Comparison of formulae used to estimate oxygen saturation of mixed venous blood from caval samples

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A comparison of several formulae used to estimate the oxygen saturation of mixed venous blood from caval samples has been made in 63 patients who had no evidence of a left-to-right shunt. For patients not on intermittent positive pressure ventilation only the formula $\frac{3SVC + HIVC}{4} = MVB$ (where SVC is superior vena cava, HIVC is high inferior vena cava, and MVB is mixed venous blood) gave a satisfactory regression and mean value. For patients on intermittent positive pressure ventilation, high inferior vena cava correlated poorly with mixed venous blood and no formula was an ideal predictor of mixed venous blood.

For the whole group, including those with and without intermittent positive pressure ventilation, $\frac{3SVC + HIVC}{4}$ most nearly approached the ideal formula for prediction of mixed venous blood. The sources of error in estimation of mixed venous blood are examined and implications for calculation of shunt size are discussed.

When mixed venous blood cannot be obtained from the pulmonary artery because of the presence of a left-to-right shunt at a more proximal level, there is considerable debate as to which caval blood sample, or combination of samples, provides the best estimate of mixed venous blood. Though a number of different formulae have been used (Barratt-Boyes and Wood, 1957; Flamm, Cohn, and Hancock, 1970; Goldman *et al.*, 1968; Scheinman, Brown, and Rapaport, 1969; Swan, Burchell, and Wood, 1954; Swan, Marshall, and Wood, 1958), there is little information comparing the reliability of the various formulae used to predict mixed venous blood from caval samples.

Since January 1970 we have used a computer based system to store all data obtained at diagnostic catheterization (Blackburn *et al.*, 1972). The existence of this large data store and the ease of access and analysis provided by computer handling made possible a re-examination and statistical comparison of various formulae used to estimate mixed venous blood in a large series of patients studied at routine diagnostic catheterization.

Patients and methods

Review of 1,800 reports of catheterizations performed between January 1970 and June 1972 was performed by computer search. Patients were selected in whom the final diagnosis at catheterization excluded a left-to-right shunt and in whom oxygen saturation had been measured in pulmonary artery, superior vena cava, and high and low inferior vena cava thus permitting comparison of true mixed venous blood (pulmonary artery) and various combinations of caval samples. In addition no patient had clinical, angiographic, surgical, or necropsy evidence of a left-to-right shunt. A total of 63 patients met these criteria of whom 9 had no cardiac disease, 33 had acquired heart disease (rheumatic or ischaemic), and 21 had congenital heart disease (isolated pulmonary stenosis 12 patients, coarctation 7, Ebsteins' anomaly 1, tetralogy of Fallot 1).

Ten patients were aged 1 year or less and the mean age of the remaining 53 patients was 14·8 years (1 to 63 years). Of the patients, 24 were studied under general anaesthesia with intubation and intermittent positive pressure ventilation, using a Brompton-Manley ventilator: 5 of these were aged less than 1 year and the mean age of the remainder was 4·4 years (1 to 10 years).

Oxygen saturation was measured by reflection oximetry (Zijlstra and Mook, 1962). In all patients samples were obtained from the superior vena cava either just above

the right atrial shadow or close to the junction with the innominate vein, and from high inferior vena cava at the level of the diaphragm and low inferior vena cava at abdominal level above the entry of the renal veins. All patients had a pulmonary arterial sample which was taken as mixed venous blood. The time elapsing from the start of catheterization was known for each blood sample and also the time interval between first and last samples. The samples were not taken in any particular sequence.

The mean time interval between first and last blood samples was 9·1 minutes (3–26 min).

Calculations

Estimates of mixed venous blood were obtained from the following formulae which have been investigated by the authors shown.

I: $SVC = MVB$ (Goldman *et al.*, 1968; Scheinman *et al.*, 1969)

II: $\dfrac{SVC + HIVC}{2} = MVB$ (Barratt-Boyes and Wood, 1957)

III: $\dfrac{3SVC + HIVC}{4} = MVB$ (Flamm *et al.*, 1970)

IV: $\dfrac{SVC + 2HIVC}{3} = MVB$ (Swan *et al.*, 1954)

V: $\dfrac{SVC + HIVC + LIVC}{3} = MVB$

VI: $HIVC = MVB$

VII: $LIVC = MVB$

Linear regressions were performed of true mixed venous blood (pulmonary arterial sample) on the estimated mixed venous blood value calculated from each of the formulae. The probability of regression slopes being equal to unity and intercepts equal to zero was examined. Also the mean differences between estimated and true mixed venous blood for each formula was compared to zero. This analysis was performed for the whole group and for four subgroups shown below.

