The O_2 Status of Arterial and Mixed Venous Blood

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The Significance of the Mixed Venous O_2 Status as a Complement to the Arterial O_2 Status

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Introduction

Central venous (v) or mixed venous ($\bar{v}$) blood gas analyses are often used in clinical practice for assessing the respiratory and metabolic condition of a patient as well as for obtaining a more complete view of hemodynamic parameters, although the diagnostic value of such data is a subject of controversy [1–3, 7, 11, 13, 19–22, 24]. The aim of this overview is to attempt a critical evaluation of the significance of the mixed venous O_2 status in the assessment of the O_2 supply and hemodynamic parameters. Data from the literature and own results from clinical investigations are presented.

Factors Determining the Mixed Venous O_2 Status

The mixed venous oxygen status is mainly influenced by two factors: on the one hand by the oxygen availability $\dot{A}O_2$ [ml O_2/min] in the arterial blood (C.O. $\times$ caO_2) to the periphery, on the other by the oxygen consumption $\dot{Q}O_2$ [ml O_2/min] within the periphery. If the peripheral O_2 consumption remains constant, an increased arterial oxygen supply (improvement of the arterial O_2 status, increase in cardiac output) leads to an increase in the venous oxygen content, and vice versa. Similarly, an increase in the peripheral consumption (e.g. increased temperature, increased rate of cell metabolism) leads to a decrease in the venous oxygen content if the oxygen supply remains constant, and vice versa [6, 8, 9]. The factors determining the mixed venous oxygen status are summarized

Table 1. Factors determining the mixed venous O_2 status

Decrease in $c\bar{v}O_2$ by:		Increase in $c\bar{v}O_2$ by:	
I. Decrease in the O_2 supply		I. Increase in the O_2 supply	
Decrease in C.O.		Increase in C.O.	
Frequency	↓	Frequency	↑
Stroke volume	↓	Stroke volume	↑
Decrease in caO_2		Increase in caO_2	
paO_2	↓	paO_2	↑
saO_2	↓	saO_2	↑
cHb	↓	cHb	↑
II. Increase in O_2 consumption		II. Decrease in O_2 consumption	
Microcirculation	↑	Microcirculation	↓
Peripheral shunts	↓	Peripheral shunts	↑
Cell metabolism	↑	Cell metabolism	↓

in table 1 based on either a decrease or an increase in the mixed venous O_2 content ($c\bar{v}O_2$).

Due to the many factors that can influence the mixed venous O_2 concentration ($c\bar{v}O_2$), an interpretation of changes in the mixed venous oxygen status is difficult. This also applies to the indirect assessment of the patient's cardiac status based on an assessment of the mixed venous oxygen saturation ($s\bar{v}O_2$) and the arteriovenous oxygen difference ($a\bar{v}DO_2$), whose relationship is described by Fick's principle [3, 6, 7]:

$$a\bar{v}DO_2 = \frac{\dot{Q}O_2}{C.O.}$$

According to this principle, the cardiac output C.O. [l/min] is inversely proportional to the oxygen content difference $a\bar{v}DO_2$ [ml/dl]. With a constant peripheral oxygen consumption, this should be suitable for assessing the cardiac output of a patient.

Site of Measurement

There is general agreement in the literature that blood taken from the pulmonary artery (PA) using a pulmonary artery catheter should be described as 'mixed venous' ($\bar{v}$), and blood from the Vena cava superior, inferior or right atrium as 'central venous' (v) [1, 11, 13, 19, 22]. This

differentiation is important because coronary venous blood does not enter the venous blood pool until it reaches the right atrium (coronary sinus). Therefore, an adequate mixing of the venous blood from all organs of the body takes place at the earliest in the right ventricle.

The mixing of the coronary venous blood thus inevitably leads to a decrease in the O_2 saturation of the blood arriving at the right atrium, although this effect is somewhat weaker than would be expected from the low proportion of the cardiac output due to the coronary blood flow (5%). This can be explained by the special situation of the venous drainage of the heart:

– ⅔ of the coronary blood flow drains into the coronary sinus,

– ⅓ of the coronary blood flow drains directly into the heart chambers via the Venae Thebesii (Venae parvae cordis and Venae cordis minimae), ⅕ of this going into the left chamber (proportion of physiological R/L shunt 0.3% of cardiac output), and ⅘ into the right chamber.

For example, for the O_2 saturation it follows that

– the O_2 saturation of the pulmonary artery blood ($s\bar{v}O_2$) must always be lower than that of the blood arriving at the right atrium (svO_2),

– any central venous saturation (VCS, VCI, RA) can only represent the situation of parts of the circulation, and

– only the pulmonary arterial blood, after sufficient mixing of all sources of central venous blood in the right ventricle (RV), can give a representative value for the entire organism.

However, this is not the only reason why the value of so-called central venous blood samples (from the Vena cava inferior, the Vena cava superior or the right atrium) should be approached cautiously as a more practical alternative [3, 4] to mixed venous blood samples for the determination of a representative venous oxygen concentration ($c\bar{v}O_2$).

A further point must also be considered: There is still no generally accepted definition of where exactly in the venous system around the heart a venous blood sample must be taken in order to be considered as central venous.

For reasons of safety (for example, to avoid the danger of perforating the Vena cava superior along its intrapericardial course or the wall of the right atrium or chamber [4]), the tip of the catheter should be placed in the Vena cava superior clearly above its junction with the right atrium. This of course requires that entry into the vascular system is made via the veins of the upper half of the body.

Vena cava superior (VCS)

The location of the catheter tip in the Vena cava superior means that the blood samples taken in this way only represent the organs which drain into the VCS (veins of the head and neck region and of the arms, pericar-

dial veins, Vv. thoracicae internae). Even the blood from the lower half of the body (segmental trunk veins and spinal veins) supplied via the Vena azygos, which joins the Vena cava superior dorsally immediately before its entrance to the pericardium, is not represented in these blood samples. Since the cerebral circulation accounts for 15% of the cardiac output, this will be the most important contributing factor in this case.

Vena cava inferior (VCI)

If one of the femoral veins is chosen as the point of entry to the central venous system (now only used in exceptional cases [4]), the correct central venous location of the catheter tip would be somewhat below the diaphragm (generally, the Vena cava inferior joins the right atrium immediately after passing through the diaphragm and does not have a significant intrapericardial aspect). Thus the circulation of the splanchnic region (25% of cardiac output) and, with a less deeply-placed catheter, the renal circulation (20% of cardiac output) will be the major factors contributing to the central venous data.

Right Atrium (RA)

A third central venous site for blood sampling, although hardly ever used in practice nowadays, is the right atrium. For safety reasons (e.g. to avoid disturbances of cardiac rhythm, endocardial lesions, perforations, see [4]), the catheter tip is not primarily positioned in the atrium. There is, however, another possibility of obtaining central venous blood from the right atrium via the injection lumen of a thermodilution catheter. The opening of this lumen is in the wall of the catheter 30 cm from the catheter tip, and there is a high probability that this side opening is in the right atrium, if the catheter is correctly positioned in the pulmonary circuit.

However, there are a number of reasons why this procedure is not to be recommended:

(1) With the catheter in place, thus providing the possibility of obtaining a mixed venous sample, taking an additional sample of central venous blood would be senseless, unless simultaneous sampling would be helpful for cardiological diagnosis (e.g. cardiac L/R shunt, transposition of the pulmonary veins).

(2) The exact position of the side opening can only be verified with difficulty (pressure curve), if at all. This depends entirely on how far the catheter must be inserted into the pulmonary circuit before reaching the wedge position. 'Falsely positioned' side lumens in the Vena cava or in the right ventricle are not uncommon.

(3) Even if the side opening is in the correct position in the right atrium, the samples taken must be interpreted with great caution, since the proportion of coronary venous blood

in the sample can vary widely, depending on the position of the opening within the atrium, and in extreme cases (e.g. large atrial loop) pure coronary vein blood will be aspirated.

