

Significance of venous oximetry in the critically ill

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Critically ill patients are threatened or affected by multi-organ failure (MOF). Tissue hypoxia is one of the most important co-factors of MOF. Venous oximetry allows the critical estimation of the global oxygen (O_2) supply-demand ratio and can be gained from mixed ($S_V O_2$) and central venous blood ($S_{cv} O_2$). Cellular requirements dominate the feedback hierarchy of the O_2 -metabolism. This review describes the history and validity of haemodynamic monitoring, illustrates the physiological background and clinical application of venous oximetry and presents carbon dioxide analysis as evidence of the usefulness of a multimodal approach in cardio-respiratory monitoring. Variation of cardiac output, optimisation of arterial O_2 -saturation and adaptation of O_2 -extraction are shown to be the relevant levels of pathophysiological adaptation as well as therapeutic intervention. We portray the functional equivalence of $S_{cv} O_2$ and $S_V O_2$ and analyse their diagnostic, therapeutic and prognostic significance, providing the basis for the efficacy of venous oximetry as an important marker of critical illness. Finally, having drawn an outline of current developments for the better understanding of the oxidative balance of individual organs, we stress the importance of a synoptic O_2 -monitoring strategy as well as the need to use its beneficial, yet unfulfilled, clinical potential.

KEY WORDS: *oxygen, monitoring, critical illness.*

IMPORTANCIA DE LA OXIMETRÍA VENOSA EN EL ENFERMO CRÍTICO

Los enfermos críticos tienen riesgo de fracaso multiorgánico (FMO) o ya lo sufren. La hipoxia tisular es uno de los cofactores más importantes de FMO. La oximetría venosa permite la estimación crítica de la ratio de aporte-demanda del oxígeno global (O_2) y puede ser obtenida de la sangre venosa mixta ($S_V O_2$) y central ($S_{cv} O_2$). Las necesidades celulares dominan la jerarquía de retroalimentación del metabolismo de O_2 . Esta revisión describe la historia y validez del control hemodinámico, ilustra el fundamento fisiológico y aplicación clínica de la oximetría venosa y presenta el análisis de dióxido de carbono como prueba de la utilidad del enfoque multimodal en el control cardiorrespiratorio. Se comprueba que la variación del gasto cardíaco, la mejora de la saturación de O_2 arterial y la adaptación de la extracción de O_2 son los niveles importantes para la adaptación fisiopatológica y la intervención terapéutica. Presentamos el perfil de $S_{cv} O_2$ y $S_V O_2$ y analizamos su importancia diagnóstica, terapéutica y pronóstica, proporcionando la base para la eficacia de la oximetría venosa como un importante marcador en el enfermo crítico. Finalmente, después de presentar un esquema de los desarrollos actuales para mejorar el conocimiento del balance oxidativo de los órganos individuales, destacamos la importancia de una estrategia sinóptica de monitorización de O_2 , así como la necesidad de utilizar su potencial clínico beneficioso, aún no aprovechado.

PALABRAS CLAVE: *oxígeno, monitorización, enfermedad crítica.*

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OXYGEN TRANSFER FROM ATMOSPHERE TO MITOCHONDRIA, AND BACK

The cardio-respiratory system provides the infrastructure for the transport of metabolic substrates to

and from the capillary beds where cells can perform effectively. Cells are strategically well positioned at the supply-demand interface, presenting a maximal surface area for the exchange of metabolites, and represent the basic functional physiological unit, as they possess the mitochondrial machinery for energy production as well as all other organelles enabling them to perform the functions of life. Oxygen (O_2) is of vital importance for the efficient running of these processes.

«Cellular respiration» neatly describes the molecular processes on the final common pathway of O_2 following its journey from atmosphere to mitochondria. On this long and complex route, O_2 is moved through conducting airways, exchanged against carbon dioxide (CO_2) in the lungs along opposing diffusion gradients on either side of the red blood cell membrane (O_2 -uptake), bound to haemoglobin and convectively transported in the major blood vessels to the tissues, there it diffuses and is distributed in the tissues. The variable fraction of O_2 finally taking part in oxidative phosphorylation to generate adenosine triphosphate (ATP) is the effective oxygen delivery (DO_2) for the cells. The arterio-venous difference of O_2 describes its extraction from DO_2 depending on the level of O_2 -demand (VO_2).

METABOLIC AUTOREGULATION OF THE CELL

Oxidative ATP production is a highly efficient process governed by metabolic autoregulation of the cell: the cumulative cellular metabolic performance signals a level of VO_2 -requirement; this global VO_2 , in turn, is the cellular feedback parameter creating the set point for a minimal DO_2 sufficient to satisfy metabolic demand.

Pflüger was the first to realise the feedback hierarchy –cellular requirement $> VO_2 > DO_2$ – as early as 1872. He described how it was not only the task of the cardio-respiratory system to act as the logistic conduit for substrates of metabolism, but also, and more importantly, that the oxygen requirement of the cells was the paramount regulator of cardio-respiratory physiology: «Herein lies the predominant secret of the regulation of the amount of oxygen consumed by the whole organism, determined only by the cell itself; (...) arterial oxygen content, aortal pressure, velocity of blood stream, mode of respiration are all incidental and subordinate, they all combine their actions in the service to the cells.»¹.

