Review

Oxygen uptake-to-delivery relationship: a way to assess adequate flow

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Abstract

Invasive and noninvasive monitoring facilitates clinical evaluation when resuscitating patients with complex haemodynamic disorders. If the macrocirculation is to be stable, then it must adapt to blood flow or blood flow must be optimized. The objective of flow monitoring is to assist with matching observed oxygen consumption (Vo_2) to pathophysiological needs. If an adequate balance cannot be maintained then dysoxia occurs. In this review we propose a simple schema for global reasoning; we discuss the limitations of Vo_2 and arterial oxygen delivery (Dao_2) assessment; and we address concerns about increasing Dao_2 to supranormal values or targeting pre-established levels of Dao_2, cardiac output, or mixed venous oxygen saturation. All of these haemodynamic variables are interrelated and limited by physiological and/or pathological processes. A unique global challenge, and one that is of great prognostic interest, is to achieve rapid matching between observed and needed Vo_2 – no more and no less. However, measuring or calculating these two variables at the bedside remains difficult. In practice, we propose a distinction between three situations. Clinical and blood lactate clearance improvements can limit investigations in simple cases. Intermediate cases may be managed by continuous monitoring of Vo_2-related variables such as Dao_2, cardiac output, or mixed venous oxygen saturation. In more complex cases, three methods can help to estimate the needed Vo_2 level: comparison with expected values from past physiological studies; analysis of the relationship between Vo_2 and oxygen delivery; and use of computer software to integrate the preceding two methods.

Introduction

Major advances have been made in monitoring the critically ill patient following the introduction in the 1970s of intravascular pressure and flow recording catheters [1]. Today, flow monitoring is one of the major reasons to admit patients into an intensive care unit (ICU), but which of the flow-based parameters are really interesting from a clinical perspective?

A reasonable assumption is that below a critical level the oxygen consumption (Vo_2) is inversely related to the risk for cell dysfunction and necrosis and to the severity of shock. Among the various haemodynamic variables that may be evaluated, a Vo_2 below the required level is most strongly related to death [2]. Once a substantial amount of cell necrosis has occurred, organ function recovery is not always possible, even when adequate Vo_2 is restored. Thus, it is intuitive that flow monitoring must be aimed at early adaptation of Vo_2 to metabolic needs [3,4]. Although this is universally accepted, its usefulness at the bedside has been challenged because of theoretical and practical limitations of Vo_2 assessment [5,6]. However, it has been shown that several of these limitations have been over-stated [4]. In addition, targeting a Vo_2 that is adequate to meet the patient's needs does not necessarily require continuous Vo_2 measurement. Monitoring Vo_2-related variables such as cardiac output (CO) and/or mixed venous oxygen saturation (Svo_2) may represent an acceptable compromise, especially as these variables can be obtained less invasively.

This review proposes a simple and comprehensive schema for understanding and adapting flow monitoring in order to stabilize the macrocirculation.

Fundamental basis of the relationship between oxygen consumption and delivery

For each cell, life requires enough energy for metabolic activity. Energy depends on oxidative reactions that require nutrients and oxygen. For each cell most of the oxygen is used for oxidative mechanisms. Nonoxidative systems have lower affinity for oxygen than do cytochrome oxidase systems. Therefore, significant activity of the non-mitochondrial oxidase systems can only be present when there is no more dysoxia.

CO = cardiac output; Dao_2 = arterial oxygen delivery; Do_2 = oxygen delivery; Eo_2 = oxygen extraction ratio; ICU = intensive care unit; PAC = pulmonary artery catheter; Svo_2 = mixed venous oxygen saturation; Vo_2 = oxygen consumption.

Hence, for each cell a match between VO_2 and needed VO_2 ($^nVO_2$) is necessary for life. This basic relationship between life and energy is also applicable to each organ and to the body as a whole. However, a whole body VO_2 that equals body needs does not guarantee that circulation is adequate for each cell because distributive mismatch may lead to nonoxidative metabolism in some areas and dysoxia in others. However, it is a prerequisite that the macrocirculation must be stabilized before one may examine the microcirculation. Consequently, the first priority is to consider the balance between whole body VO_2 and $^nVO_2$.