Table 2, based on data from the literature, shows how inconsistent the connection between central venous and mixed venous oxygen saturation – which has recently again been vigorously postulated [21] – is, and that it is not only dependent on the choice of the central venous position for taking the sample, but also on the condition of the monitored patient. It is amazing that the majority of authors are nonetheless in agreement that an assessment of the course of a disease – e.g. the development of an intrapulmonary right-left shunt – can be carried out with sufficient accuracy by measuring the central venous saturation (notwithstanding the additional problem of a potential cardiac right-left shunt existing at the same time [5]).

The table also shows that only a blood sample taken from the right ventricle can be considered accurately representative of a mixed venous sample (see the results of Barratt-Boyes [1]). The correlation of svO_2 (from the right atrium) and $s\bar{v}O_2$ in the entire group of intensive care patients described by Scheinmann [19] is a purely cumulative effect of positive and negative variations (see table 2). The high correlation between mixed venous and central venous data which is continually being postulated [21] can no longer stand up to a critical examination of the literature.

Preliminary Conclusions

The mixed venous, and unfortunately, also the central venous oxygen status are used considerably more often than the arterial status in routine clinical care in departments of anesthesia (central vein catheter), intensive care (central vein catheter and pulmonary artery catheter), and in heart catheter laboratories (pulmonary artery catheter) to assess the current condition of the patient. One reason for this is that mixed venous (and even central venous) blood samples are easier to obtain, which is especially important when repeated controls are necessary. In addition, it is important to consider that an accurate assessment of the patient's hemodynamic condition is only possible with the help of thermodilution catheters for determining cardiac output. A third reason for the preference shown to pulmonary artery catheters is the additional possibility which this affords of assessing the functioning of the left ventricle via the pulmonary capillary wedge pressure (PCWP).

Thus, using a pulmonary artery catheter allows a detailed assessment of the hemodynamic condition (cardiac output, left and right ventricular load) of the critically ill patient. The question remains as to whether or not the additional possibility of obtaining the parameters of the mixed venous

Table 2. Relationship between the sO_2 in central venous (svO_2) and mixed venous ($s\bar{v}O_2$) blood samples as a function of the central venous site of blood sampling and the condition of the patient (correlation coefficient r)

Author	Catheter tip	Subjects	svO_2 Deviation	r
Barret-Boyes (1957; [1])	VCI	Volunteers	$> s\bar{v}O_2$	
	VCS		$< s\bar{v}O_2$	
	RA		$> s\bar{v}O_2$	
	RV		$= s\bar{v}O_2$	
Brandl (1981; [2])	VCS	Ventilated		0.91[a]
Goldman (1968; [8])	VCS	Cardiac infarct	$> s\bar{v}O_2$	
Kersting (1986; [11])	VCS	Before anesthesia	$< s\bar{v}O_2$	0.87
		During anesthesia	$> s\bar{v}O_2$	0.70
		After anesthesia	$< s\bar{v}O_2$	0.80
		Intensive care	$> s\bar{v}O_2$	0.68
		Sepsis	$> s\bar{v}O_2$	0.68
		Organ donor	$> s\bar{v}O_2$	0.48
Miller (1974; [13])	VCS	Cardiac catheter	$< s\bar{v}O_2$	0.86
	VCI[b]		$> s\bar{v}O_2$	0.57
	VCI[c]		$> s\bar{v}O_2$	0.74
Scheinmann (1969; [19])	VCS	Intensive care[d]	$> s\bar{v}O_2$	0.86
	RA		$= s\bar{v}O_2$	0.95
	VCS	Group 1	$< s\bar{v}O_2$	0.99
	VCS	Group 2	$> s\bar{v}O_2$	0.59
	RA		$< s\bar{v}O_2$	0.83
	VCS	Group 3	$> s\bar{v}O_2$	0.55
	RA		$> s\bar{v}O_2$	0.97
Sladen (1981; [20])	VCS	Under anesthesia	$> s\bar{v}O_2$	
Specht (1889; [21])	?	Awake	$< s\bar{v}O_2$	
		General anesthesia	$> s\bar{v}O_2$	
		Peridural anesthesia	$< s\bar{v}O_2$	
Tahvanainan	VCS	Intensive care		0.79
(1982; [22])	RA		$> s\bar{v}O_2$	0.88

[a] The correlation coefficient refers to the calculation of the shunt fraction using each of the saturation values

[b] The catheter tip was inserted into the Vena cava inferior at the diaphragm

[c] The catheter tip was inserted into the Vena cafa inferior at the junction of the kidney veins

[d] Summary of the values of all three patient groups

Group 1: intensive care patients without cardiac failure

Group 2: intensive care patients with cardiac failure

Group 3: patients in shock

oxygen status also allows to some extent the assessment of the respiratory situation (O_2 availability).

Parameters

$c\bar{v}O_2$

The optimal parameter for describing the mixed venous oxygen status is the O_2 concentration ($c\bar{v}O_2$), since this includes the amounts of both physically dissolved and chemically bound oxygen. The arterial venous oxygen difference (in concentration units) can only be obtained from the O_2 concentration (arterial and mixed venous). In practice, however, this is too complicated (van Slyke method or galvanic cell).

The concentration calculated using the CO-oxymeter only includes the chemically bound O_2 and is therefore only useful under normoxic, but not hyperoxic, conditions.

$s\bar{v}O_2$

The mixed venous oxygen saturation ($s\bar{v}O_2$) is only suitable for determining the venous oxygen status if the Hb concentration remains unchanged. Its value is further limited under hyperoxic conditions, since a saturation value of 100% saO_2 on the arterial side cannot be surpassed. This means that, in hyperoxia, the arteriovenous oxygen difference ($a\bar{v}DO_2$ in %) is no longer proportional to oxygen consumption, since part of the O_2 demand is met by the physically dissolved proportion (during hypothermia in a cardiopulmonary bypass the peripheral oxygen demand can under certain conditions be met by the physically dissolved porportion; Brandt, unpublished data).

$p\bar{v}O_2$

The mixed venous oxygen partial pressure ($p\bar{v}O_2$) is of no value and should therefore be rejected for the assessment of the oxygen demand, since it represents a completely different part of the oxygen binding curve (steep part) than the arterial O_2 partial pressure (paO_2) (upper flat part).

In summary, the following conclusions can be drawn from the above considerations:

– There is no accurately predictable relationship between the central venous and the mixed venous oxygen status. Therefore, a central venous

blood sample cannot be taken in place of a mixed venous sample, since as a rule this only represents a blood sample from part of the circulation.

– The two main factors determining the mixed venous oxygen status are the arterial oxygen supply and the oxygen consumption of the tissues.

– The ideal value for determining the mixed venous oxygen status is the oxygen concentration.

– With a constant hemoglobin concentration and in normoxia the mixed venous oxygen saturation could also be a useful parameter.

– With the arteriovenous oxygen difference calculated from the oxygen concentration or oxygen saturation ($a\bar{v}DO_2$; ml/dl, %), it is not possible to differentiate between a change in oxygen supply and a change in oxygen consumption.