OXYGEN SUPPLY AND DEMAND

Respiration is a tidal process, DO_2 and VO_2 have to be constantly balanced and energy is permanently generated, chemically bound in and released from its molecular storage form of ATP. Tissue hypoxia ensues when this balance (DO_2/VO_2) is disturbed and oxygen consumption outstrips delivery. Oxidative phosphorylation stalls, cellular stress programmes

are triggered and anaerobic oxidation occurs. The inefficient anaerobic generation of ATP is quickly exhausted and leads to the development of lactic acidosis representing, and in turn, further worsening, global cellular dysfunction. As tissue hypoxia constitutes one of the most important co-factors of multi-organ failure (MOF)², it serves to illustrate the paramount regulatory function of the cell in its strategic frontline position.

Of all metabolic substrates, O_2 has the highest percentage of extraction and O_2 -reserves are exhausted within a few minutes³. While this physiological fact renders O_2 , together with its immense biological importance, a very precious commodity, the phenomenon also promotes measurement of arterial and venous O_2 -saturation as a highly effective clinical tool to monitor the cardio-respiratory system. Different organ systems display heterogeneous oxygen extraction levels, representing their differential metabolic activity as well as their respective position in various capillary zones of the circulation together with the unhomogenous share of cardiac output (CO) they receive per unit weight. The spectrum of venous saturation figures for different organs is, therefore, wide already under physiological conditions (fig. 1) and can be further varied by pathophysiological adaptation.

VENOUS OXIMETRY

The two principal sources for venous oximetry at the bedside are either a pulmonary artery catheter (PAC) or a central venous catheter, generating mixed (S_vO_2) and central venous saturation ($S_{cv}O_2$) measurements, respectively. $S_{cv}O_2$ is clinically more readily available as it is less invasive. It forms a constituent part of S_vO_2 , rendering the true mixed venous saturation the more representative indicator of global tissue oxygenation. As various organs display physiological differences in DO_2/VO_2 , and DO_2 as well as VO_2 can both individually fluctuate acutely under pathophysiological conditions, S_vO_2 does not yield information on oxygen reserves or adequate tissue oxygenation of individual organs. Furthermore, several disease states, such as hepatic failure or severe sepsis leading to arterio-venous shunting, limit the interpretation of absolute S_vO_2 values as indicators of tissue oxygenation. Here, normal or even supranormal S_vO_2 levels can co-exist with severe tissue hypoxia. This is also possible for conditions disturbing the unloading of oxygen from haemoglobin through left shift of the oxygen dissociation curve or blockage of the respiratory chain, such as in cyanide poisoning and, less well defined, in distributive, for example septic shock.

In 1870, Fick explored the relationship between CO, global oxygen demand and oxygen extraction and stated that «total uptake or release of any substance by an organ is the product of blood flow to the organ and the arterio-venous concentration difference of the substance» (Fick's principle)⁴. As O_2 is in global cellular demand and the whole CO passes the

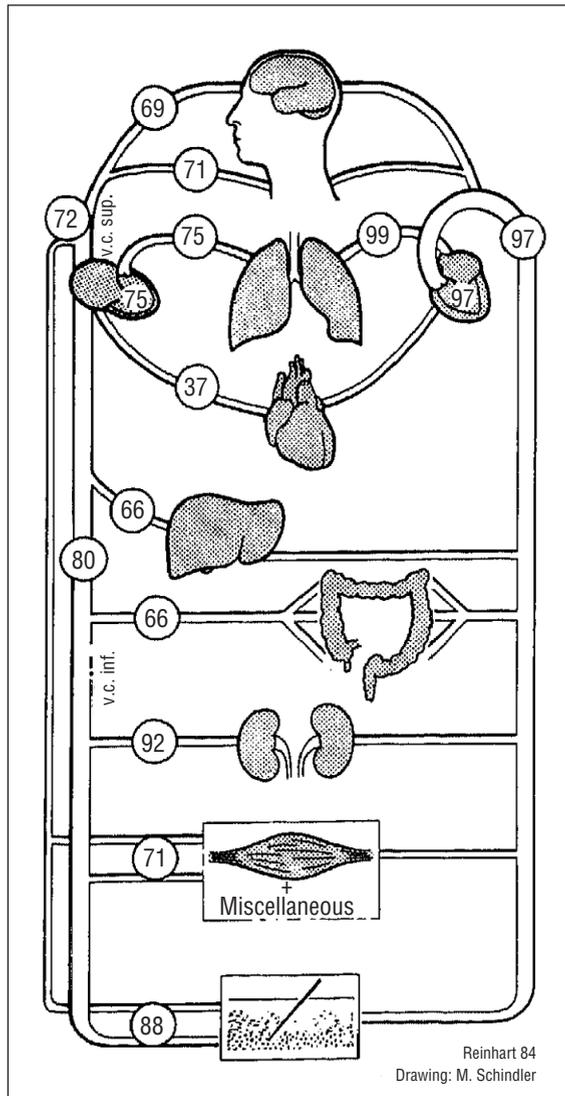


Figure 1. Average percentage figures of physiological arterial (right) and venous (left) oxygen saturation of various organ regions: their heterogeneous O₂-extraction levels explain the wide venous O₂-saturation spectrum.