For all systems, VO_2 is the difference between the input flow and the output flow. For the whole body circulation, the input flow is the arterial oxygen delivery (DaO_2) and the output flow is the venous oxygen delivery. If one considers the oxygen extraction ratio (EO_2) to be the ratio between VO_2 and DaO_2, then VO_2 can be represented by the product $DaO_2 \times EO_2$. The simple equation $VO_2 = DaO_2 \times EO_2$ is conventionally used to represent the macrocirculatory balance.

The VO_2 observed ($^oVO_2$) by a clinician (either measured or calculated) is the product of an observed DO_2 and an observed EO_2, such that $^oVO_2 = {}^oDO_2 \times {}^oEO_2$. Similarly, the specific patient's requirements ($^nVO_2$) may be formulated as the product of the needed DO_2 and the needed EO_2: $^nVO_2 = {}^nDO_2 \times {}^nEO_2$. The ratio between these two equations represents the balance between what the doctor sees and what the patient needs: $^oVO_2/^nVO_2 = {}^oDO_2/^nDO_2 \times {}^oEO_2/^nEO_2$. Any change in $^oDO_2/^nDO_2$ must be balanced by an inverse change in $^oEO_2/^nEO_2$ to maintain $^oVO_2/^nVO_2 = 1$ and *vice versa*. When $^oVO_2/^nVO_2 = 1$ cannot be maintained, dysoxia occurs. Consequently, three indices of performance may be described: $^oVO_2/^nVO_2$ is an index of global performance, with a value below 1 indicating shock; $^oDO_2/^nDO_2$ is an index of circulatory performance, with a value below 1 indicating circulatory failure; and $^oEO_2/^nEO_2$ is an index of tissue performance, with a value below 1 indicating tissue failure.

We do not propose that these indices be calculated for each and every patient, but they should perhaps be borne in mind to facilitate, at any time, empirical review of the patient's likely status and to determine the probable results of any therapeutic intervention.

Clinical means to deal with concepts

Evaluation of whether macrocirculatory adaptation is adequate requires one to answer several simple questions.

Is oxygen consumption equal to the patient's needs?

Otherwise stated, is the expression $^oVO_2/^nVO_2 = 1$ true? Three levels of complexity may be defined.

First, clinical improvement is a good indicator of adequate resuscitation [7]. In practice, the $^nVO_2$ is usually met by decreasing metabolic requirement, optimizing the haematocrit and arterial haemoglobin oxygen saturation, and increasing blood flow empirically until the clinical status improves. This situation does not require invasive haemodynamic investigation.

Second, a clear improvement in blood lactate clearance is also a good and minimally invasive indicator of adequate resuscitation [7]. The blood lactate concentration alone fails to discriminate between dysoxia and aerobiosis [8]. Although more reliable, the time course of lactate levels is not an ideal marker [2,7,9]. The limitations of lactate were recently reviewed [8]. Diabetes mellitus, liver dysfunction, tissue reperfusion, catecholamine infusion, cellular metabolic alterations and inhibition of pyruvate dehydrogenase can all result in a marked increase in blood lactate concentrations, despite improvement in tissue dysoxia.

Finally, in more complex situations in which clear clinical improvement and normalization in blood lactate are not observed, evaluation of oxygenation is required, followed by an evaluation of $^oVO_2$ and $^nVO_2$. The $^oVO_2$ can be measured at the bedside using expired gases [10] or it may be calculated from the product of CO and the arteriovenous difference in blood oxygen content. Demonstrating that $^oVO_2/^nVO_2 = 1$ requires one to evaluate $^nVO_2$ concomitantly. When $^oVO_2$ is evaluated alone, this provides no information of prognostic interest [2].

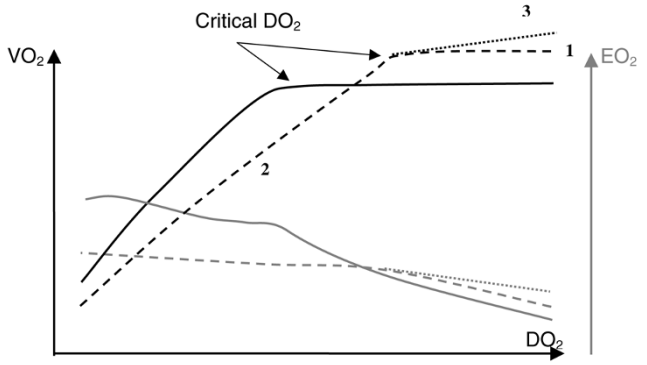
How may we estimate the needed oxygen consumption?

