</i>	<i>Linear Regression</i>	<i>R</i>	<i>Sy-x</i>
Arterial Pre-Bypass n = 15	Y = .73x + 4.95	.89	1.15	Y = .73x + 4.94	.89	1.14
All Arterial n = 63	Y = .96x + .83	.97	.56	Y = .94x + 1.59	.97	.60
All Venous n = 63	Y = .97x + .39	.97	.53	Y = .96x + 2.15	.85	1.14
Samples >32°C n = 35	Y = .96x + .74	.97	1.02	Y = .95x + 1.03	.97	.99
Samples 28-32°C n = 66	Y = .94x + .93	.97	.56	Y = .79x + 3.76	.93	.84
Samples <28°C n = 40	Y = 1.05 - .35	.99	.44	Y = .92x + 2.47	.93	.94
O ₂ Content All Samples n = 141	Y = .98x + .53	.97	.68	Y = .84x + 3.01	.94	.97
O ₂ Consumption All Samples n = 63	Y = 1.03x + 8.86	.95	13.38	Y = .43x + 39.73	.71	29.93

man's technique was contrasted against the virtually uncorrected Group 1.

Normothermic arterial pre-bypass samples are high

in oxygen content. Results from linear regression and correlation coefficients in Table 3 indicate that calculated oxygen content for arterial pre-bypass samples by group 4 technique was not closely correlated with the direct measurement since the line generated by the

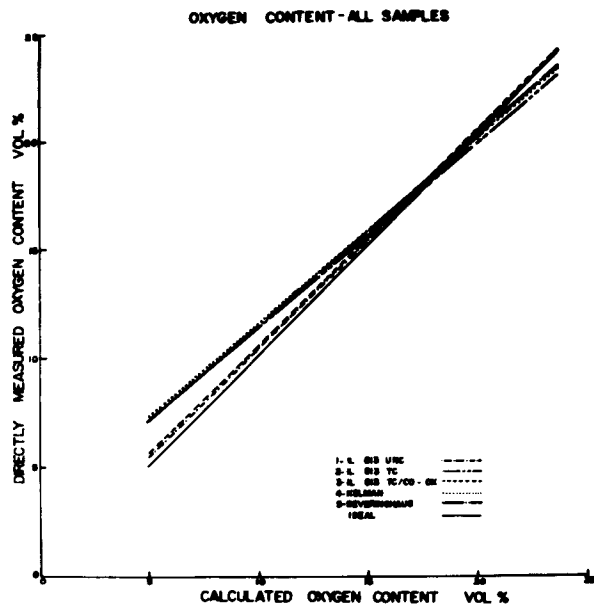


FIGURE 1. Comparison of oxygen content for all samples (n = 141) by a direct measurement against calculated oxygen content by all groups studied.

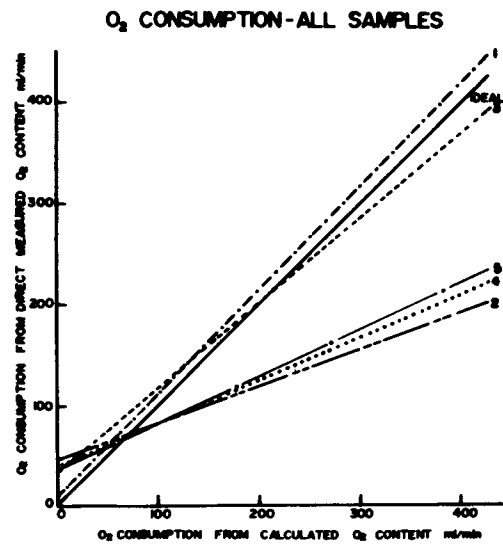


FIGURE 2. Comparison of oxygen consumption for all samples (n = 63) derived from directly measured oxygen content against oxygen consumption derived from calculated oxygen content by all groups studied.