entire cardio-respiratory system, mathematical rearrangement of the physiological equation deducing VO₂ illustrates the clinical usefulness and monitoring potential of SvO₂:

$$VO_2 = CO \times (C_aO_2 - C_vO_2) \text{ [Fick's principle]}$$

$$CO = VO_2 / (C_aO_2 - C_vO_2) \sim CO = VO_2 / 13.4 \times Hb \times (S_aO_2 - S_vO_2) \text{ and hence:}$$

$$S_vO_2 \sim S_aO_2 - (VO_2 / CO) \times k$$

In other words: for a given VO₂, S_vO₂ represents the supply-demand ratio of oxygen. A DO₂/VO₂ imbalance indicates mismatch: in clinical terms, shock. Notwithstanding some methodological limitations, as with all technology, venous oximetry provides extremely useful information for the evidence-based evaluation of the critical global oxidative balance and, therefore, makes for a good monitor.

VALIDITY AND HISTORY OF HAEMODYNAMIC MONITORING

Sophisticated monitoring greatly enhances speed and quality of diagnosis and allows to guide and control therapy, provided it is based on validated parameters. The Latin monitor translates as “I am being warned/reminded”. Critical synoptic analysis of the correlation coefficients of the haemodynamic parameters SvO₂, mean arterial pressure (MAP) and heart rate (HR) for DO₂/VO₂ (fig. 2) demonstrates that while the first is a reliable warning sign of oxidative imbalance, the latter two are no reminders of oxygen delivery.

The most frequently measured monitoring parameters deliver the least information on oxygen transport and cellular oxygenation. In the cellular regulation framework of cardio-respiratory pathophysiology, however, evidence of O₂-transport and requirements carries the highest validity, as information on the oxidative state of the cells most closely reflects their bioenergetic status, and those surrogate parameters, in turn, indicate most accurately what constitutes «critical» illness.

While MAP, especially if measured directly arterially, remains a valuable clinical parameter and firmly established in haemodynamic monitoring, a further problem of validity arises with its use. In 1928, Jarisch pointed out that «for the development of the science of circulation it was fateful that it is comparatively so awkward to measure flow, yet so easy to measure pressure: this is why the blood pressure manometer gained almost fascinating influence, while most organs do not require pressure, but flow volume»⁵.

The second half of the twentieth century ushered in an era of wider distribution and greater understanding of monitoring technology for the reduction of morbidity and mortality, stimulated particularly by anaesthesiological practice in peri-operative and intensive care medicine. Pulse oximetry (S_pO₂) for the continuous, real-time measurement of peripheral arterial oxygen saturation, as well as capnography (respiratory [end-tidal] CO₂-monitoring, ET_{CO2}) are non-invasive and have both proven so significant as to have been promoted into the rank of obligatory monitoring standards for the safe conduct of clinical anaesthesia.

THE CARBON FOOTPRINT OF CELLULAR RESPIRATION

CO₂-monitoring offers a perspective of demand orientation not dissimilar to that of venous oximetry, as the amount of carbon dioxide produced (VCO₂) for oxygen consumed are intrinsically linked through the respiratory quotient: RQ = VCO₂/VO₂. The RQ describes the carbon footprint of oxidative phosphorylation depending on the substrates used for ATP-production; for a diet of pure carbohydrates the RQ is 1 as the exothermic conversion of glucose (C₆H₁₂O₆) with oxygen produces equimolar quantities of carbon