Needs can initially be estimated as the sum of VO_2 at basal metabolism, as indicated by age-specific and sex-specific normative data, and the additional VO_2 that results from other metabolic requirements. The latter can be approximated based on a number of factors, such as body temperature ($^nVO_2$ changes by ±13% for each 1°C above or below 37°C). Pathologic situations such as respiratory failure and severe sepsis also increase metabolic needs. Based on metabolic conditions, $^nVO_2$ can vary from 0.7-fold to 3-fold the basal metabolism.

Needs can also be estimated by using the specific VO_2/DO_2 relationship (Figure 1). A biphasic relationship between oxygen use and resources has been established [6]. When DO_2 is greater than a threshold value, VO_2 remains stable (oxygen supply independency) because the EO_2 changes proportionally. When DO_2 falls below this threshold, a proportionate increase in EO_2 cannot be maintained and the VO_2 drops linearly to zero (oxygen supply dependency). There is consensus that the inflection point between the two slopes indicates the critical level of DO_2 (Figure 1). Oxygen supply dependency is associated with increased blood lactate concentration, denoting possible activation of the anaerobic pathway.

Assessment of the VO_2/DO_2 relationship is a theoretical means to evaluate the gap between actual VO_2 and $^nVO_2$. When DO_2 increases, an increase in VO_2 suggests that oxygen supply is

Figure 1



Pathophysiological changes in the VO_2/DO_2 relationship. Normal relationship is shown in a solid black line, and abnormal relationships in dotted lines. 1: Increased VO_2 needs; 2: impaired EO_2; 3: other mechanisms (see text). The grey curves are the corresponding EO_2/DO_2 relationships. DO_2, oxygen delivery; EO_2, oxygen extraction ratio; VO_2, oxygen consumption. Reproduced with permission from Squara [4].

inadequate. In contrast, a stable VO_2 value when DO_2 increases suggests either that VO_2 matches needs when it is associated with decreasing lactate levels [11,12] or that VO_2 is limited by mechanisms other than oxygen supply when it is associated with increasing lactate levels [13,14].

In pathophysiology, two mechanisms delay achievement of the VO_2 plateau and account for a rightward shift in the critical DO_2 point (Figure 1). When VO_2 needs are excessive (uncoupling and/or increased metabolic activity), the VO_2 plateau is reached at a higher level of VO_2 [15,16]. When oxygen tissue diffusion is impaired (impaired microcirculation and/or impaired oxygen mitochondrial use), the slope of the dependant part of the VO_2/DO_2 relationship is decreased [17,18].

Three other mechanisms result in an increase in VO_2 as DO_2 increases beyond the critical point, so that a slight upward slope – usually of less than 5% – replaces the expected VO_2 plateau. Although more difficult, identification of the critical DO_2 inflection point remains possible when these mechanisms are operative because the slope of the VO_2/DO_2 dependency segment ranges from 20% to 50% [19]. The first mechanism occurs during a DO_2 challenge involving an increase in CO, because the VO_2 needs of kidneys [20], stomach [21] and muscle [22] increase in direct proportion to flow. Furthermore, infusion of inotropic agents increases myocardial oxygen consumption [11,12,19]. Another mechanism is additional oxygen uptake due to non-mitochondrial oxidase systems when dysoxia has resolved [23]. The final mechanism, termed conformance, is a decrease in the metabolic needs of cells that occurs in response to a gradual decline in available oxygen. Although secondary to a chronic change, this phenomenon has been observed in acute situations [24]. Schumacker and coworkers [25] reported that a VO_2 increase occurred in unshocked patients after aortic stenosis valvuloplasty.

