

The Value of Venous Oxygen Levels During General Anesthesia

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Right atrial and superior vena caval O_2 saturations were measured in premedicated adult patients under anesthesia, 5 with ether and 5 with halothane, during surgical treatment of varicose veins. Sampling catheters were positioned by electrocardiographic techniques. Saturations were determined by *in vitro* reflection oximetry.

Average venous O_2 levels were higher during ether than during halothane anesthesia. The differences were small, however, and not considered to be of functional import. Average right atrial O_2 levels agreed well with mixed-venous O_2 levels predicted from previous studies of cardiac output and O_2 uptake during ether or halothane anesthesia. Such measurements of right atrial O_2 saturation offer advantage in clinical investigations on anesthesia.

Venous oxygen levels have been helpful in management of patients during whole-body perfusion¹ and in the postoperative period.^{2,3} These applications are based upon the manner in which venous O_2 levels reflect relations in the O_2 transport system. When the Fick equation (1) is rearranged (2), it is apparent that mixed-venous O_2 content is related directly to arterial O_2 content and inversely to the ratio of O_2 uptake and cardiac output.

$$\begin{aligned} \text{Cardiac output} \\ &= \frac{O_2 \text{ uptake}}{(\text{Arterial} - \text{mixed venous}) O_2 \text{ content}} \quad (1) \end{aligned}$$

$$\begin{aligned} \text{Mixed-venous } O_2 \text{ content} \\ &= \text{Arterial } O_2 \text{ content} - \frac{O_2 \text{ uptake}}{\text{Cardiac output}} \quad (2) \end{aligned}$$

Thus a decrease in mixed-venous O_2 indicates a change in the O_2 transport system which in-

cludes a reduction of arterial O_2 content or reduction of cardiac output *relative* to O_2 uptake, or a combination of both. Similar considerations apply to the interpretation of an increase in mixed-venous O_2 .

While knowledge of mixed-venous O_2 content alone does *not* provide a quantitative estimate of arterial O_2 content, O_2 uptake, or cardiac output, it does make possible certain deductions about relations within the O_2 transport system. For example, if mixed-venous O_2 content is normal (15 ± 1 ml./100 ml. blood) no profound disparity exists in arterial O_2 content or in the relation of cardiac output to O_2 uptake. If mixed-venous O_2 content is abnormally low—for example, 10 ml./100 ml. blood—a disparity exists in the O_2 system, the precise nature of which could be elucidated only by further laboratory or clinical observations. The abnormality might be: (1) reduced arterial O_2 content (anemia, low inspired O_2 tension, CO poisoning, and so on), or (2) low cardiac output relative to metabolic consumption of O_2 (myocardial failure, coronary occlusion, hypovolemia, hyperthermia, shivering, and such), or (3) a combination of (1) and (2).

The present study explored the practicality and utility of measuring venous O_2 levels in anesthetized patients. The hemodynamics of clinical situation obtaining had been studied previously in detail.⁴⁻⁶ This circumstance facilitated comparison of right atrial O_2 levels observed in the present study with mixed-venous O_2 levels predicted for this situation from previous investigations.

Materials and Methods

Ten adult patients free of known metabolic or cardiorespiratory disorders were studied during operative treatment of varicose veins. Each received ethchlorvynol (Placidyl) (500

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TABLE 1. Arterial, Right Atrial (RA), and Superior Vena Caval (SVC) O₂ Saturations (%) During Anesthesia With Ether and With Halothane (Average of Triplicate Determinations)

Anesthetic	Case	First Hour			Second Hour		
		Arterial	RA	SVC	Arterial	RA	SVC
Ether	1	100	78	83	100	83	85
	2	99	72	78	100	77	81
	3	100	83	85	100	81	83
	4	100	74	78	100	77	82
	5	99	69	60	98	70	66
	Avg.	100	75	77	100	78	79
Halothane	6	98	68	65	99	65	66
	7	100	72	69	99	71	69
	8	98	74	80	98	71	78
	9	100	72	59	100	73	59
	10	100	77	69	100	72	72
	Avg.	99	73	68	99	70	69

mg. orally) the night before operation. Pre-medicants consisted of pentobarbital (100 mg. orally) 2 hours before and meperidine (50 to 100 mg. intramuscularly) and atropine sulfate (0.4 mg. subcutaneously) 1 hour before the start of anesthesia. After induction with thiopental (100 to 275 mg. intravenously) and intubation with the aid of succinylcholine (40 to 60 mg.), anesthesia was maintained with 6 liters per minute of nitrous oxide (65 per cent) and oxygen (35 per cent) and additional ether (5 patients) or halothane (5 patients). The concentration of ether or halothane was adjusted in each case to the level just sufficient to maintain unconsciousness and lack of movement, without the use of additional relaxants. Manual hyperventilation was used with a semiclosed-circle carbon-dioxide absorption system. Expiration took approximately twice as long as inspiration. Mean airway pressure was 3 to 4 mm. of mercury. All patients were awake and responded soon after operation (3 to 9 hours in duration) and left the hospitals without serious postoperative complications.