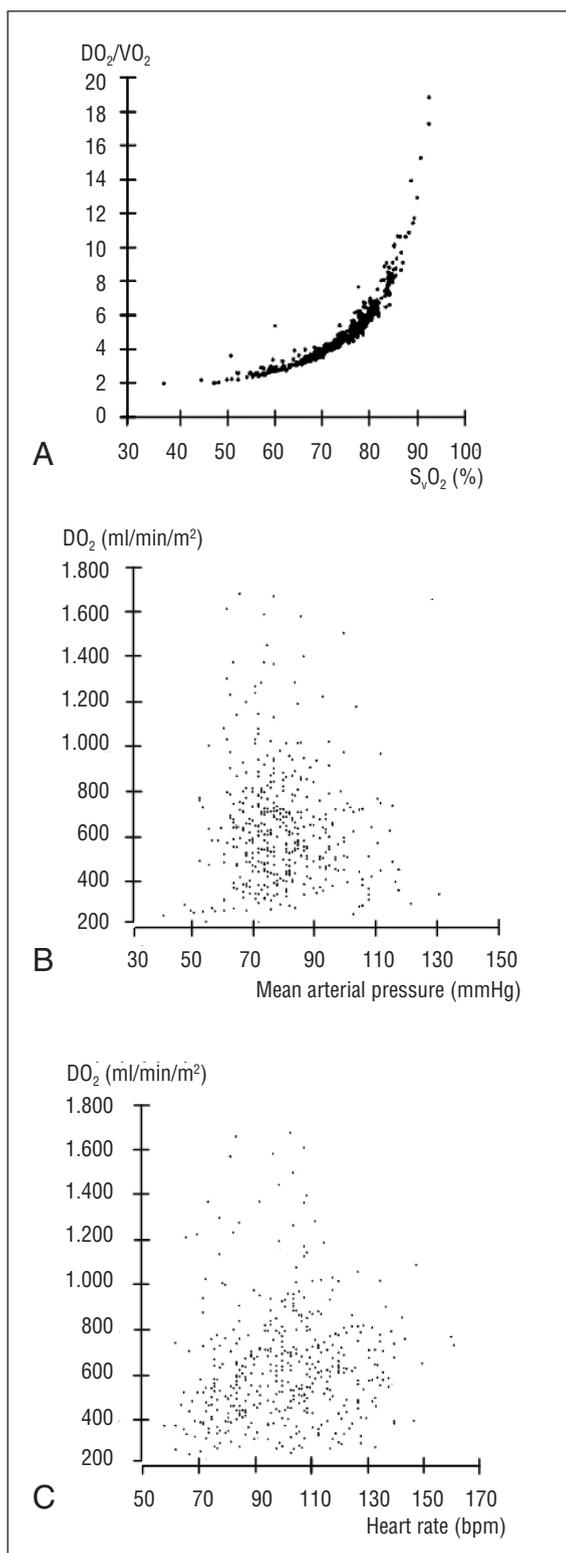


Figure 2. Critical synoptic analysis of the correlation between the haemodynamic variables mixed venous oxygen saturation (S_vO_2) (A), mean arterial blood pressure (MAP) (B), as well as heart rate (HR) (C) and oxygen supply/demand (DO_2/VO_2) reveals that S_vO_2 accurately reflects oxidative balance while the most frequently measured parameters MAP and HR deliver the least information on O_2 -transport and cellular oxygenation.

dioxide (and water [H_2O]): $C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O + \Delta heat$.

As the average diet in the industrialised world consists of a mix of carbohydrates (50%), fatty acids (30%) and proteins (20%) as sources for energy conversion, and the caloric value of fats and proteins is higher than that of sugar, the mean RQ of a healthy male European (75 kg) at rest is approximately 0.8, that is 200 ml/min of CO_2 generated for 250 ml/min of O_2 consumed (basal metabolic rate).

Looking at the substrate-specific conversion formula for oxygen is instructive in several ways. It sheds light on the alveolar gas exchange where, on the one hand, water and heat serve to humidify and warm the gases, O_2 and CO_2 , taking part; on the other, however, CO_2 and water vapour, along with nitrogen, occupy volume that cannot be used for optimised alveolar O_2 -uptake (Boyle's law of partial pressures). The disturbance of the evolutionarily old pulmonary unit, filled with high concentration nitrogen displaying a splinting effect, and protected by the physicochemical properties of water on the alveolar fluid-gas interface with low-concentration CO_2 and medium-concentration O_2 , partially explains the detrimental long-term consequences of the exposure of the lungs to high O_2 -concentrations by way of denitrogenation, with the therapeutic intent to maximize S_aO_2 . Exceeding a threshold of the fractional concentration of inhaled O_2 (F_iO_2), in addition, has a negative feedback impact on the CO. Trying to increase the effective DO_2 can thus paradoxically lower it.

While a synoptic analysis of O_2 -monitoring including capnography is, therefore, highly desirable, diet-dependency of the RQ represents only one of the methodological problems for the indirect monitoring of O_2 -supply-demand adequacy via CO_2 -monitoring. The elegant idea of gauging dysoxia via PCO_2 gradients (ΔPCO_2) provides the basis for gastro-intestinal tonometry, one of the few clinical tools presently available for the monitoring of tissue oxygenation⁶. At first regarded as a promising candidate for the early detection of dysoxia and regional hypoperfusion, critical concerns about methodological inaccuracies⁷ suggest a reduced, albeit still valuable role of ΔPCO_2 for the monitoring of the microcirculation only. However, as it cannot reliably detect anaerobic metabolism when flow is preserved, gastro-intestinal tonometry fails to reflect the oxygen supply dependency during hypoxic episodes witnessed under conditions of oxidative stress in the critical vascular bed of the gut.

Nevertheless, additional surrogates of impaired oxygen supply to peripheral tissues, such as ΔPCO_2 or plasma disappearance rate of indocyanine green (PDR_{icg})⁸, help to widen the scope of the global oxygenation parameter $S_{(e)v}O_2$, adding valuable information on individual organ regions.