A controversy arose during the late 1980s from several studies on acute respiratory distress syndrome and/or sepsis, in which the expected VO_2 plateau was not observed in patients who were recovering from shock and had high DO_2 values [26,27]. This was interpreted as evidence of 'pathologic oxygen supply dependency', possibly related to hidden oxygen deficit and contributing to multiorgan failure and death. However, increasing DO_2 to supranormal values was beneficial in some studies [28,29] but not in others [30,31]. Furthermore, it has been suggested this so-called 'pathologic supply dependency' may result from spurious upsloping of the VO_2/DO_2 relationship due to mathematical coupling of measurement errors when using a pulmonary artery catheter (PAC), because in some studies simultaneous independent VO_2 assessment revealed a plateau [5,6,32]. In addition, VO_2 and DO_2 assessment are limited by theoretical and practical concerns [5,6]. However, these limitations were recently reviewed [4]. Use of the most recent generation of devices for continuous CO monitoring and blood gas analysis minimizes the variability in measurement. It has been proposed that the relevance of the VO_2/DO_2 relationship could be increased by combined analysis of the VO_2/time relationship (Figure 2) [4]. Thus, although difficult, acceptable identification of the VO_2 plateau, and of the ${}^{n}VO_2$, is possible when necessary.

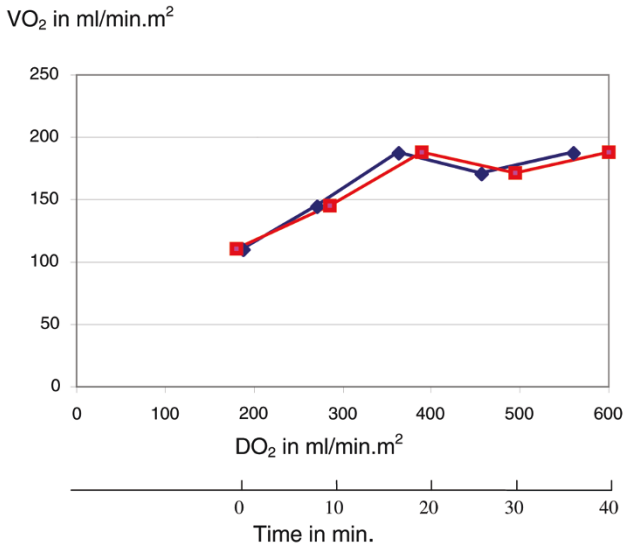
Finally, it may be concluded that ${}^{o}VO_2 = {}^{n}VO_2$ when one or several of the following factors is present: clinical improvement, decrease in blood lactate concentration, and ${}^{o}VO_2$ inside the expected range and/or inflexion point in the ${}^{o}VO_2/DO_2$ curve. The two methods can be combined. When the ${}^{o}VO_2$ plateau is reached at a value close to the estimated needs, the patient's real needs are probably met. Handling the large amount of information required to assess oxygen needs can be difficult [33,34], and computer assistance may be helpful [2,35,36].

Are there other means to balance oxygen consumption and needs?

Supraphysiologic targets

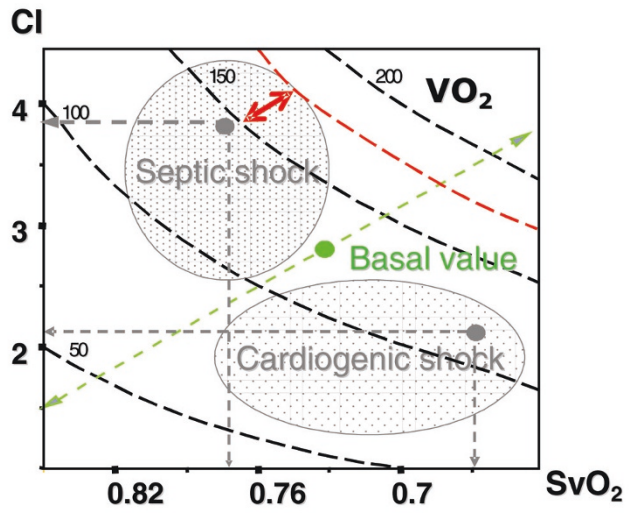
Some investigators have recommended that DO_2 be increased to supranormal values, greater than the usual critical level, without paying much attention to VO_2. This simplification of the method based on the VO_2/DO_2 relationship was associated with favourable outcomes in homogeneous populations of patients undergoing high-risk surgery [37,38], with cardiogenic shock following myocardial infarction [39] and with acute respiratory failure [15,40]. However, those studies failed to demonstrate any beneficial effects after the onset of organ failure [38] or when different aetiologies of shock were pooled together [15,40].