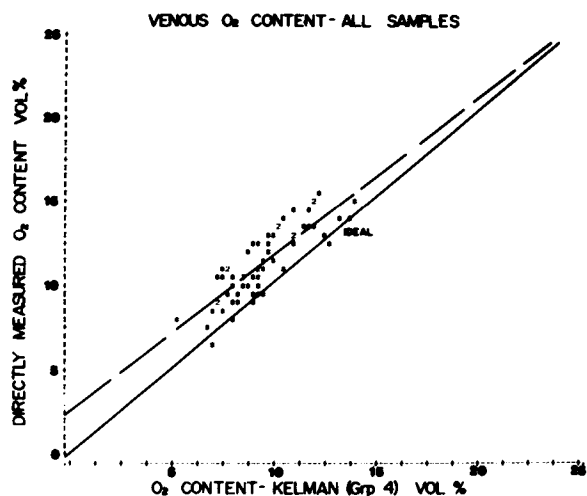


FIGURE 3. Comparison of oxygen content for venous samples only (n = 63) by a direct measurement and against calculated oxygen content by Group 4 (Kelman); $r = .85$, linear regression $Y = .96x + 2.15$.

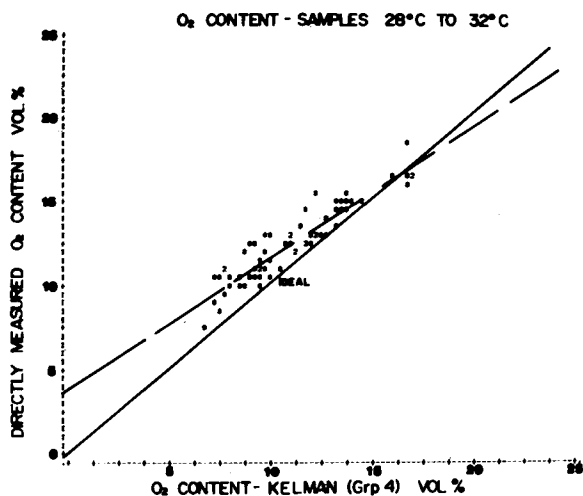


FIGURE 4. Comparison of oxygen content for samples between 28°C and 32°C (n = 66) by a direct measurement and against calculated oxygen content by Group 4 (Kelman); $r = .93$, linear regression $Y = .79x + 3.76$.

data points was deviant from the ideal. In fact no groups were satisfactorily correlated with the direct measurement for arterial pre-bypass samples.

The "all arterial" category includes hypothermic and hemodiluted samples. Again Table 3 describes the results of Group 4 compared with the ideal. Data in this category have lower content values due to hemodilution. However, all arterial samples have high oxygen partial pressures. The shape of the oxyhemoglobin dissociation curve predicts that any sample with a pO_2 over 100 mmHg will have a hemoglobin saturation of 97% or greater. The slowly changing slope of the dissociation curve in the higher pO_2 's indicates that it is not necessary to predict pO_2 precisely in this range to get an accurate saturation value. A large change in pO_2 in the higher range causes only a small change in saturation. Thus content calculations for arterial samples by all techniques will be fairly accurate as demonstrated by the results in Table 3.

Lower values for venous pO_2 fall on the oxyhemoglobin dissociation curve where the slope is quite steep. A slight error in pO_2 measurement causes a large change in saturation. A wider variation of saturation values is probable, and when they are used in different correction techniques, they result in large variances of venous oxygen content between the groups. The large deviance from ideal for venous samples is observed with Group 4 in Figure 3. Kelman's formula appears inaccurate in the venous range.

Data were also analyzed according to different temperature ranges. Arterial, venous, and pre-bypass

blood samples greater than 32°C were evaluated for a change in oxygen content using the various techniques. Little deviation from ideal was indicated for Group 4 as shown in Table 3.