LEVELS AND LEVERS OF PATHOPHYSIOLOGICAL ADAPTATION

When the variation of S_vO_2 (ΔS_vO_2) is correlated to that of S_aO_2 (ΔS_aO_2) in the critically ill, it becomes

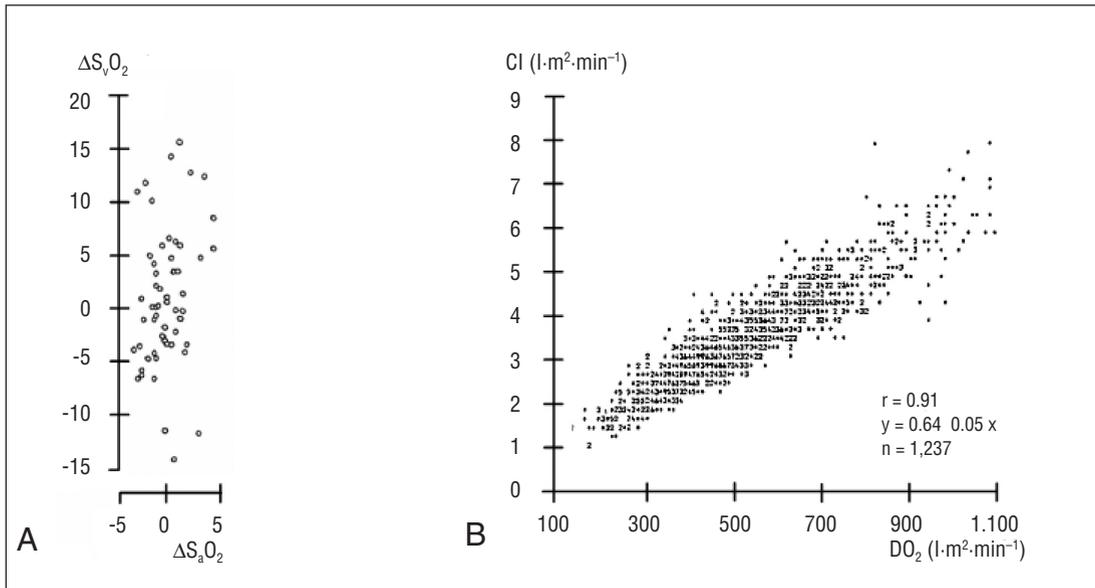


Figure 3. Arterial oxygen saturation (S_aO_2), cardiac index (CI) and oxygen extraction, here represented by mixed venous saturation (S_vO_2), are the three relevant systemic mechanisms of adaptation to demand-supply-fluctuations (DO_2/VO_2). A) Correlation between the respective variations of saturation ($\Delta S_vO_2/\Delta S_aO_2$) illustrates the functional importance and monitoring capability of S_vO_2 as it fluctuates much more than S_aO_2 . B) Tight positive correlation of DO_2 and CI marks their physiological interdependence.

apparent that venous saturation fluctuates much more than its arterial equivalent over time (fig. 3), illustrating the functional importance of O_2 -extraction as well as rendering ΔS_vO_2 the more specific and sensitive parameter to indicate adaptive changes, particularly in times of oxidative stress.

Optimisation of arterial O_2 -saturation, variation of CO and adaptation of oxygen extraction are the three relevant systemic mechanisms to adjust the organism to fluctuations in DO_2/VO_2 ; they present themselves at the same time as therapeutic levers for haemodynamic management.

Without evidence of venous saturation, cardio-respiratory monitoring, based solely on the measurement of heart rate and rhythm, arterial blood pressure and oxygen saturation, central venous pressure and CO, be it invasive or non-invasive, is half blind. Information on oxygen supply does not answer the decisive question whether it is sufficient to meet cellular oxygen demand. While clinical monitoring that allows the satisfactory quantification of the bioenergetic status of the cells is still some way off, it is all the more regrettable that venous oximetry has not yet attained the position befitting a global monitoring parameter of such relevance and importance.

In view of the astonishing technological progress revolutionizing the generation, acquisition, processing, display and analysis of monitoring information, it is important not to forget the original meaning of «monitor» as an aid supporting the human decision-making process. The first Harvard criterion for good monitoring practice is, therefore, the constant presence of adequately qualified anaesthesia personnel throughout the course of any

anaesthetic intervention. «Keeping a finger on the pulse» means just that.

S_vO_2 AND $S_{cv}O_2$ – NOT IDENTICAL, BUT FUNCTIONALLY EQUIVALENT

While S_vO_2 is the true mixed venous parameter, indicating global oxidative balance and correlating best with DO_2/VO_2 , $S_{cv}O_2$ is its constituent part and as such only representative of the organs of the upper body. At the same time, $S_{cv}O_2$ measurements are less invasive and widely and quickly attainable in clinical reality; S_vO_2 necessitates an intensive care environment. Frequently, neither the time nor the place for PAC-dependent monitoring are available.

What is more, PAC usage, per se, has been shown not to affect outcome in critically ill patients⁹, whereas the implementation of treatment strategies that incorporate $S_{cv}O_2$ (or S_vO_2 , where available) monitoring as part of a dynamic monitoring philosophy along the lines of bioenergetic cellular integrity have succeeded in reducing their mortality considerably¹⁰⁻¹⁴.