Figure 2



Comparison between the VO_2/DO_2 relationship and the VO_2/time relationship in one hypothetical example. For this figure, DO_2 increased linearly with time. This helps to identify the critical VO_2 point and eliminates the possible effect of mathematical coupling of error. DO_2, oxygen delivery; VO_2, oxygen consumption. Reproduced with permission from Squara [4].

Figure 3



Nomogram showing CI, SvO_2 and VO_2 isopleths (dotted black lines). The green point shows the expected values for a 59-year-old woman at basal metabolism, and the green dotted arrow indicates the expected normal variations in case of hypo- or hypermetabolism. The real position of the patient in the nomogram can be continuously monitored. This is adequate for diagnostic purposes. The patient's position can move from the normal profile to a characterized area of septic or cardiogenic shock (grey dotted arrows and areas). However, for therapeutic objectives, this nomogram gives no idea of needs. If we made the hypothesis that the $^{n}VO_2$ (red isopleth) is higher than the $^{o}VO_2$, then the red double arrow indicates the difference between $^{n}VO_2$ and $^{o}VO_2$. Units for CI are l/min per m^2 and for VO_2 they are ml/min per m^2. CI, cardiac index; $^{(n/o)}VO_2$, (needed/observed) oxygen consumption; SvO_2, mixed venous oxygen saturation.

Monitoring of cardiac output and mixed venous oxygen saturation

Other studies suggest that sequential DO_2 and VO_2 calculations can be advantageously replaced by continuous measurement of CO [41], SvO_2 [42], or central venous oxygen saturation [43]. The use of these variables avoids compounding of measurement errors and allows for continuous comparison between measured values and targeted values.

However, targeting a pre-established value for DO_2, CO, or SvO_2 does not prove that these values meet the needs of an individual patient [16]. These pre-established targets are derived from normal findings or from survivors in selected populations of patients [44,45]. Determination of the needed value of one given variable must take into consideration the limitation in other variables that are specific to the patient, his past history, the actual pathologic event, the delay before onset of shock and often recent therapeutic interventions (Figure 3). Intuitive evaluation of the needed value of each variable in each specific case requires considerable expertise. Misinterpretation of information derived from PAC placement and heterogeneity in the medical decision process is frequent [30,31]. Even for experts, intuitive evaluation of needs may be subject to errors [16]. In some conditions, such as coronary disease, efforts to increase CO in order to 'normalize' the cardiac index to more than 2.5 l/min per m^2 or the SvO_2 value to more than 70% can be harmful (see examples given below). In addition, there is some evidence that an excessive oxygen supply may be deleterious, either via the useless metabolic cost of an excessive increase in DO_2 or via activation of nonoxidative systems. Failure to consider these latter two mechanisms may also account for the poor results obtained in controlled studies targeting nonspecific 'supranormal' values of DO_2 [30,31]. Thus, treatment efforts should be limited to what is necessary – no less and no more.

The relationship between cardiac output and mixed venous oxygen saturation

All haemodynamic variables are interrelated, and ensuring that VO_2 meets needs is the best tool to ensure that global haemodynamic status is adequate. VO_2, whether calculated by spirometry, indirect calorimetry, or using a PAC, is similar to the plateau of VO_2 in the VO_2/DO_2 relationship. No other relationship between two variables allows a clear identification of a plateau or a clear inflection point between anaerobiosis and aerobiosis. The shape of the CO/SvO_2 relationship or the CO/EO_2 relationship is bi-curvilinear and similar to the DO_2/EO_2 relationship shown in Figure 1. A clear inflexion point between aerobiosis and anaerobiosis is much more difficult to identify than the VO_2/DO_2.

Table 1

Clinical parameters of two patients admitted to the ICU (sedative infusions and mechanical ventilation required)

	Patient 1 (male, 84 years)		Patient 2 (male, 24 years)		
Parameters	H_0	H_2	H_0	H_5	H_6
Temperature (°C)	35.2	36.8	40.2	38.5	38.5
MAP (mmHg)	65	68	55	99	97
Heart rate (beats/min)	65	74	117	113	111
Sp_{O_2} (%)	100	100	97	96	97
Haemoglobin (g/l)	11.0	11.1	13.6	13.0	13.0
Serum lactate (mEq/l)	3	2	10.3	6.6	6.2
Cardiac index (l/min per m^2)	2.1	2.3	4.1	6.5	6.4
Sv_{O_2} (%)	65	68	75	76	75
$^{o}V_{O_2}$ (mL/min per m^2)	88	119	178	240	237

H, delay in hours; ICU, intensive care unit; MAP, mean arterial pressure; Sv_{O_2}, mixed venous oxygen saturation; $^{o}V_{O_2}$, observed oxygen consumption.