Group A: Patients with intermittent positive pressure ventilation.
Group B: Patients without intermittent positive pressure ventilation.
Group C: Patients with samples taken in 11 minutes or less.
Group D: Patients with samples taken in greater than 11 minutes.

In addition, comparison of correlation coefficient, slope, and intercept for each formula was made between Groups A and B, and Groups C and D.

Statistical analysis of all comparisons was made by Student's 't' test (Armitage, 1971).

Results

The regression lines for the whole group for formulae I to VI are shown in the Fig. and the relevant statistical values are shown in Table 1. The mean of differences between true and estimated mixed venous blood was significantly different from zero for all formulae except formula III. Mean values for formula VI (high inferior vena cava) and VII (low inferior vena cava) were especially high and this was reflected in formula V which incorporates both. The mean value for formula I (superior vena cava) was significantly lower than the regression for high inferior vena cava and low inferior vena cava. Only the regression for formula V had a slope not significantly different from 1·0 and an intercept not significantly different from zero. The slopes and intercepts of the other regressions differed to varying degrees from 1·0 and zero, respectively, but this was least pronounced for formula III. The correlation coefficients of regressions for formula IV and formulae VI and VII were significantly lower than that for the other formulae (Table 1).

For those without intermittent positive pressure ventilation (Group B) as for the whole group, only formula III gave a mean difference between true and estimated values of mixed venous blood not significantly different from zero. The slope and intercept were not significantly different from 1·0 or zero for this formula and also for formulae II, IV, V, and VI.

Comparison between Groups A and B showed no significant differences in correlation coefficient, slope, or intercept for the regressions of formulae I, III, and V, but the regression for formulae II, IV, and VI which weight high inferior vena cava to varying degrees showed pronounced differences in these parameters (Table 2). The regression for formulae VI (high inferior vena cava) has a low correlation coefficient (0·33) for patients on intermittent positive pressure ventilation (Group A).

Comparison of regressions for Groups C and D showed no significant differences between those with shorter and those with longer sampling times.

Discussion

A formula which satisfactorily predicts mixed venous blood from caval blood samples would give a mean of differences between true and estimated mixed venous blood not significantly different from zero and a regression with a slope close to unity, a negligible intercept, and a high correlation coefficient. For Group B (not on intermittent positive pressure ventilation), comprising 62 per cent of the total, formulae III, $\dfrac{(3SVC + HIVC)}{4}$, meets all of
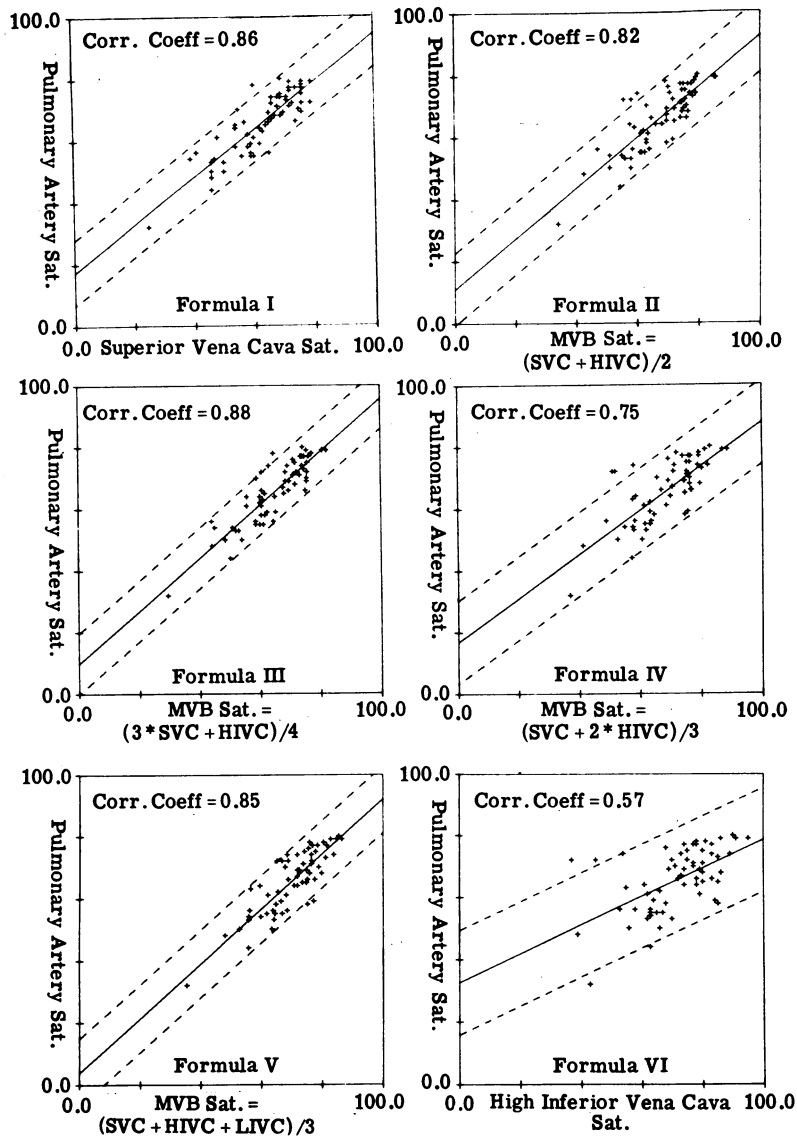
FIG. *The linear regressions for formulae I–VI are shown. Dashed lines indicate 95 per cent confidence limits.*