«Critical illness» can be defined as a state of disease that threatens the life of a patient by endangering the function of one or more vital organ systems. Tissue hypoxia is a pivotal co-factor of multi-organ dysfunction syndrome (MODS), and venous oximetry, therefore, well suited to describe this situation. Critical, in this context, is not only the biographic nadir as such, but also the narrowness of the window of opportunity and with it the timing of therapeutic interventions: sub-stratification analysis of haemodynamic strategy in high-risk patients¹⁵ reveals that optimisation attempts are futile once organ failure is

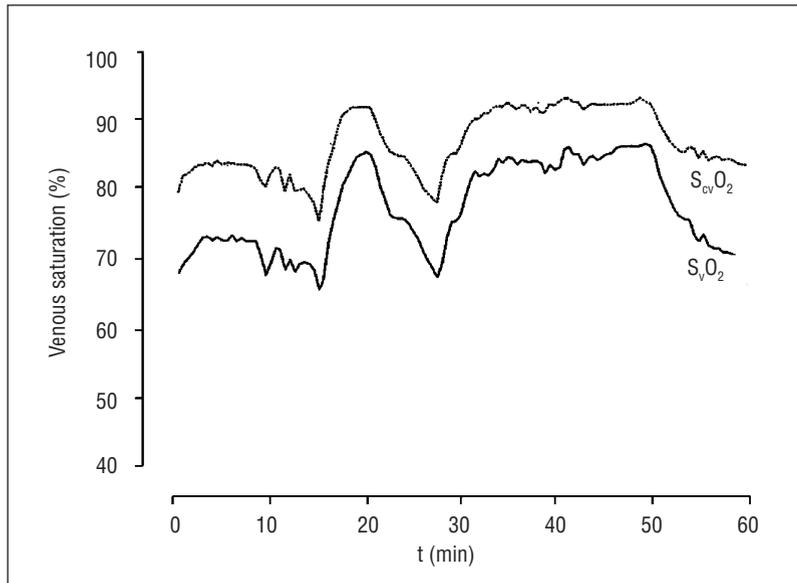


Figure 4. Simultaneous registration of S_vO_2 and $S_{cv}O_2$; numerically different, consistently parallel, functionally equivalent.

firmly established. $S_{cv}O_2$ serves as an early warning sign for the developing shock entity; it has the potential to drag cryptic shock out into the open. It allows the monitoring of the critical oxidative balance in the decisive period before both MODS and a PAC are established on the intensive care unit. Herein lies the beauty and main advantage of $S_{cv}O_2$ over S_vO_2 .

The long-running discussion about the equivalence of S_vO_2 and $S_{cv}O_2$ has been addressed in several studies¹⁶⁻¹⁸. These have illustrated $S_{cv}O_2$ and S_vO_2 levels to be numerically different, yet consistently parallel. Recognising a discrepancy of absolute numbers is primarily of academic interest when their correlation is tight and, as a consequence, their physiological trend patterns are equal as demonstrated in animal studies¹⁹ as well as human clinical observations²⁰ (fig. 4). «Mixed vs central venous oxygen saturation may be not numerically equal, but both are still clinically useful»²¹ was the blunt title of a recent editorial summing up conclusively the supposed dilemma of lack of absolute congruence between $S_{cv}O_2$ and S_vO_2 .

SIGNIFICANCE OF VENOUS SATURATION MONITORING

It is of much greater value for the clinician to know to what extent CO and S_aO_2 are able to meet the oxygen requirements of the capillary beds dictated by global cellular VO_2 (Pflüger) than just to know the supply side values in isolation, and nowhere more so than in critically ill patients constantly threatened or affected by MOF.

In addition, valuing trend lines over absolute figures is an important principle of clinical measurement where biosensitive systems have to be calibrated often by multi-point analysis to detect and correct shift and drift, as well as in biostatistics where only a satisfactory quantity of data allows the description of

a phenomenon as a trend or correlation in the first place.

Continuous measurements display real-time trends on-line and lead, as a consequence, to more sensitive and powerful monitoring data records than the discrete numbers generated by intermittent gathering of reference points. This is of particular importance for the close, accurate and precise monitoring of episodically and unforeseeably fluctuant parameters such as DO_2 and VO_2 . As VO_2 exerts a physiological feedback on DO_2 , it is instructive to measure and correlate them both. If an increase in DO_2 , that is a raised CO, leads to a relevant increase in VO_2 , then this O_2 -flux test indicates the improvement of a previously inadequate tissue oxygenation²².

Altogether, there can be no doubt that the benefits of (trend analysis of continuous) $S_{cv}O_2$ -monitoring by far outweigh the slight, predominantly academic and clinically irrelevant discrepancy in absolute numerical values when compared to S_vO_2 .

Deduction from Fick's principle elucidated the role of S_vO_2 as a functional monitoring parameter for the critical estimation of the global balance of DO_2 and VO_2 . Three components of the equation (balance, supply, demand) on one side find their numerical expression in the venous saturation on the other.