During moderate hypothermia, between 28°C and 32°C, there is poor correlation between calculated oxygen contents using Kelman's Group 4 technique and a direct measurement of oxygen content. This deviation is represented in Figure 4. Moderate hypothermia is used extensively in extracorporeal bypass surgery. The failure of the Kelman correction to provide an accurate evaluation of a moderately hypothermic patient is

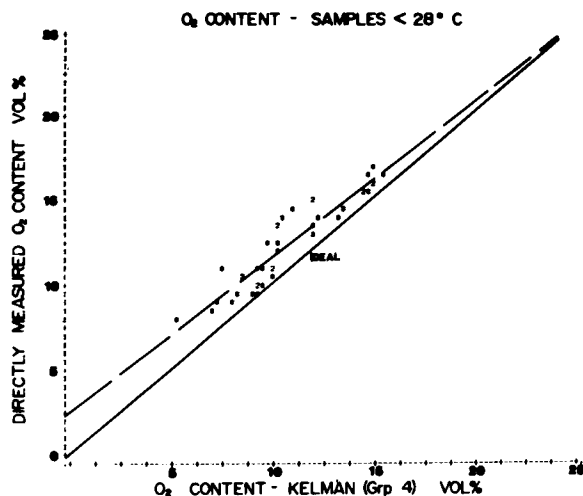


FIGURE 5. Comparison of oxygen content for samples less than 28°C (n = 40) by a direct measurement and against calculated oxygen content by Group 4 (Kelman); $r = .93$; linear regression $Y = .92x + 2.47$.

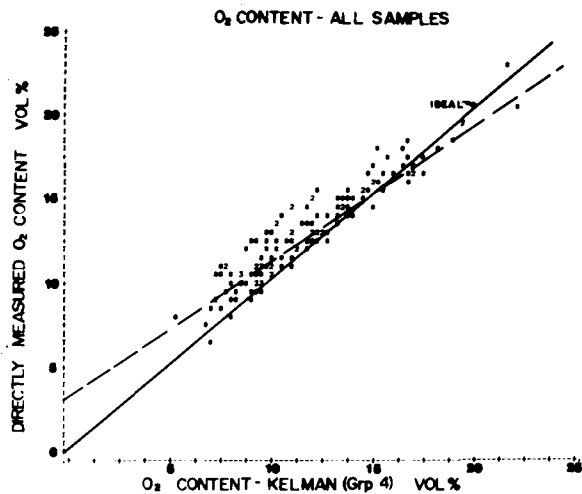


FIGURE 6. Comparison of oxygen content for all samples ($n = 141$) by a direct measurement and against calculated oxygen content by Group 4 (Kelman); $r = .94$; linear regression $Y = .84x + 3.01$.

important. Likewise, Group 4 shows poor correlation with the direct measurement for blood temperatures less than 28°C as illustrated by the data in Figure 5.

This study has shown that values obtained using Kelman's correction formula do not agree with direct content measurement of venous samples during moderate and deep hypothermia. When Kelman's technique for correction is applied to all samples for content analysis, regardless of source or temperature, as in Figure 6, the Pearson correlation coefficient is .94. The standard deviation from linear regression²² is a good indicator of the predictability of obtaining direct oxygen content values from blood gas determinations. The standard deviation from regression for content in Group 4 is .97 vol%.

The conversion of content data to consumption data for all samples from Group 4 illustrates the variance between Kelman's and ideal in Figure 7. The discrepancy occurs because venous content by Group 4 is so much lower than directly measured values for oxygen content. Thus when A-V O_2 content difference is used to derive oxygen consumption, a decrease in venous content will cause oxygen consumption by Group 4 technique to appear much greater. The Pearson correlation coefficient is .71 and the standard deviation from linear regression is 29.93 ml/min. Other methods in this study which exhibited similar trends were Group 2, the IL 813 temperature-corrected, and Group 5, by Severinghaus and Rosenthal.

A formula is sought which conforms more closely to

the ideal line than Groups 4, 2 and 5. From the methods explored in this study the technique (Group 1) using uncorrected values is most accurate. This technique involves temperature-uncorrected data from the IL 813 blood gas analyzer to calculate content. A review of the remaining figures indicates the superiority of the uncorrected technique over Kelman's Group 4.

Calculated content using the uncorrected technique (group 1) for arterial pre-bypass samples is poorly correlated with the corresponding direct measurement. All groups in this study exhibited poor correlation for the arterial pre-bypass category as suggested by the linear regression results in Table 3.

Under the category of "all arterial" samples, a high correlation of Group 1 with the direct measurement was expected. The data on Table 3 indicate this. Besides having the highest correlation coefficient, the slope and y intercept approach the ideal, however only slightly superior to the Kelman technique.