Oxygen saturation was determined on triplicate samples removed from the right atrium (RA) and superior vena cava (SVC) at 1 hour and at 2 hours or more after induction of anesthesia. At these times the O₂ saturation, P_{CO₂}, pH, and concentration of hemoglobin were de-

termined on brachial-artery samples (Teflon needle). RA and SVC samples were obtained via catheters introduced percutaneously via a needle in a medial antecubital vein, passed centrally, and positioned by electrocardiographic (ECG) means. For these purposes the catheter (PE90, S36: Clay-Adams, New York City) was freed of bubbles, filled with saline, and connected to an ECG lead. In all essential respects, the technique including characteristic position profiles (ECG) was not different from that previously described for positioning ventriculo-atrial shunt catheters.⁷ Roentgenographic confirmation of appropriate positioning was obtained in a number of cases. Precaution against accidental induction of ventricular fibrillation included testing of the ECG assembly (Section of Engineering, Mayo Clinic) and disconnecting all other electrical equipment attached to the patient or operating table during catheter placement.

Percentage saturation of hemoglobin with oxygen (O₂ saturation) was determined by reflection oximetry (American Optical Model 10800). This instrument⁸ makes measurements at two wavelengths (650 and 805 millimicrons), requires a 2-ml. sample, and reads directly in saturation units (S.U.). In repeated determinations on aliquots of blood samples, a systematic difference existed between dial readings and O₂ saturations deter-

mined by the method of Van Slyke. Therefore, all dial readings were corrected by referring to a calibration curve constructed and repeatedly checked by Van Slyke determinations. Readings were reproducible (± 0.5 S.U.), little affected by actual hemoglobin concentration (up to twofold dilution), only slightly temperature-sensitive (1 S.U. per 10° C.), and not influenced by the presence of anesthetic agents. In 35 of 45 consecutive comparisons, corrected oximeter readings differed from saturations determined by the Van Slyke procedure by not more than ± 2 S.U. The range of differences was 0 to 4 S.U. These differences are comparable to the magnitude of error inherent in the Van Slyke determination. Hemoglobin (grams per 100 ml.) was determined by the cyanmethemoglobin method (Fisher Hemophotometer Model 55). Dilutional error was minimized by the use of quality pipettes (± 0.3 per cent) and larger than usual volumes of blood (0.1 ml.) and diluent (20 ml.). Hemoglobin values determined by this technique did not differ from known values (Van Slyke) by more than ± 0.2 g. Electrodes (Instrumentation Laboratories) maintained at esophageal temperature were used for the determination of pH and P_{CO_2} . Buffer base (BB⁺) values were obtained by appropriate substitution in the Singer-Hastings nomogram.

Mixed-venous O_2 saturations were predicted for this anesthetic and surgical situation by means of the rearranged Fick formula (2)

after appropriate conversion of O_2 content to O_2 saturation terms. In this calculation, average observed values were used from previous⁴⁻⁶ (O_2 uptake, cardiac output) and the present (arterial O_2 saturation, hemoglobin) studies. The difference in content of O_2 in physical solution between arterial and mixed venous blood was assumed to be 0.2 ml. of O_2 /100 ml. of blood.

Results

Arterial and venous O_2 saturations observed during the first and second hour of ether or halothane anesthesia are listed as individual and group-average values in table 1. Arterial O_2 saturations were similar and within a narrow range (98-100). Venous O_2 saturations were more variable, although within each set of triplicate samples the range of saturations averaged 1 and did not exceed 3 S.U. Venous O_2 saturations tended to be greater and to increase with time in the ether group and to be lower and remain the same or fall in the halothane group. Generally, in the ether group, SVC saturations were the same as or higher than right atrial saturations. In patients receiving halothane, SVC saturations tended to be lower than RA saturations. Despite these trends, considerable individual variability existed and the ranges of group-venous O_2 saturations were broad and overlapping. Mixed-venous saturations predicted for each group are listed in table 2 and compared with average observed RA and SVC saturations in table 3. Good