Oxidative balance in the critically ill is represented by a $S_{(c)v}O_2$ level of 70%. If oxygen demand outstrips supply the saturation scales are slanting towards tissue hypoxia - $S_{(c)v}O_2$ figures less than 65% are an early and urgent warning sign pointing towards development of MODS and shock. The (physio)logical interpretation of $S_{(c)v}O_2$ levels exceeding 75% is that of a reverse imbalance with DO_2 greater than VO_2 (fig. 5). As long as all metabolic requirements are being met, this imbalance is irrelevant: supranormality accounts for physiological reserve. Not so in shock, though, where insufficient metabolic performance is

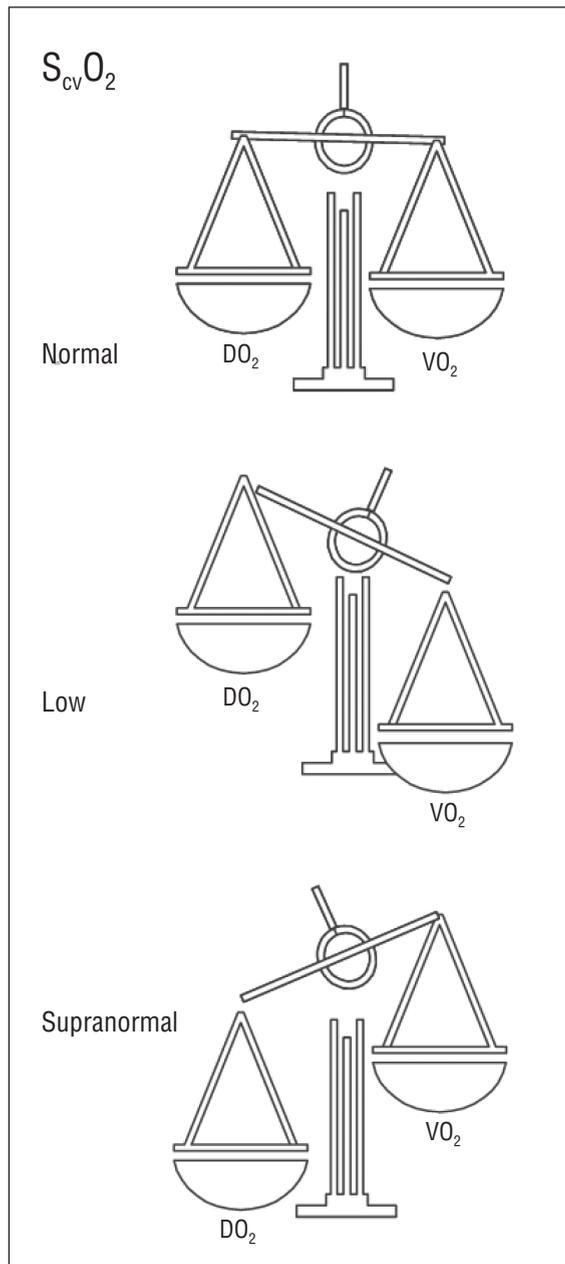


Figure 5. Disease-induced oxidative stress in critical illness: oxidative balance ($S_{cv}O_2$ 70%) indicates an adequately raised DO_2 in response to an increased VO_2 . Tissue hypoxia ensues when VO_2 outstrips DO_2 : $S_{cv}O_2 < 65\%$, an urgent warning sign. Supranormality is a marker of poor prognosis too, as it highlights a reverse imbalance ($S_{cv}O_2 > 75\%$): VO_2 cannot be adequately up-regulated to satisfy cellular metabolic requirements and is outweighed by a raised DO_2 .

the very defining, pathognomonic feature. The patients' maximal oxygen uptake and metabolism ($VO_2[\max]$) cannot fulfill the acutely increased mitochondrial requirements in critical illness. Supranormal venous saturation in this context cannot be regarded as a useful or luxury reserve. Rather, it represents a desperately needed, yet unused resource.

Focussing on the supply side alone does not meet excessive demand requirements. The balance is not right: oxygen uptake is too low, indicating either shunts forming at the level of the micro-circulation (effective DO_2 too low) or highlighting the inability of the mitochondria to pass electrons through the respiratory chain, that is a utilisation disturbance (effective VO_2 too low)²³.

Cardio-pulmonary exercise testing (CPET) provides a constructive analogy, as it is a clinically validated protocol stratifying at-risk-patients into categories with prognostic relevance based on their capacity to mount a measurable response ($VO_2[\max]$) to a potentially life-threatening situation of oxidative stress (major surgery). A patient presenting with signs of MODS is, in contrast to the elective setting of CPET, a medical emergency and necessitates a robust and streamlined approach. $S_{cv}O_2$ is currently the best evidence-based parameter to guide and monitor the direction of treatment strategies in critical illness towards the goal of an adequately raised DO_2/VO_2 ratio dynamically balanced on the level of a higher metabolic set point as dictated by the disease-induced surge in oxidative stress.

BETWEEN A ROCK AND A HARD PLACE: A SAFETY CORRIDOR OF $S_{cv}O_2$ -VALUES

This is why $S_{cv}O_2$ is a cornerstone of an outcome-oriented algorithm such as early goal-directed therapy (EGDT) as a constituent part of the Surviving Sepsis Campaign. Furthermore, obtaining a specimen for blood gas analysis to establish a $S_{cv}O_2$ in the critically ill should be a primary motivation when indicating the need for the placement of a central venous catheter. What is more, persistent signs of tissue hypoxia should then prompt continuous monitoring of the $S_{cv}O_2$, underpinning its importance as an end point of critical and early prognostic, diagnostic and therapeutic significance.