Clinical Investigations

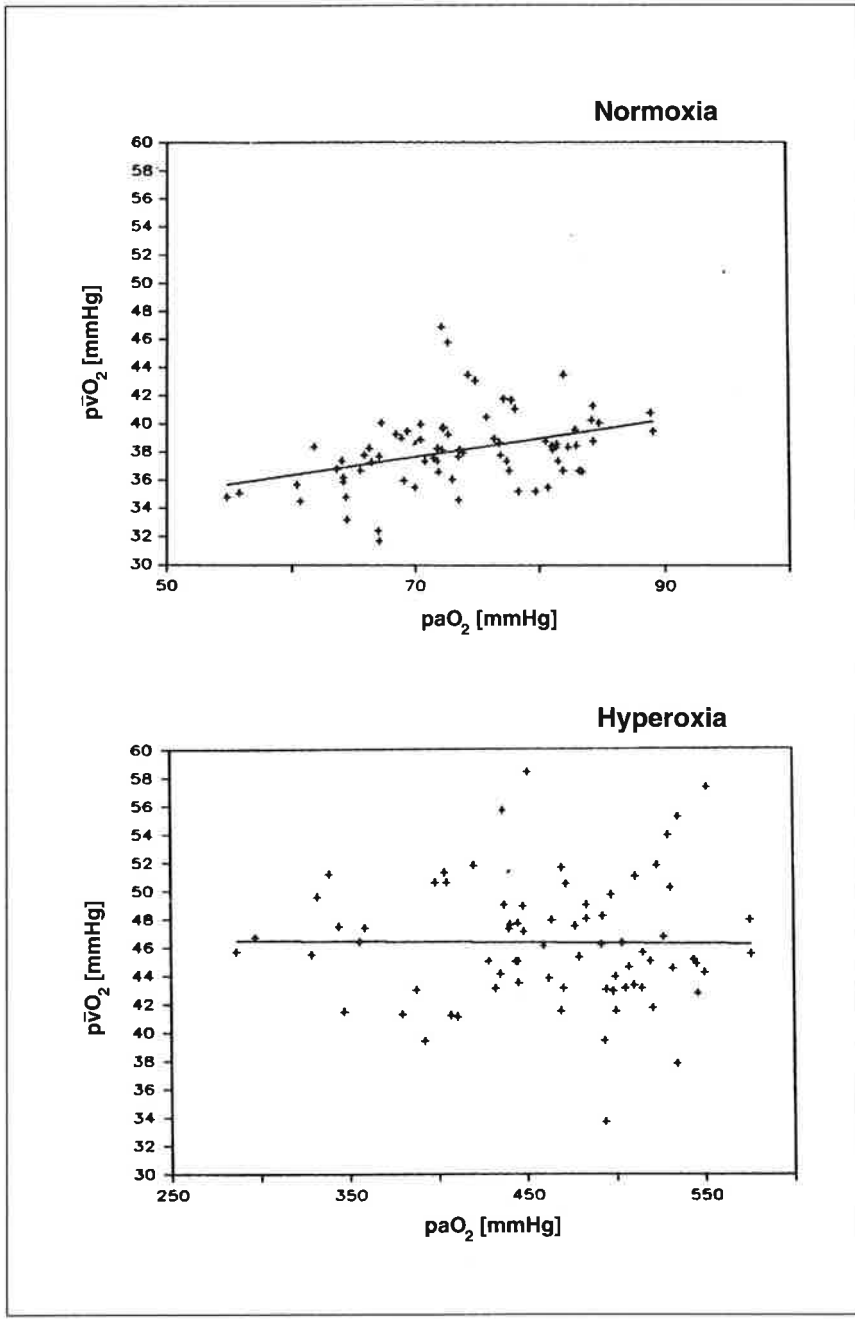
In a clinical investigation to study the behavior of blood gases and hemodynamic parameters during the use of various anesthetic techniques, the question of the relevance of mixed venous oxygen status per se and as an adjunct to the arterial oxygen status was examined. In 75 patients who underwent an aortocoronary bypass operation in our clinic, the relationships between the mixed venous and the arterial oxygen status during normoxia and hyperoxia were studied, as well as the value of the mixed venous oxygen status in assessing the cardiac situation of the patient.

All patients had an arterial cannula inserted into the radial artery and a 4-lumen thermodilution catheter inserted via the internal jugular vein, right or left. The oxygen pressure and the oxygen saturation as well as the calculated oxygen content of the arterial and mixed venous blood were determined in vitro using the Corning 170 pH/blood gas analyzer and the 2500 CO-oxymeter during normoxia and hyperoxia following the onset of anesthesia.

The statistical evaluation of the measured values was carried out by calculating the regresson line and by determining the correlation coefficient r.

Results

Whereas during normoxia there is an apparent 'linear' correlation between paO_2 and $p\bar{v}O_2$ within a paO_2 range of 60–90 mmHg ($r = 0.38$; regression line $y = 0.13\ x + 28.34$), during hyperoxia the mixed venous oxygen pressure (paO_2 280–580 mmHg) has a constant value of 46.7 mmHg (fig. 1).


Normoxia
$p\bar{v}O_2$ [mmHg]
60
58
56
54
52
50
48
46
44
42
40
38
36
34
32
30
50
70
90
paO_2 [mmHg]
Hyperoxia
$p\bar{v}O_2$ [mmHg]
60
58
56
54
52
50
48
46
44
42
40
38
36
34
32
30
250
350
450
550
paO_2 [mmHg]

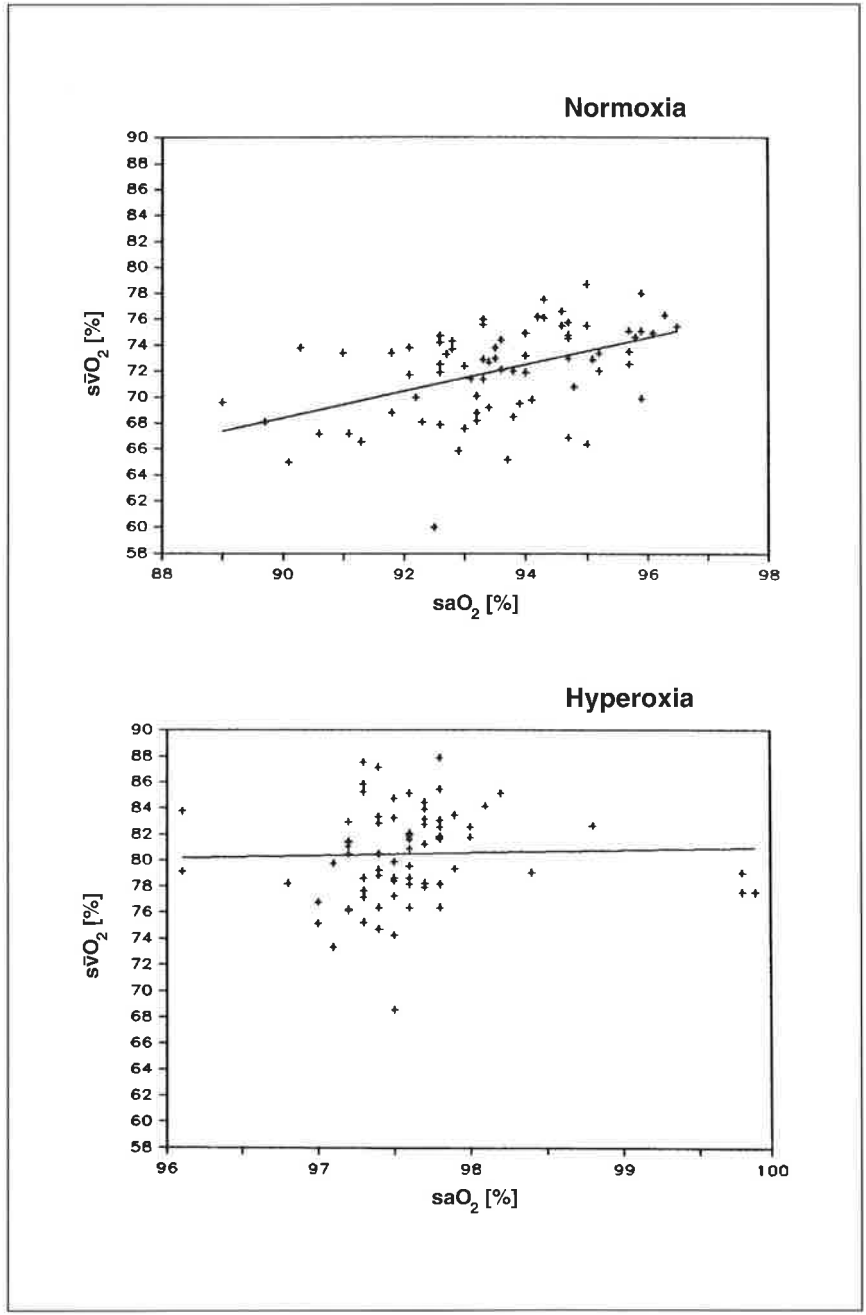
As expected, similar results were found for the oxygen saturation. Whereas during normoxia (saO_2 89–96%), with varying cardiac efficiency and oxygen consumption (CI 1.7–3.6 l/min × m^2 BSA; $\dot{Q}O_2$ 55–175 ml/min × m^2 BSA; awake, premedicated patient!), the mixed venous saturation also increases with increasing arterial saturation ($r = 0.46$; regression line $y = 1.02\ x - 23.30$), this correlation is lost during hyperoxia (saO_2 96–100%). Mixed venous saturation is only influenced by cardiac output (CI 1.2–3.3 l/min × m^2 BSA) and oxygen consumption (35–130 ml/min × m^2 BSA; anesthetized) (fig. 2).