Large deviance from the ideal was demonstrated previously by Kelman's Group 4 for venous samples. Note in Figure 8 that the uncorrected data of Group 1 does not exhibit this deviance. Instead the data points demonstrate a very close fit to the ideal. A high degree of correlation in the venous samples is highly desirable and exclusive to Group 1 in this study.

Table 3 indicates that the uncorrected Group 1 technique has high correlation with the direct measurement for all samples with temperatures greater

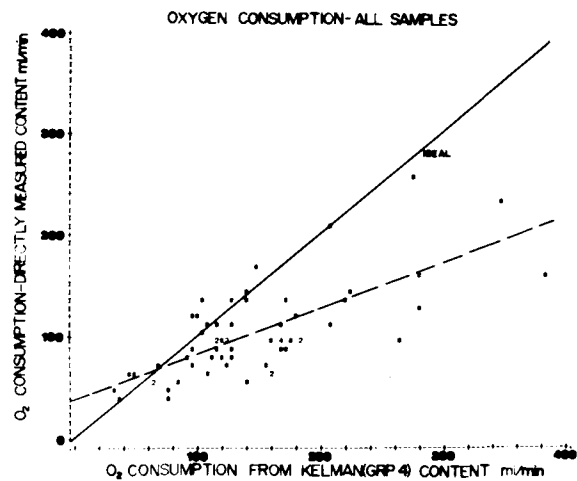


FIGURE 7. Comparison of oxygen consumption for all samples ($n = 63$) derived from directly measured oxygen content and against oxygen consumption derived from calculated oxygen content by Group 4 (Kelman); $r = .71$, linear regression $Y = .43x + 39.73$.

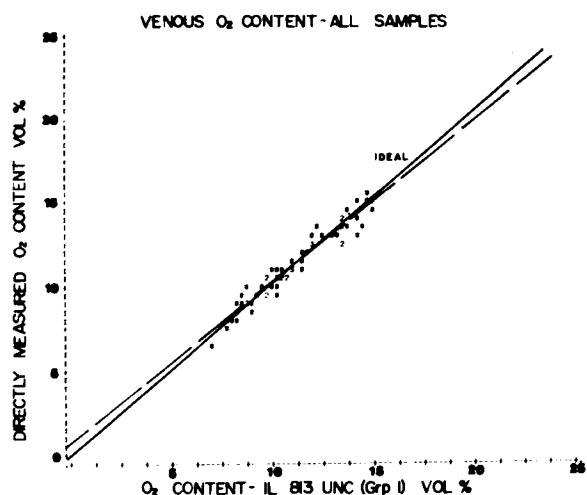


FIGURE 8. Comparison of oxygen content for venous samples only ($n = 63$) by a direct measurement and against calculated oxygen content by Group 1 (IL 813 UNC); $r = .97$ linear regression $Y = .97x + .39$.

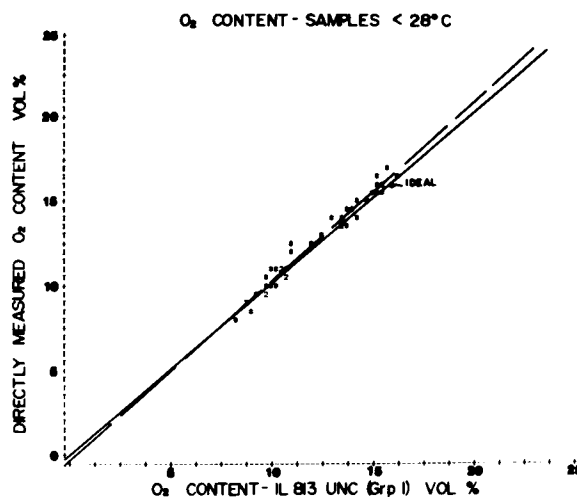


FIGURE 10. Comparison of oxygen content for samples less than 28°C ($n = 40$) by a direct measurement against calculated oxygen content by Group 1 (IL 813 UNC); $r = .99$, linear regression $Y = 1.05x - .35$.

than 32°C . In moderate hypothermia, 28°C to 32°C , Group 1 technique surpasses all other methods in correlating with direct measurement; minimal deviance from the ideal line is noted from Figure 9. Kelman's Group 4 previously exhibited great deviancy from ideal in this temperature range as well as deep hypothermia. Figure 10 shows data indicating that even in deep hypothermia, the total amount of oxygen in the blood is very accurately calculated by the Group 1 technique.