Clinical examples

Example 1

Patient 1, receiving sedative drugs and mechanical ventilation, was admitted to an ICU immediately after an aortic valve replacement. He was hypothermic, with marbled and cold extremities. Haemodynamic variables are listed in Table 1. In this patient, cold extremities may be due to hypothermia, and the supranormal serum lactate may result from postoperative washout. Therefore, clinical evaluation including lactate level is not relevant in evaluating macrocirculatory performance relative to metabolic needs. Other means to explore the balance between V_{O_2} and needs are conflicting. The Sv_{O_2} (65%) was below the expected value and may be considered a marker of unacceptably low CO and oxygen flow [45,46]. In contrast the calculated $^{o}V_{O_2}$ (88 ml/min per m^2) is close to expected $^{n}V_{O_2}$ (90 ml/min per m^2) when assessed using the basal V_{O_2} value for this 82-year-old man (119 ml/min per m^2, as indicated by age-specific and sex-specific normative data), corrected according to the low body temperature. It would be difficult to exploit the V_{O_2}/D_{O_2} relationship. No V_{O_2} plateau is expected in the early postoperative period because of increasing metabolic needs.

The clinician on duty disregards the Sv_{O_2} threshold and concluded that the haemodynamic status was adequate to the patient's needs and no specific treatment was given. Two hours later (Table 1), a decrease in lactate serum value, normalization in Sv_{O_2} and a calculated $^{o}V_{O_2}$ = basal V_{O_2} demonstrate that metabolic needs were probably covered.

In this case, a rough interpretation of Sv_{O_2} below 70% as an indicator of insufficient CO as compared with needs would have led to an unjustified increase in CO. An Sv_{O_2} below 70% can be normal in elderly patients, especially if haemoglobin level is low, as is frequently observed postoperatively.

Example 2

Patient 2, requiring sedation and mechanical ventilation, was admitted to an ICU with a history of sudden shock and hyperkinetic state (Table 1). Was V_{O_2} adequate to needs? There is agreement between the clinical signs of shock with elevated lactate level and a calculated $^{o}V_{O_2}$ below the needed value (216 ml/min per m^2) according to basal V_{O_2} for a 24-year-old man (152 ml/min per m^2) corrected for the high temperature. In contrast, the Sv_{O_2} value, higher than normal values, suggests that CO and oxygen flow are adequate.

Once again, the clinician on duty disregards the Sv_{O_2} threshold and concluded that the haemodynamic status was inadequate for the patient's needs. A resuscitation regimen combining cooling, fluid optimization, and dobutamine and noradrenaline (norepinephrine) was instituted in addition to antibiotics. CO increased, Sv_{O_2} remained stable (Table 1) and calculated $^{o}V_{O_2}$ increased over its needed value, whereas lactate serum decreased, suggesting that metabolic needs were covered.

In this case, an interpretation of the Sv_{O_2} above 70% as an indicator that the hyperkinetic state was adequate to needs would have led to insufficient resuscitation. Sv_{O_2} can be above 70% in pathological states, for instance involving severe impairment in tissue oxygen diffusion.

Practical implications

The rationale for incorporating the V_{O_2}/D_{O_2} relationship into clinical management strategies is supported by several studies in which most of the limiting factors listed above were avoided [13,14]. In contrast, the chances of survival are very small in patients whose D_{O_2} and V_{O_2} fail to increase with treatment, despite evidence of an oxygen deficit [13,14]. Thus, reaching the critical D_{O_2} and ensuring that V_{O_2} needs

are met are crucial objectives, even though these two variables are calculated or intuitively estimated. To increase the likelihood of identifying clinical benefits related to bedside VO_2 guided therapy, we suggest a number of practical guidelines. As stated above, computer assistance may be helpful in harmonizing the diagnostic reasoning processes of different clinicians for different patients [2,35].