Also as expected, cardiac output increases (independently of the current Hb concentration) with increasing oxygen consumption. During hyperoxia this correlation can be seen much more clearly ($r = 0.37$; regression line $y = 22{,}89\ x + 40.67$) than during normoxia ($r = 0.26$; regression line $y = 15.27\ x + 65.14$). This is due, among other things, to the correlation between arterial and mixed venous saturation already described (calculation of oxygen consumption using Fick's equation) (fig. 3).

The correlation between cardiac output and mixed venous O_2 saturation is also implied in Fick's equation and can be seen in figure 4. It is identical during normoxia ($r = 0.59$; regression line $y = 5.55\ x + 58.33$) and hyperoxia ($r = 0.59$; regression line $y = 6.29\ x + 68.91$). Here the two factors Hb concentration and oxygen consumption are not taken into consideration (scattering of the values).

Similar relationships were also found for the negative correlation between cardiac output and arteriovenous oxygen content difference (fig. 5) during normoxia ($r = 0.40$; regression line $y = -1.3\ x + 6.78$) and during hyperoxia ($r = 0.32$; regression line $y = -1.09\ x + 6.58$). However, here too, it must be remembered that the third main factor, oxygen consumption, is not taken into consideration (scattering of the values).

Fig. 1. Relationship between paO_2 and $p\bar{v}O_2$. *Normoxia:* The non-linear correlation between the two values is predictable if the current $a\bar{v}DO_2$ and the two current O_2 binding curves are known. The regression line represents one of many 'pseudolinearities'. *Hyperoxia:* A correlation between the two values can no longer be seen (paO_2 in the upper flat part, $p\bar{v}O_2$ in the steep lower part of the O_2 binding curve). This is supported by the straight line shown.


Normoxia
$s\bar{v}O_2$ [%]
saO_2 [%]
Hyperoxia
$s\bar{v}O_2$ [%]
saO_2 [%]

Discussion

An assessment of the arterial O_2 availability on the basis of the mixed venous oxygen status is very much dependent on the marginal conditions existing ($a\bar{v}DO_2$, e.g. changes in cardiac output and/or oxygen consumption):

In alert patients with normoxia the correlations between arterial and mixed venous oxygen pressure, which are revealed in the oxygen binding curve, can be shown indirectly. A linearity in the correlation between the two values – as demonstrated in figure 1 – can at most be deduced for very limited sections of the O_2 binding curve (pseudolinearity). At a constant $a\bar{v}DO_2$ the correlation is seen in the course of the given oxygen binding curve.

By contrast, the correlation between mixed venous and arterial oxygen saturation must be linear at a constant $a\bar{v}DO_2$, since it is exactly this arteriovenous O_2 difference that is described here. For this reason the position of the straight lines in figure 2 only describes the (constant) mean $a\bar{v}DO_2$ of the patient group above the given saturation range. A decrease in the $a\bar{v}DO_2$ results in an upward parallel shift of the straight lines, while an increase in the $a\bar{v}DO_2$ results in a parallel downward shift.

In the anesthetized and relaxed patient with hyperoxia (reduced oxygen consumption with a proportionally much higher oxygen supply) both the mixed venous oxygen pressure and the mixed venous oxygen saturation are constant at varying arterial values: over a range of 300 mm Hg arterial O_2 pressure difference (280–580 mmHg) the mixed venous O_2 pressure remains constant at 46–47 mmHg (upper flat part of the O_2 binding curve). The change in arterial saturation between 96 and 100% also has no effect on the mixed venous oxygen saturation.

From this it is clear that, as mentioned earlier, the mixed venous oxygen pressure is not suitable as a parameter describing an adequate oxygen supply. Even the smallest changes in the $p\bar{v}O_2$ lead to considerable changes in the $s\bar{v}O_2$, a fact which can result in dangerously false assess-

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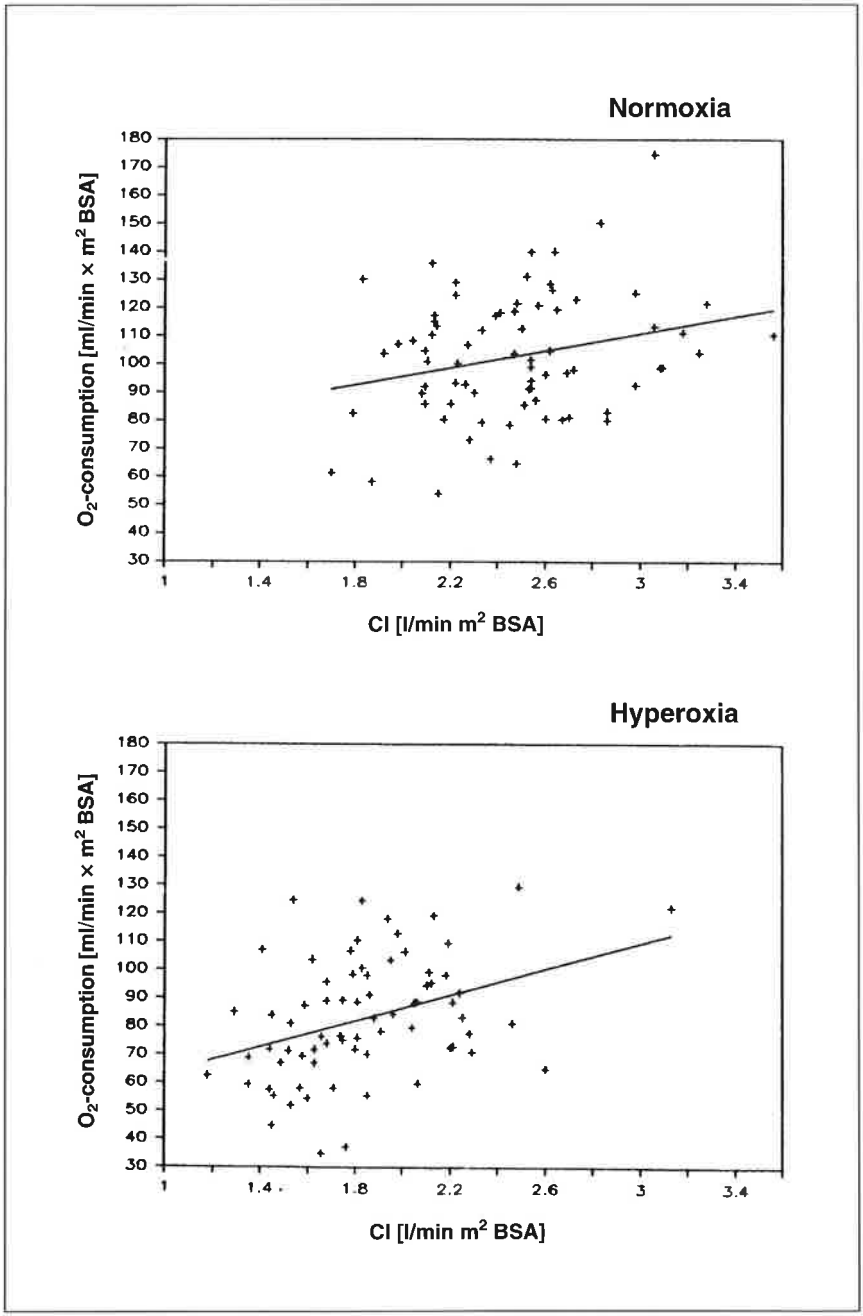
Fig. 2. Relationship between saO_2 and $s\bar{v}O_2$. *Normoxia:* The scatter in the measured values is due to variations in the $a\bar{v}DO_2$; the straight line represents the mean $a\bar{v}DO_2$ of all patients. *Hyperoxia:* A correlation between the two values can no longer be seen (saO_2 is limited at 98%; increase in the $a\bar{v}DO_2$ is at the cost of the physically dissolved O_2). This is supported by the straight line shown.