these fairly strict requirements but the other formulae fail on at least one score. Formula III therefore is the expression of choice for this group. However, the results for Group A (intermittent positive pressure ventilation) are less satisfactory. Though several formulae have satisfactory mean values, only the regression for formula V has a satisfactory slope and intercept but the mean value for this formula is higher than true mixed venous blood. Comparison of regressions for Group A and B shows that the correlation coefficient for the regression for Formula VI (high inferior vena cava) is much lower for Group A than B and the regressions of other formulae which weight high inferior vena cava are similarly affected. As only formula I (superior vena cava) excludes high inferior vena cava the regressions for Group A are in general less satisfactory and incorporation of Group A in the whole group has a deleterious effect on regressions for the whole group. For the whole group only

TABLE I *Statistical data*

Group	Formula	Mean estimated mixed venous blood	P_M	SEE	r	Slope	P_S	Intercept	P_I
All									
	I	63·6	<0·001	5·3	0·86	0·77	<0·001	17·3	<0·001
	II	67·1	0·05	5·8	0·82	0·81	0·01	11·0	<0·05
Pulmonary artery	III	64·8	NS	4·9	0·88	0·86	<0·05	9·8	<0·02
mean=65·5	IV	68·5	<0·01	6·7	0·75	0·71	<0·01	16·9	<0·01
No.=63	V	70·0	<0·001	5·4	0·85	0·88	NS	3·9	NS
	VI	71·4	<0·001	8·4	0·57	0·46	<0·001	32·6	<0·001
	VII	76·0	<0·001	7·4	0·69	0·61	<0·001	19·2	<0·01
	I	59·9	<0·001	4·6	0·88	0·73	<0·01	20·6	<0·01
	II	65·3	NS	6·8	0·70	0·60	<0·01	24·8	<0·01
Group A (IPPV)	III	62·6	NS	4·9	0·86	0·79	<0·05	15·0	<0·05
PA mean=64·3	IV	67·1	NS	7·9	0·56	0·43	<0·001	35·2	<0·01
No.=24	V	69·6	<0·001	6·5	0·74	0·74	NS	13·1	NS
	VI	70·8	0·05	9·0	0·33	0·19	<0·001	50·6	<0·001
	VII	78·2	<0·001	8·3	0·51	0·44	<0·01	30·0	<0·05
	I	64·3	0·05	5·7	0·85	0·81	<0·05	14·0	<0·02
Group B (not	II	68·1	<0·02	4·7	0·90	0·97	NS	0·3	NS
IPPV)	III	66·2	NS	4·9	0·89	0·92	NS	5·7	NS
Pulmonary artery	IV	69·3	<0·001	4·9	0·89	0·96	NS	−0·5	NS
mean=66·3	V	70·2	<0·001	4·6	0·90	0·95	NS	−0·6	NS
No.=39	VI	71·9	<0·001	6·2	0·85	0·85	NS	4·9	NS
	VII	74·6	<0·001	6·2	0·74	0·74	<0·01	11·2	NS

IPPV=intermittent positive pressure ventilation; NS=not significant; P_S=probability that slope is 1; P_M=probability that mean (PA=estimated MVB) is zero; PA=pulmonary artery; r=correlation coefficient between PA and estimated MVB; P_I=probability that intercept is zero; SEE=standard error of regression estimate.

TABLE 2 *Comparison of regression for Groups A and B*

| | Formula | | | | | | |
	I	II	III	IV	V	VI	VII
Correlation co-efficient	NS	0·05	NS	0·001	NS	0·01	0·05
Slope	NS	0·02	NS	0·001	NS	0·001	NS
Intercept	NS	0·02	NS	0·001	NS	0·001	NS

NS=not significant.

formula V gives a satisfactory regression and only formula III gives a satisfactory mean value. As formula III is the expression of choice for Group B and its regression departs only slightly from the ideal, it is probably the best formula for the whole group as well.