Early detection of shock states

Shock responds better to haemodynamic resuscitation in the early stages [43]. Although the final objective is to provide sufficient oxygen to each cell, there is some evidence that rapidly achieving a sufficient total body VO_2 is a prerequisite. Late-stage shock is a far more complex situation that involves not only the macrocirculation and microcirculation but also cell metabolism and the consequences of cell necrosis, which cannot be corrected by haemodynamic resuscitation alone.

Matching oxygen consumption to needs is the first objective

In most situations, targeting a clinical improvement, a decrease in lactate level, or a pre-established value for CO or SvO_2, or both, is an acceptable and intuitive means of achieving adequate VO_2. In complex situations, by plotting VO_2/DO_2 over time during a DO_2 challenge, the critical DO_2 value can be evaluated rapidly by identifying the inflection point on the curve, and resuscitation efforts can then be limited to what is necessary. Because the critical DO_2 value can be determined visually with a 95% confidence interval of 20%, it is reasonable to limit DO_2 to its observed critical value +20%. When lactate remains high despite evidence that a VO_2 plateau has been reached, increasing DO_2 further does not seem to add benefit [13,14]. Continuous efforts to decrease oxygen demand and to improve the microcirculation may be more appropriate [47]. Combined analysis of the VO_2/DO_2 and VO_2/time relationships provides the most useful approach, because the effects of mathematical coupling of errors and the theoretical limitations resulting from DO_2 variability in the regression line derivations are minimized. A mild up-sloping of the VO_2 plateau (slope <10%) should not be confused with oxygen dependency. When necessary, the critical DO_2 point can be determined more accurately using the method developed by John-Alder and coworkers [48].

To reach this objective, the best compromise must be identified, mostly based on metabolic cost

Hyperthermia, acute respiratory failure and/or pain all increase VO_2 needs sharply. In contrast, cooling, sedation and mechanical ventilation often produce a 50% decrease in VO_2 needs. The latter has exactly the same favourable effect as doubling the CO or doubling the EO_2. Improving EO_2 must be always considered, although this rarely produces a rapid increase in VO_2. Treating infection, excessive sedation, or excessive water retention, for example, may increase EO_2 [43]. When the only possibility is to increase DO_2, clinicians must choose among various agents that presumably differ in their caloric effects. Arterial vasodilatation improves DO_2 and decreases myocardial oxygen requirements. In contrast, inotropic agents and vasoconstrictors have major caloric effects. Whatever the method used, a metabolic price must be paid for improving VO_2 and DO_2 up to critical values. This metabolic price (a part of VO_2 needs) must also be limited to what is strictly necessary.

Conclusion

Matching the VO_2 and $^nVO_2$ is a crucial objective in critically ill patients, and must take into account the specific situation of the patient and its pathological limitations. Achieving this objective requires one to decrease oxygen needs first, to improve EO_2 when possible and then to improve DO_2. In most situations, targeting a clinical improvement, a decrease in lactate level, or a pre-established value for CO, SaO_2, or SvO_2 (or all of these) is an acceptable and intuitive means of achieving an adequate VO_2. However, intuitive evaluation of the needed value for each variable in each specific case requires considerable expertise, considering all available variables, and may be subject to error.

In complex situations, by plotting VO_2/DO_2 over time during a DO_2 challenge, the critical DO_2 value can be rapidly identified as the inflection point on the curve, and resuscitation efforts can then be limited to what is necessary. Whatever the method used, a metabolic price must be paid for improving VO_2 and DO_2 to the critical values, and must be limited to what is strictly necessary. Thus, the more complex the critically ill presentation, the greater the number of global haemodynamic variables that are needed.

Flow monitoring is of major interest in terms of stabilizing the macrocirculation. A stabilized macrocirculation is a global pre-requisite, and must be achieved before one looks at the local microcirculation.

> *Although we do not have direct evidence of any clinical benefits from invasive hemodynamic monitoring, we believe that more intensive monitoring (invasive or non-invasive) is needed to ensure the safety of acutely ill patients, otherwise we would not have ICUs.*
>
> Bellomo and Uchino [49]

Competing interests

PS is a consultant for Edwards Lifesciences. This manuscript was written from a slide presentation as part of a European PAC course promoted by Edwards Lifesciences.

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