Normoxia
O_2-consumption [ml/min × m² BSA]
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
1
1.4
1.8
2.2
2.6
3
3.4
CI [l/min m² BSA]
Hyperoxia
O_2-consumption [ml/min × m² BSA]
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
1
1.4
1.8
2.2
2.6
3
3.4
CI [l/min m² BSA]

ments of the oxygen supply to the patient (due to ignorance of the actual position of the oxygen binding curve). Similarly, the extent of a hyperoxia cannot be estimated on the basis of the $p\bar{v}O_2$.

On the other hand, under conditions of normoxia, it is possible to detect at least the tendency towards an insufficient O_2 supply on the basis of the mixed venous oxygen saturation, independently of the position of the oxygen binding curve. In hyperoxia the same applies for $s\bar{v}O_2$ as for $p\bar{v}O_2$.

The correlation between cardiac output (C.O.) and oxygen consumption ($\dot{Q}O_2$) is described by Fick's principle:

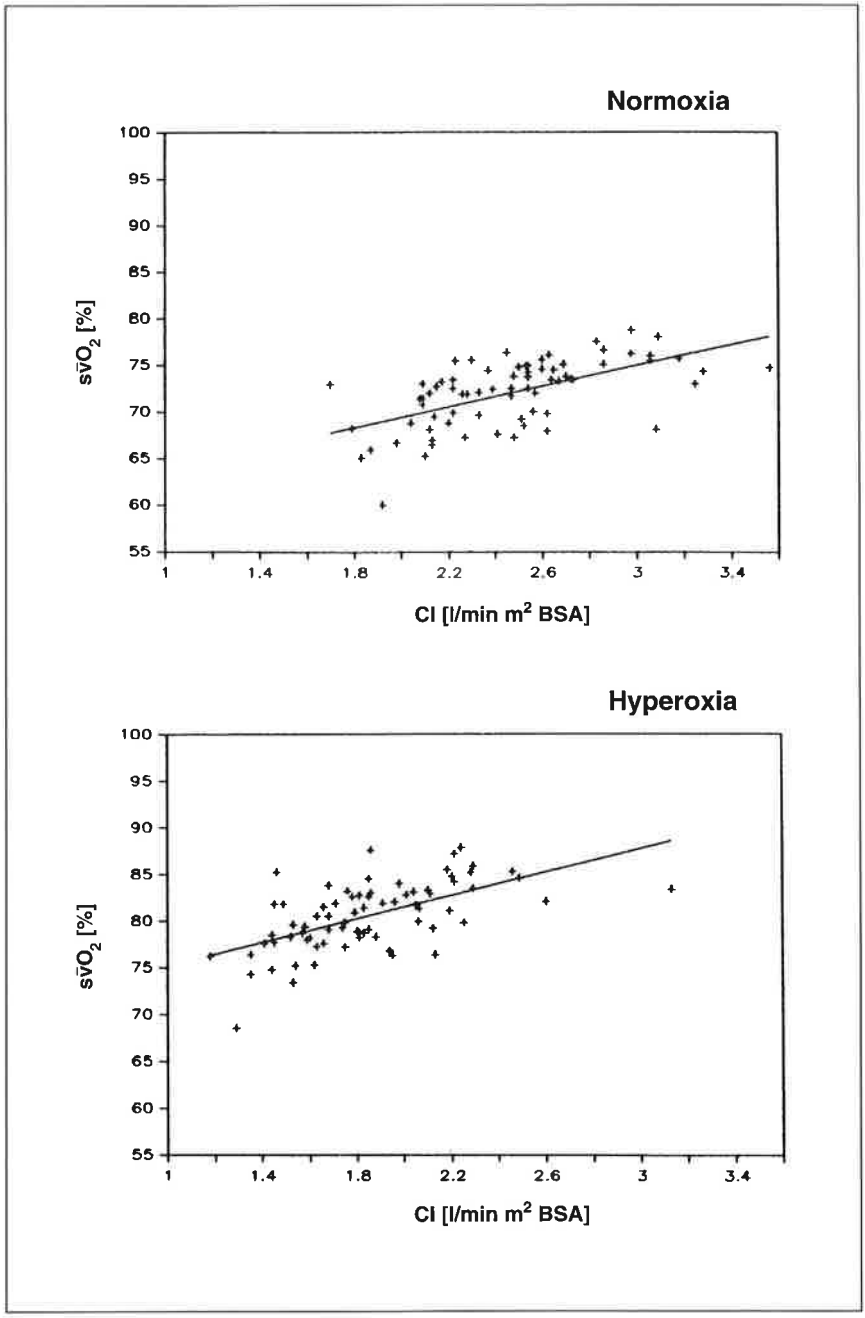
$$\text{C.O.} = \frac{\dot{Q}O_2}{a\bar{v}DO_2}$$

It can be assumed that with increasing oxygen consumption cardiac output also increases, and vice versa. However, an approximately linear correlation between the two values can only be expected if the arteriovenous oxygen difference remains more or less constant, i.e. if the cardiac output can accomodate an increased peripheral oxygen consumption. This is obviously not the case in the patients investigated. The $a\bar{v}DO_2$ varies among the patients between 2.5 and 7.0 ml/dl. As a result of this random variation in the $a\bar{v}DO_2$, there is also a random linear correlation between the two values. The same applies for hyperoxia.

The correlations between cardiac output and mixed venous saturation shown in figure 4 can be explained as follows:

The two values are again related by Fick's equation, the variable not taken into account being oxygen consumption. With a variable oxygen consumption, as was the case with the patient group investigated (50–175 ml/min × m^2 BSA in normoxia, and 35–130 ml/min × m^2 BSA under anesthesia and hyperoxia), the correlation between the two values can again only show a 'random linearity' and is predictable when the oxygen consumption is known (Fick's equation). The same applies (reciprocally)

Fig. 3. Relationship between cardiac index (CI) and oxygen consumption. *Normoxia:* This figure shows a considerable scatter in the measured values (random linearity), since the $a\bar{v}DO_2$, being a variable parameter, is not taken into account. *Hyperoxia:* The scatter of the values remains (random linearity). O_2 consumption and cardiac index are reduced by anesthesia to approximately the same extent; the $a\bar{v}DO_2$ remains largely constant.


Normoxia
100
95
90
85
80
75
70
65
60
55
$sv\bar{O}_2$ [%]
1
1.4
1.8
2.2
2.6
3
3.4
CI [l/min m^2 BSA]
Hyperoxia
100
95
90
85
80
75
70
65
60
55
$sv\bar{O}_2$ [%]
1
1.4
1.8
2.2
2.6
3
3.4
CI [l/min m^2 BSA]

to the correlation between cardiac output and arteriovenous oxygen difference shown in figure 5.