Figure 11 represents the distribution of oxygen content for all samples in Group 1. Minimal variation exists between the direct measurement on the y-axis and the calculated content by Group 1 on the x-axis. The Pearson correlation coefficient for this distribution is $.97$, and the standard deviation from regression is $.68$ vol% for Group 1 content.

In contrast to the consumption graph for all samples in Group 4, Figure 12 indicates that Group 1 had only slight deviance from ideal consumption. The Pearson

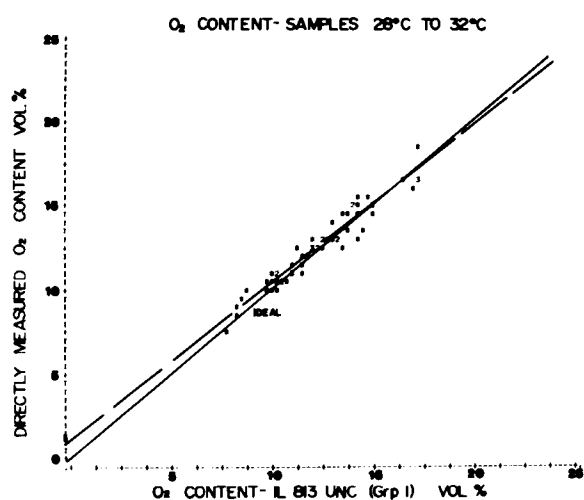


FIGURE 9. Comparison of oxygen content for samples between 28°C and 32°C ($n = 66$) by a direct measurement and against calculated oxygen content by Group 1 (IL 813 UNC); $r = .97$, linear regression $Y = .94x + .93$.

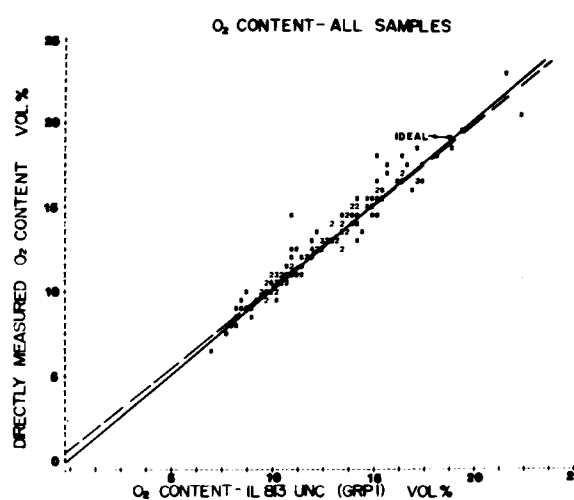


FIGURE 11. Comparison of oxygen content for all samples ($n = 141$) by a direct measurement and against calculated oxygen content by Group 1 (IL 813 UNC); $r = .97$; linear regression $Y = .98x + .53$.

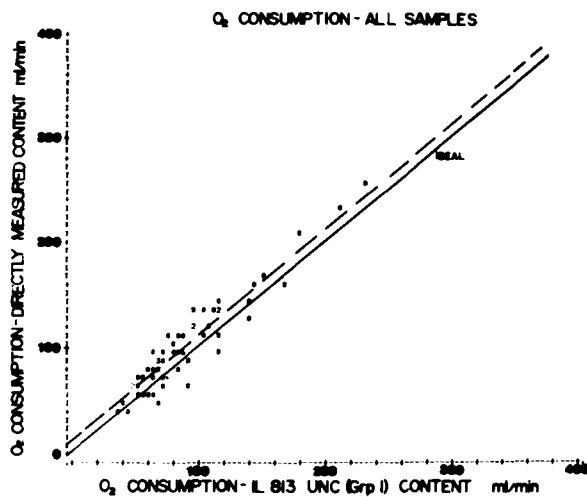


FIGURE 12. Comparison of oxygen consumption for all samples ($n = 63$) derived from directly measured oxygen content and against oxygen consumption derived from calculated oxygen content by Group 1 (IL 813 UNC); $r = .95$, linear regression $Y = 1.03x + 8.86$.