The effect of intermittent positive pressure ventilation on the regression lines is unexpected and might be due to a number of factors including changes in regional blood flow, sampling inaccuracies due to streaming in the inferior vena cava, or patient differences between Groups A and B, such as age.

There was an equal number of infants in Group A and B but the remaining patients in Group B were younger, which was usually the reason for general anaesthesia and ventilation being used. As the number of very young patients was the same, it is unlikely that this difference in age is a relevant factor in explaining the observations, and in other ways the groups appeared similar.

Classical studies by Cournand *et al.* (1948) showed that intermittent positive pressure ventilation had no significant effect on cardiac output, provided that inspiratory pressure increased slowly, expiratory pressure decreased rapidly, and expiration was at least as long as inspiration. The Brompton-Manley ventilator used in this study incorporates these features and is unlikely to have affected cardiac output. However, it is not known whether intermittent positive pressure ventilation can cause changes in regional blood flow which could result in a change in oxygen saturation of high inferior vena caval blood (Davis, 1972).

Sampling in the high inferior vena cava is always liable to inaccuracies caused by streaming of blood of different oxygen saturation, but this factor is unlikely to affect preferentially those with intermittent positive

pressure ventilation. However, if several high inferior vena cava samples had preferentially sampled poorly saturated hepatic venous blood, this could produce the observed regression for high inferior vena cava (Fig.).

The choice of a formula for estimation of mixed venous blood has been influenced by interpretation of the effect of different blood flows in the vena cavae and their slightly different oxygen saturations (Barratt-Boyes and Wood, 1957). There is direct evidence that blood flow in the superior vena cava is approximately half that in the inferior vena cava (Wexler et al., 1968). This supports the suggestion that any formula estimating mixed venous blood from caval samples should at least include a sample from the inferior vena cava either averaging it with the superior vena cava or weighting it in keeping with its higher flow and oxygen saturation. Others have avoided inferior vena cava samples because wide variation in oxygen content of hepatic and renal veins together with laminar blood flow may lead to inaccuracies in sampling (Storstein and Efskind, 1963). Sampling from two sites in the inferior vena cava, one high favouring hepatic blood and one low favouring renal blood, might avoid this by providing an average inferior vena cava sample. This study shows that incorporation of this in formula V has some advantage in that formula V alone gave a satisfactory regression for the whole group but it results in too high a mean value caused by the high oxygen content of low inferior vena cava blood. All formulae ignore the contribution of coronary sinus blood which, though only 5 per cent of the total, is very desaturated (Wade and Bishop, 1962). Flamm et al. (1970) observed that when this blood mixes with inferior vena cava blood it will reduce about half inferior vena cava blood to superior vena caval saturation. Because of this they favour weighting the superior vena cava (formula III) in spite of the reduced superior vena cava flow. In our study this formula is the one of choice for patients not on intermittent positive pressure ventilation and for the whole group is also the most satisfactory, though the regression line departs slightly from the ideal.

The standard error of the regression for formula III for all patients was 4·9 and was greater than this for other regressions. Any single estimate of mixed venous blood therefore has 95 per cent confidence limits of about ± 10 per cent. This variation reflects several factors including inaccuracies in the method of measurement of oxygen saturation, inaccuracies of sampling due to laminar blood flow, and genuine variation in oxygen saturation with time caused by spontaneous changes in cardiac output. The method used to measure oxygen saturation in this study may show slight errors in absolute values of ± 1·8

per cent (Zijlstra and Mook, 1962). Inaccuracies caused by sampling have already been discussed. The spontaneous variation in cardiac output may be considerable. Barratt-Boyes and Wood (1957) found that in normal subjects variation in pulmonary artery oxygen saturation for samples taken more than two minutes apart could range from 0 to 10 per cent because of this effect. This range is similar to the standard error of the present series. They found that this range could only be reduced by very rapid sampling in two minutes or less, and this may be difficult to achieve under routine conditions. It is noteworthy that there were no significant differences between regressions for Group C with shorter sampling times compared to Group D where these were prolonged. Presumably sampling was not sufficiently rapid in Group C to produce an effect. It remains likely, therefore, that the time factor is a major determinant of the variation in predicted mixed venous blood for all the formulae in this study.

If mixed venous blood is estimated from caval samples obtained under the conditions described in this study, any calculation of systemic blood flow or left-to-right shunt is subject to the same variation. For example, if one assumes pulmonary artery saturation of 85 per cent and systemic arterial saturation of 98 per cent then an estimated mixed venous blood of 70 per cent with an error of ± 10 per cent leads to calculation of shunt size ranging from 1·4 to 2·8. Calculation of shunt size, therefore, should not be allowed to infer a false impression of precision.

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