O_2 Supply Adjusted to Consumption: C.O., saO_2, $s\bar{v}O_2$ or $a\bar{v}DO_2$?

Can the question as to whether the O_2 supply is adjusted to the current metabolic requirements by the cardiopulmonary system be answered with the help of parameters which are as simple as possible but still reliable?

The O_2 supply is defined as:

$\dot{A}O_2$ [ml/min] = C.O. [l/min] × caO_2 [ml/dl]

Oxygen consumption is calculated as:

$$\dot{Q}O_2 \text{ [ml/min]} = \text{C.O. [l/min]} \times (caO_2 - c\bar{v}O_2) \text{ [ml/dl]}$$
$$= \text{C.O. [l/min]} \times a\bar{v}DO_2 \text{ [ml/dl]}$$

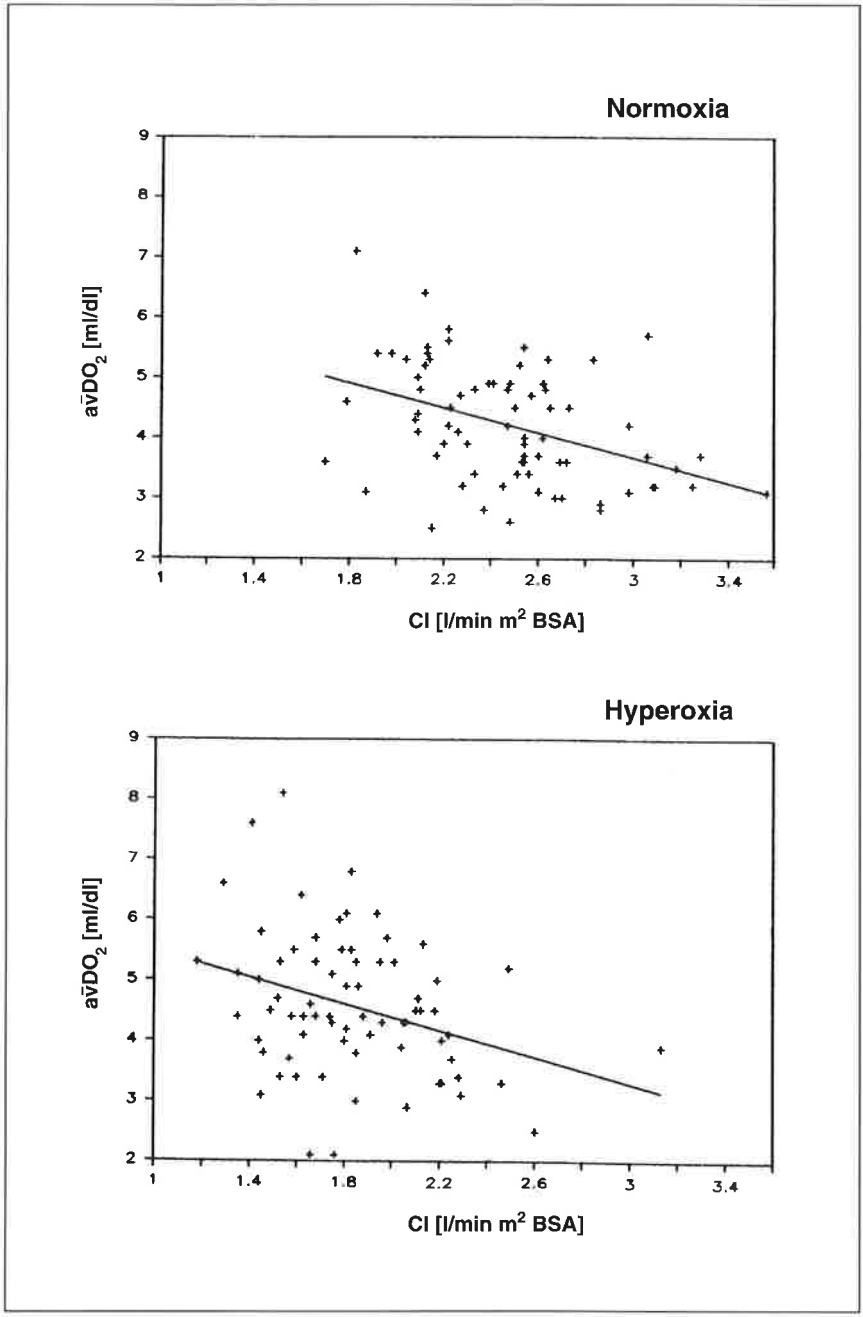
Since the proportion of physically dissolved O_2 normally plays a minor role in the arterial O_2 supply (in normoxia approx. 2% of the $\dot{A}O_2$) and no simple method of determining caO_2 was until now available, the saO_2 was used in clinical practice as the main factor determining the caO_2.

Therefore, simplified for routine clinical practice, the three parameters with which both the $\dot{A}O_2$ and the $\dot{Q}O_2$ and consequently the status of the O_2 supply to the organism can be determined are:

- cardiac output,
- arterial oxygen saturation saO_2, and
- mixed venous oxygen saturation $s\bar{v}O_2$.

However, the availability of all three values is limited due to the invasive measures necessary to obtain them: with increasing invasiveness the specific complications associated with the measurement techniques also increase [4]. Weighing the risks against the benefits necessarily leads to the question as to which of the three parameters or which combination of the parameters yields the most information on the current cardiopulmonary situation with the least invasiveness.

Fig. 4. Correlation between cardiac index (CI) and mixed venous oxygen saturation ($s\bar{v}O_2$). *Normoxia:* The scatter of the values (random linearity) is due to the fact that O_2 consumption is not taken into account as a variable parameter. *Hyperoxia:* The scatter of the values remains unchanged (random linearity). In comparison to the situation in normoxia, the $s\bar{v}O_2$ increases markedly, since part of the $a\bar{v}DO_2$ requirement, which remains more or less constant, is supplied by physically dissolved O_2.


Normoxia
$a\bar{v}DO_2$ [ml/dl]
9
8
7
6
5
4
3
2
1
1.4
1.8
2.2
2.6
3
3.4
CI [l/min m^2 BSA]
Hyperoxia
$a\bar{v}DO_2$ [ml/dl]
9
8
7
6
5
4
3
2
1
1.4
1.8
2.2
2.6
3
3.4
CI [l/min m^2 BSA]

For obvious reasons, C.O. (determination of *only* the pumping capacity of the heart) and the saO_2 (determination of *only* the pulmonary oxygenating capacity) are inadequate. Even the availability of *both* parameters only makes possible an assessment of the $\dot{A}O_2$.

Therefore, it was obvious that the $s\bar{v}O_2$ should be considered the global parameter since it is derived from both supply and consumption [14]. However, due to the many factors which can influence this value (see tables 1 and 2), its interpretation turned out to be difficult, since the causes of an increase or decrease in the $s\bar{v}O_2$ are not always as easy to detect as would appear from aspiration or the administration of catecholamines [14, 17]. For the same reasons, a direct interpretation in terms of changes in the C.O. is also not possible [14]. As the clinical investigation discussed here has shown, linear correlations turn out to be 'pseudolinear'.

Nevertheless, the value of the $s\bar{v}O_2$ as an 'alarm parameter' indicating a disparity between the $\dot{A}O_2$ and $\dot{Q}O_2$ is undisputed. However, this does not mean that correlations should be attempted for validating this parameter which, although existing mathematically, are totally meaningless for clinical practice.