TABLE 2. Cardiac Output, Oxygen Uptake, and Mixed-Venous Oxygen Levels During Anesthesia With Ether (E) and With Halothane (H)

Observations	Mean Observed Values*						Calculated Values	
	Cardiac Output (l./min./m. ²)		Oxygen Uptake				Mixed-Venous Saturation (%)‡	
			(%) Predicted Basal		ml./min./m. ² †			
	E	H	E	H	E	H	E	H
First hour	2.31	1.96	92	84	110	101	75	73
Final hour	2.59	1.82	95	95	114	114	77	67

* Individual values have been published elsewhere.⁴⁻⁶

† Based on average predicted basal values of 120 ml./min./m.²

‡ Based on hemoglobin 13.5 g./100 ml. (present study), arterial blood saturation 100 per cent, (A-V) O_2 physical solution 0.2 ml./100 ml.

TABLE 3. Predicted and Observed Venous Oxygen Saturations (%)*

	Predicted Mixed Venous	Observed	
		RA	SVC
Ether Early Later	75	75	77
	77	78	79
Halothane Early Later	73	73	68
	67	70	69

*Based on tables 1 and 2.

TABLE 4. Arterial pH, P_{CO_2} , Hemoglobin, and Buffer Base (BB⁺) During Anesthesia With Ether and With Halothane

Anesthetic	Case	Arterial			
		pH	P_{CO_2} (mm. Hg)	Hemoglobin (g./100 ml.)	BB ⁺
Ether	1	7.55	26	13.4	49
		7.41	35	13.4	45
	2	7.57	27	13.6	51
		7.49	31	13.6	48
	3	7.55	30	13.4	51
		7.60	27	13.5	53
	4	7.63	23	14.4	52
		7.59	24	14.5	50
Halothane	5	7.47	30	14.0	46
		7.50	31	14.0	49
	Avg.		28	13.8	49
	6	7.55	29	12.5	51
		7.55	31	12.7	52
	7	7.59	25	13.7	51
		7.53	29	13.2	50
	8	7.42	37	14.9	47
		7.43	38	15.0	48
	9	7.60	26	11.8	52
		7.58	27	12.2	52
	10	7.61	26	12.8	52
		7.62	26	13.0	52
	Avg.		29	13.2	51

agreement exists between early predicted mixed-venous and observed RA O_2 saturations. The direction and magnitude of change with time were similar in predicted and observed values. A similar distribution of individual arterial pH, P_{CO_2} , hemoglobin, and BB⁺ values (table 4) was present in each group.

Comment

The observations of the present study (table 1) are consistent with the prediction (table 2) that in this anesthetic and surgical situation mixed-venous O_2 levels are slightly higher during ether than during halothane anesthesia. The small differences are not believed to have functional significance. The greater average SVC saturation than RA saturation during ether anesthesia suggests a greater blood flow in relation to O_2 consumption in the area drained by the SVC than in the body as a whole. During halothane anesthesia blood flow apparently was less in relation to O_2 consumption in the area drained by the SVC than in the body as a whole. These differences in distribution during halothane anesthesia were less apparent in later observations. While considerable variability was present between the O_2 saturations observed in different individuals, the magnitude was similar to that expected from the individual differences in cardiac output and O_2 uptake previously observed.⁴⁻⁶

In addition to confirming a prediction, this experience suggests a method particularly appropriate for the clinical situation. Whole-body O_2 levels are reflected in mixed-venous O_2 levels since both are determined by the relation of O_2 consumption rate, cardiac output, and arterial blood O_2 content. While this is evident from examination of the Fick relation, it may become more so from analysis of the observations in table 2. During the first hour cardiac output was greater during ether than during halothane anesthesia. Superficially, this suggests better cardiac performance and more "adequate" perfusion with ether. However, when O_2 consumption rates during the same period are considered, it becomes evident that the ratios of O_2 consumption to cardiac output with the two agents are similar. Accordingly, since arterial O_2 contents were simi-

lar, it can be concluded that mixed-venous O_2 levels and accordingly, whole-body O_2 levels, with each agent were similar. The point of the present study is, of course, that a similar quality of information was obtained by following right atrial O_2 saturations alone with considerable savings in time, money, and labor. It is to be remembered, of course, that mixed-venous O_2 levels provide only indirect information about tissue O_2 levels and that such information pertains only to the body as a whole. There would be hesitancy in predicting a specific organ or tissue O_2 level from mixed-venous O_2 levels alone since a wide range of organ blood flows and metabolic consumption rates exist even in normal unanesthetized man.⁹