correlation coefficient for consumption in Group 1 was .95, as opposed to .71 for Group 4. Excellent correlation in Group 1 consumption data was expected because temperature uncorrected venous samples were highly correlated with direct measurement. Therefore minimal error is introduced by A-V difference when computing consumption. The standard deviation from linear regression for consumption data were 13.38 ml/min.

Group 1 data indicates that values of uncorrected temperature data can be used to obtain accurate content values in relation to a direct measurement for all conditions studied, and are much superior to other techniques considered. This includes high correlation with direct content measurements for venous samples and at all tested levels of hypothermia. This high correlation is attributable to the fact that the blood gas sample is analyzed at 37°C and an accurate oxyhemoglobin dissociation curve is readily available for that temperature.

If some form of temperature correction is desired, Group 3 technique correlates fairly well with direct content measurement for most categories including venous samples and at all levels of hypothermia. Group 3 consists of IL 813 temperature-corrected blood gas analyzer values and saturations by co-oximetry.

Groups 2 and 3 are very similar groups in that both are represented by IL 813 temperature-corrected blood gas analyzer values. Saturations in Group 2, however,

are found by using the IL slide rule whereas the hemoglobin saturations in Group 3 are obtained by co-oximetry. High correlation between these methods would be expected if the slide rule technique and co-oximetry were equally effective in determining saturation. Upon investigation it was found that these two methods did not correlate with each other as highly as desired (correlation coefficient equals .93). In addition it was found that Group 3 was more highly correlated to the direct content measurement than Group 2 (.96 and .93 respectively). This data illustrates that cooximetry is probably a better means of determining saturation than the IL slide rule.

Conclusion

Results of this study indicate that oxygen content and consumption values computed from uncorrected pO_2 values most nearly equal the direct measurement of oxygen content. For oxygen content, the standard deviation of the observed points around the fitted line range from .68 vol% for uncorrected Group 1 to 1.07 vol% in Group 2, where .97 vol% represents Kelman's Group 4. In terms of oxygen consumption, standard deviation from linear regression ranges from 13.13 ml/min in uncorrected Group 1 to 31.82 ml/min in Group 2. Group 4 by Kelman's technique has a standard deviation from linear regression of 29.93 ml/min.

The temperature correction formulae reviewed in this paper were least accurate under the conditions of venous sampling and moderate hypothermia. With a known blood flow rate an arterial sample is drawn to determine the oxygen delivered to the patient. Blood gas data from a venous sample, drawn simultaneously, is used to evaluate a patient's oxygen consumption. The partial pressure of oxygen, corrected or uncorrected, in venous blood is a poor estimate of oxygen consumption. The best reflection of oxygen consumption is by a direct measurement of arterial and venous blood. However for institutions without direct measurement, this study has determined that the best correlation to direct measurement occurs when using uncorrected pH and pO_2 applied to a standard oxygen dissociation curve at 37°C (IL slide rule) for oxygen saturation determination. Co-oximetry also has a strong correlation with direct content determination when used in a formula to also account for oxygen in plasma.

Acknowledgments

The authors are grateful for the financial support of the Association for Circulation Technologists, Ohio State University Undergraduate Research Scholarship Fund, the assistance of Mr. David Holt and Mr. Edward Kray, and the cooperation of the perfusionists and laboratory personnel at Harper-Grace Hospital.

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APPENDIX A
Temperature Conversion Table for pO₂

Temp. °C	T	Multiplier for pO ₂
37	0	1.0
36	1	0.93
35	2	0.87
34	3	0.81
33	4	0.75
32	5	0.70
31	6	0.65
30	7	0.61
29	8	0.57
28	9	0.53
27	10	0.50
26	11	0.46
25	12	0.43
24	13	0.40