An example of such an empirical confirmation of a mathematical correlation is the relationship between the $\dot{A}O_2/\dot{Q}O_2$ quotient and the $s\bar{v}O_2$, which has recently appeared repeatedly in the literature [15–17]. The hyperbolic curve as shown in figure 6 is due to the following equation:

$$y = \frac{100}{100 - x}$$

On the condition that

$0 <= x <= 100$ (range of possible variations in $s\bar{v}O_2$)

and

$1 <= y < \infty$ (range of possible variations in $\dot{A}O_2/\dot{Q}O_2$)

Fig. 5. Correlation between cardiac index (CI) and arteriovenous oxygen difference ($a\bar{v}DO_2$). *Normoxia:* The scatter of the values (random linearity) is due to the fact that O_2 consumption is not taken into account as a variable parameter. *Hyperoxia:* The scatter of the values remains unchanged (random linearity), while O_2 consumption and cardiac index are reduced more or less to the same extent by anesthesia, and $a\bar{v}DO_2$ remains more or less constant.

this function is the mean curve of the scattered points obtained empirically and shown in figure 7:

$$\frac{\dot{A}O_2}{\dot{Q}O_2} = \frac{100}{100 - s\bar{v}O_2}$$

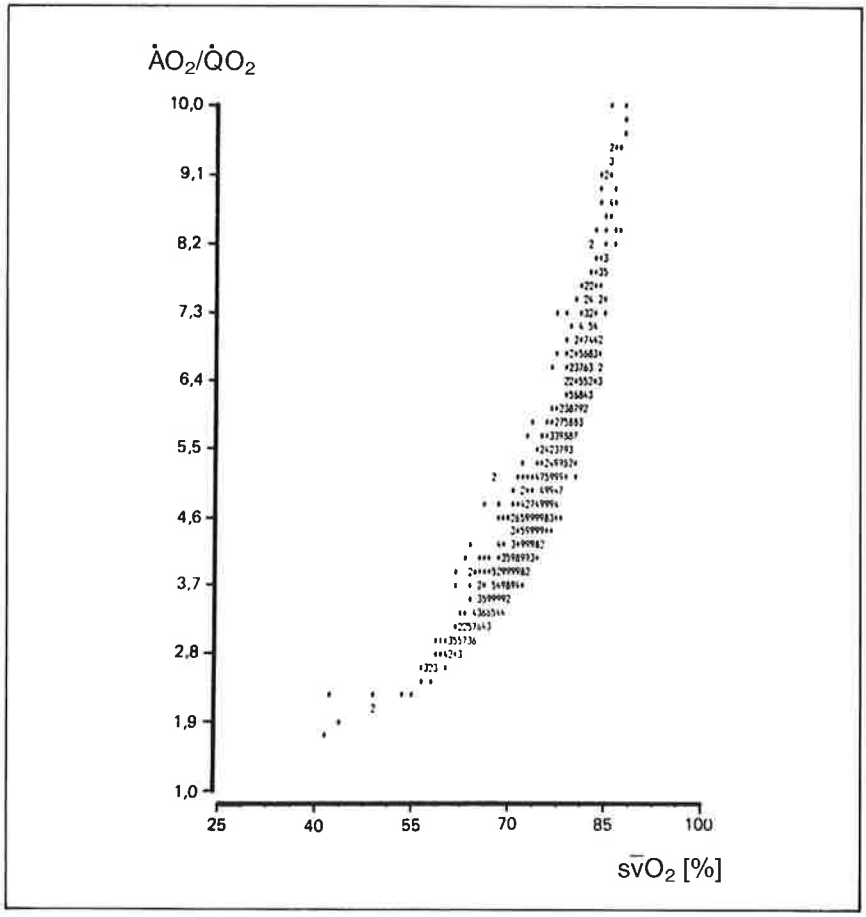


Fig. 6. Clinically determined relationship between the quotient $\dot{A}O_2/\dot{Q}O_2$ and mixed venous O_2 saturation (from Reinhart [15–17]). Empirical confirmation of the mathematical function $y = 100/(100 - x)$ shown in figure 7.

Examples:

(1) If supply is exactly the same as consumption ($y = 1$), the O_2 extraction is 100% ($x = s\bar{v}O_2 = 0\%$; intersection of the y-axis).

(2) If supply is twice as great as consumption ($y = 2$), O_2 extraction is only 50% ($x = s\bar{v}O_2 = 50\%$).

(3) If supply is 5 times as great as consumption ($y = 5$), O_2 extraction is only 20% ($x = s\bar{v}O_2 = 80\%$).

(4) If supply is 10 times as great as consumption ($y = 10$), O_2 extraction is only 10% ($x = s\bar{v}O_2 = 90\%$).

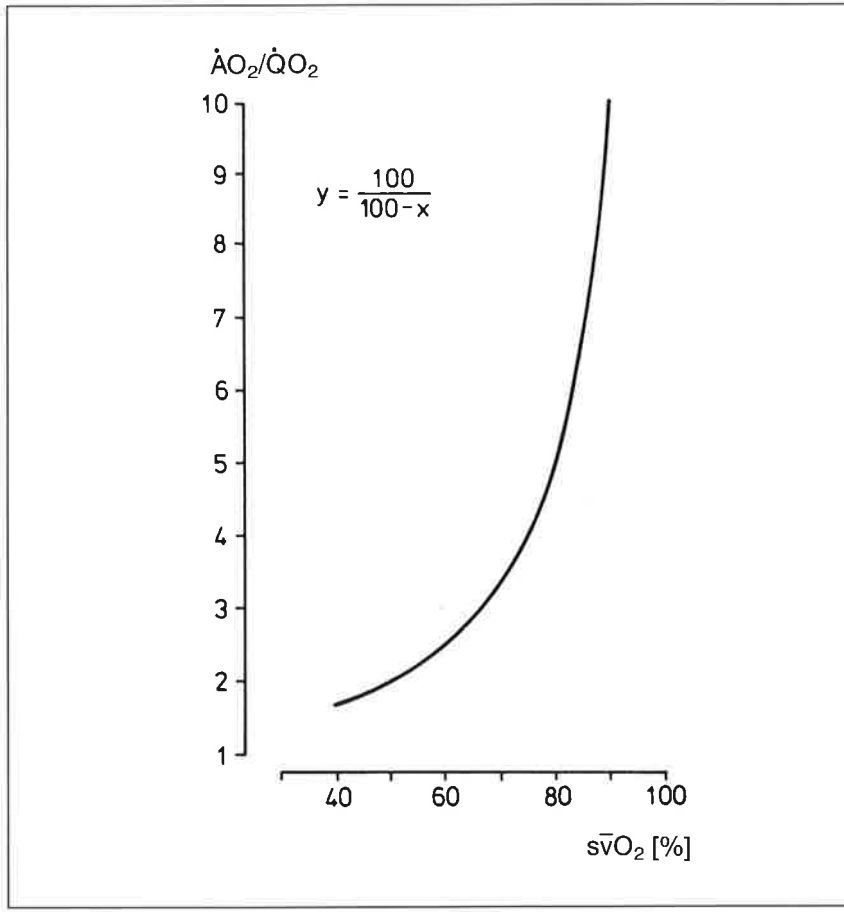


Fig. 7. Graphic representation of the mathematical function $y = 100/(100 - x)$.

Table 3. Examples of the problems involved in the interpretation of mixed venous parameters (assumption: C.O. + $\dot{Q}O_2$ = constant)

Arterial hyperoxia	$p\bar{v}O_2$	(↑)
	$s\bar{v}O_2$	↑
	$c\bar{v}O_2$	↑
Arterial hypoxia	$p\bar{v}O_2$	↓
	$s\bar{v}O_2$	↓
	$c\bar{v}O_2$	↓
Acidosis	$p\bar{v}O_2$	↑
	$s\bar{v}O_2$	→
	$c\bar{v}O_2$	→
Anemia	$p\bar{v}O_2$	↓
	$s\bar{v}O_2$	↓
	$c\bar{v}O_2$	↓

It is superfluous in the context of this discussion to point out that a mathematical correlation which has no relevance for clinical practice does not have to be proven by empirical – and dangerous – measurements in several hundred patients [15–17].