The use of RA samples to estimate mixed-venous O_2 levels is a compromise dictated by the practicalities of clinical research. Mixed-venous blood is by definition a homogeneous mixture of all blood draining from all parts of the body. In normal, unanesthetized man the SVC O_2 levels are lower than those of mixed-venous blood¹⁰ and the IVC O_2 levels are higher. The latter differential apparently results from the high blood flow and low O_2 extraction rates in the kidney and liver. These caval streams of different O_2 levels and the stream from the coronary sinus are incompletely mixed prior to reaching the outflow tract of the right ventricle or the pulmonary artery.¹⁰ Accordingly, there is a considerable chance that RA sampling will draw preferentially from the SVC, IVC, or coronary-sinus stream; and only by chance would a single sample from an indeterminate RA site be representative of all blood draining from all the body. While sampling from a *specific* site in the right atrium has been defended in the past as a means of obtaining a mixed-venous sample,¹¹ modern practice recognizes as reliable only samples from the pulmonary artery.^{6, 10} At this point, however, the practicalities of clinical research must be considered. Catheterization of the pulmonary artery is time-consuming, ordinarily requires fluoroscopy, and has a small incidence of serious cardiac arrhythmias. These obstacles are lessened by RA catheterization with localization by intracardiac electrocardiography. Theoretically,

sampling the unmixed streams in the right atrium would introduce variability in the results but no bias if the sampling were done often enough in a random manner. This perhaps accounts for the good agreement between predicted mixed-venous O_2 levels and the average observed RA O_2 levels of the present study, although some measure of good fortune cannot be discounted.

Summary

Right atrial and superior vena caval O_2 saturations have been measured in premedicated adult patients under anesthesia—5 with ether and 5 with halothane—during surgical treatment for varicose veins. Sampling catheters were positioned by electrocardiographic techniques. Saturations were determined by *in vitro* reflection oximetry.

Average venous O_2 levels at these sites were higher during ether than during halothane anesthesia. The differences were small, however, and not considered to be of functional import. Average right atrial O_2 levels agreed well with mixed-venous O_2 levels predicted from previous separate studies of cardiac output and O_2 uptake during ether or halothane anesthesia. Such measurements of right atrial O_2 saturation offer important utilitarian advantages in clinical research of anesthesia.

Dr. T. T. Myers, Section of Peripheral Vein Surgery, carried out the operative procedures during which these observations were made.

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CORTISONE DEPRIVATION After bilateral adrenalectomy dogs and rats were given desoxycorticosterone and hydrocortisone for several days until they recovered from the immediate effects of surgery. Then the hydrocortisone was discontinued. Loss of the protective action of the glucocorticoid caused the heart to behave as if it was in failure, both functionally and metabolically. SCOT levels rose significantly but SCPT levels did not. Microscopic changes in the hearts could not be demonstrated. (Degerli, I. U., Webb, W. R., and Lockwood, W. R.: *The Glucocorticoid Deprived Myocardium*, *Arch. Surg.* 89: 457 (Sept.) 1964.)

TOLERANCE OF CARDIAC ISCHEMIA Duration of ischemia which permits complete restoration of full body function is limited by post-ischemic congestive heart failure and not by the length of time it takes the brain to recover. In order to determine the limit of time the heart can withstand ischemia with subsequent immediate sufficiency to sustain life of the organism, cardiac ischemia of different durations was induced by clamping the arterial outflow of dog hearts at heart temperatures ranging from 36° C. to 28° C. during extracorporeal perfusions in 100 dogs. The investigations showed that the critical duration of ischemia at a body temperature of 37° C. is 4½ minutes. No animal survived ischemia of 5 minutes for longer than 12 hours. At 34° C. the time limit for ischemia was 5½ minutes; at 32° C. it was 6½ minutes; and at 28° C. it was 8½ minutes. Histologic changes were found to be most marked in hearts of animals which died 10, 12, or more hours after ischemia. However, the majority of animals which survived also showed histologic destruction of individual heart muscle fibers, circumscript necrotic foci, and more extensive destructions of cell areas in both ventricles though the hearts were functioning fully in the post-ischemic stage. (Schlosser, V., and Strecker, H.: *Studies of the Length of Time the Heart Will Tolerate Ischemia in Normo- and Hypothermia*, *J. Cardio. Surg.* 48: 430 (Sept.) 1964.)