The $s\bar{v}O_2$ is certainly not an easily interpretable parameter of the $\dot{A}O_2$. As shown in tables 2 and 3, the $s\bar{v}O_2$, even at a constant C.O. and $\dot{Q}O_2$, is influenced by a whole series of variables which make further differential diagnostic steps necessary [3].

In addition, in the interpretation of the $s\bar{v}O_2$ it must be taken into consideration that no information about the O_2 supply to individual organ systems can be obtained. Even during rest the degree of extraction by the various organs is extremely variable, as shown in table 4 with the list of specific svO_2 of various organs. These relationships also change depending on the functional state of the individual organs.

While these limitations already apply to mixed venous saturation ($s\bar{v}O_2$), there is an additional complication in the case of central venous saturation (svO_2) in that it is also influenced by the position of the catheter tip. Depending on the functioning state of the primarily drained organs, the svO_2 will also differ from the $s\bar{v}O_2$ more or less positively or negatively; this can be seen clearly by the data in tables 2 and 4. This has already been shown for the sampling site 'injection lumen of the pulmonary artery catheter' (probable dominating drainage organ: the CNS), even though it was incorrectly concluded that the central venous saturation (svO_2) could be used to quantitatively estimate the global relationship of the O_2 supply and O_2 consumption [21].

However, the C.O. and/or saO_2 or $s\bar{v}O_2$ (or even svO_2 [2]) cannot be considered as an alternative for correctly assessing cardiocirculatory function. Rather, supply and consumption must be examined, which is only possible if both parameters, saO_2 and $s\bar{v}O_2$, are available, especially since the determining factor in an imbalance between $\dot{A}O_2$ and $\dot{Q}O_2$, the arteriovenous O_2 difference $a\bar{v}DO_2$, can only be obtained using both parameters. In fact, the $a\bar{v}DO_2$ [ml/dl] is the only value with which an ade-

Table 4. sO_2 (%) in the blood of various organ systems (at a normal cHb of 14.5 g/dl) showing in each case the appropriate proportion of the cardiac output (own data [12] and data from the literature [10])

Organ	sO_2 (%)	$\dot{Q}$ (% of C.O.)
Pulmonary veins	98	> 99[a]
Left ventricle	96	100
Aortic root	96	100
'Central venous system'	72–76	~ 94[b]
Pulmonary arteries		
Awake	74	~ 99[c]
Anesthesia	81	
Kidneys	87–91	20
Skin	88	8
Muscles		
At rest	77–87	20
During exercise	25–48	
Gastrointestinal tract	70	25
Liver	72–77	
CNS		
Awake	59	15
Anesthesia	65	
Heart		5
At rest	35–40	
During exercise	20	
Other organs		7

[a] Less 0.3% C.O. of the Vv. cordis minimae (Vv. Thebesii, drainage veins of the left heart)

[b] Less 5% C.O. of the coronary system and ~1% C.O. of the bronchial veins draining into the pulmonary veins

[c] Less ~1% C.O. of the bronchial veins draining into the pulmonary veins and 0.3% C.O. of the Vv. cordis minimae (Vv. Thebesii, drainage veins of the left heart)

quate circulation can be verified independently of C.O., as demonstrated by the following example:

In the clinical study presented here the cardiac index (CI) fell from 2.47 l/m^2 BSA during normoxia (before anesthesia) to 2.03 l/m^2 BSA during hyperoxia (anesthesia and relaxation). In contrast, the $a\bar{v}DO_2$ remained nearly constant at 4.22 ml/dl and 4.27 ml/dl. This means that oxygen consumption (due to anesthesia) also fell and that oxygen supply was still adequate with peripheral perfusion remaining unchanged, despite a reduced C.O. The reduction in C.O. caused by anesthesia therefore has no relevance for the oxygen supply. For this reason the $a\bar{v}DO_2$ shows in this situation a change which is 'requirement-adapted' much clearer than the C.O. itself, whose absolute value per se is meaningless for the assessment of oxygen supply.

Conclusions Drawn from the above Information

(1) Cardiac output, oxygen consumption and arteriovenous O_2 difference of the blood are known to be connected to one another according to the Fick equation. A correlation between two equation values – e.g. between cardiac output and arteriovenous oxygen difference – can only be calculated if the third value, oxygen consumption, remains constant. If this is not the case – as in the clinical investigation presented here – the result will always be influenced also by this third component. The described correlations are therefore always of a random nature.

(2) If two values are known – e.g. oxygen consumption and cardiac output – the third value is always predictable from the mathematical relationship defined by the Fick equation.

(3) An accurate assessment of the circulation only on the basis of the $s\bar{v}O_2$ is also impossible as is one based only on cardiac output or a combination of C.O. and saO_2 or $s\bar{v}O_2$. The $a\bar{v}DO_2$, being the difference between the caO_2 and $c\bar{v}O_2$, could be a parameter which, together with assessment of the clinical condition of the patient, would allow a rough estimate of both the supply and consumption sides, although further differential diagnostic considerations are also necessary in pathological situations.

(4) Nevertheless, the $a\bar{v}DO_2$, and the $s\bar{v}O_2$ to a limited extent (but never the svO_2), can be a useful diagnostic indication of a cardiocirculatory imbalance, if the clinical condition of the patient is taken into account [3].

Additional Examples

An $a\bar{v}DO_2$ of, for example, >6 ml/dl is always a danger signal for a discrepancy between O_2 supply and O_2 consumption. On the basis of the clinical condition of the patient, however, a differential diagnosis must be made between the causes of a possibly reduced oxygen supply (reduced C.O., reduced arterial O_2 concentration) or of an increased oxygen consumption (increased cell metabolism with various causes) (see table 1). The same applies to the $s\bar{v}O_2$. Even if further parameters are unknown, a fall to under 60% should always be seen as a danger signal and an indication that further differential diagnostic steps should be taken.

By contrast, an $a\bar{v}DO_2$ which has fallen to <4 ml/dl should not necessarily be seen as a sign of a lavish perfusion of the periphery (peripheral a.v. shunt, e.g. during shock). Nevertheless, a lower $a\bar{v}DO_2$ is always an indication of a discrepancy between O_2 supply and O_2 requirement. It can only be explained, however, within the context of the patient's clinical condition. The same applies to a $s\bar{v}O_2 > 80\%$. Thus the $a\bar{v}DO_2$ alone can in certain circumstances be a more useful parameter than cardiac output when the clinical situation of the patient is known.

Taking into account the reservations mentioned above, both the $a\bar{v}DO_2$ and (with restrictions) the $s\bar{v}O_2$ are valuable additional parameters particularly in the assessment of variable hemodynamic situations (e.g. during anesthesia) in clinical practice.

Summary

The O_2 status measured as 'central venous' in the Vena cava superior, inferior or in the right atrium is not suitable for monitoring the course of clinical conditions. More accurate information can only be obtained with the mixed venous O_2 status measured in the pulmonary artery.

The $p\bar{v}O_2$ is not suitable for determining arterial hypoxemia due to the relationships described by the O_2 binding curve.

The $s\bar{v}O_2$, based on its relationship to the $a\bar{v}DO_2$, is more useful as an indicator of a change in the arterial oxygen status. However, a differentiation between O_2 supply (C.O., oxygenation) or O_2 consumption is not possible. This applies particularly in hyperoxia.

An assessment of the cardiocirculatory condition of a patient on the basis of the $s\bar{v}O_2$ is only possible under constant marginal conditions (arterial oxygen status, peripheral oxygen consumption), while an assessment on the basis of the $a\bar{v}DO_2$ is only possible if peripheral oxygen consumption remains constant.

Nevertheless, in the context of the patient's clinical condition, the $s\bar{v}O_2$ can be useful (although the $a\bar{v}DO_2$ is better) in the assessment of cardiopulmonary dynamics, especially with regard to 'requirement-adapted' changes in the cardiac output or oxygen consumption.

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