In a series of 205 patients undergoing elective cardiac surgery we observed a similar hypoxic burden as indicated by increased lactate levels (> 4 mmol/l) along with comparable morbidity and mortality in patients with $S_{cv}O_2$ measurements below 65% as well as above 75%, respectively (own unpublished observation). These data suggest a three-tiered sub-stratification along $S_{cv}O_2$ cut-off points gained by trend analysis of continuous measurements: while the well oxygen-balanced patient cohort had the best chances of survival, both cohorts with $S_{cv}O_2$ values falling outside a «corridor of safety» of $70 \pm 5\%$ performed significantly worse and similarly to each other.

IMPORTANCE OF A SYNOPTIC MONITORING STRATEGY OF O_2 IN DYNAMIC EQUILIBRIUM

Contemporary oxygen monitoring is sophisticated, universally available and yields important information to put intensive care for the critically ill on a sound and solid evidence base as an eminent part of a

synoptic evaluation strategy for a substrate in dynamic equilibrium. Despite its great significance, (patho)physiological plausibility and clinical practicability, venous oximetry is not used to its full potential yet.

Additional surrogates of impaired oxygen supply to individual organs and functional cellular units, such as PDR_{icg} or gastro-intestinal tonometry, are technically achievable and clinically available today at least for some capillary beds. The near future will see the introduction of more devices for the specific surveillance of organs and their functions in relation to their individual DO₂, VO₂, their respective interaction and further important O₂-dependent variables. These highly desirable instruments for prognostic, diagnostic and therapeutic management of the critically ill threatened or affected by MOF allow a direction of focus away from what Pflüger so poignantly defined as «incidental and subordinate».

The challenge today is to move on from this state of affairs and to raise understanding of the existing possibilities of O₂-monitoring and its significance for survival of the critically ill, characterised by a heterogeneity of outcome which has less to do with access to high-tech medicine than with the will to consequently implement, at local level and into clinical routine, what has to be regarded as best practice at the present time.

Venous oximetry should play the role of the first violinist in the orchestrated approach necessary to do justice to the complex and dynamic network of interactions that classifies oxygen metabolism and its clinical monitoring as a symphony constantly in the making –or breaking– in the critically ill patient.

CONCLUSION

The cardio-respiratory system provides the infrastructure for the transport of O₂ from atmosphere to mitochondria, and back. Global cellular requirement determines effective VO₂, setting the point for a minimally sufficient effective DO₂. The cell is at the top of the feedback hierarchy of metabolic autoregulation. Tissue hypoxia ensues when global and/or individual organ DO₂/VO₂-balance are disturbed; it constitutes one of the most important co-factors of MOF with highly significant morbidity, mortality and cost implications for the critically ill. Of all metabolic substrates, O₂ has the highest percentage of extraction. It is further characterised by heterogeneous organ saturation levels and a quickly exhaustable reserve. This dynamic equilibrium promotes monitoring of arterial and venous O₂-saturation as a very effective clinical tool. Arterial O₂-saturation is routinely monitored invasively (S_aO₂) or non-invasively (S_pO₂); in contrast to that, venous oximetry is not used as consistently or effectively. There are two principal sources for venous oximetry: S_vO₂ and S_{cv}O₂. S_vO₂ is the more representative indicator of global tissue oxygenation; S_{cv}O₂, however, is less invasive and more readily available (they are not identical, but functionally equivalent). Both represent the supply-

demand ratio for O₂ and, therefore, provide highly significant evidence for the critical synoptic analysis of cardio-respiratory monitoring data. Unfortunately, the most frequently measured haemodynamic parameters -arterial blood pressure and HR- deliver the least information on cellular oxygenation. Furthermore, a multi-modal O₂-monitoring approach elucidates the useful function of CO₂-monitoring with its perspective of demand orientation similar to that of venous oximetry; VO₂ and CO₂-flux (VCO₂) are intrinsically linked through alveolar ventilation in the respiratory quotient: $RQ = VCO_2/VO_2$. Optimisation of S_aO₂, variation of CO and adjustment of oxygen extraction ($\Delta S_{(cv)}O_2$) are the three relevant systemic physiological mechanisms of adaptation as well as therapeutic levers for haemodynamic management. They are half blind without evidence of venous saturation, as it is much more important to establish to what extent CO and S_aO₂ are able to meet oxygen requirements than just to know the supply side values in isolation. In the critically ill, sustained S_{cv}O₂ levels below 65% indicate ineffective DO₂ while those above 75% characterise an ineffective VO₂, with a safety corridor of 70 ± 5% in between. S_{cv}O₂ is currently the best evidence-based parameter to guide and monitor treatment strategies of patients threatened or affected by MOF. Obtaining S_{cv}O₂-values should be a primary motivation when indicating the placement of a central venous catheter. Contemporary, multi-modal O₂-monitoring is sophisticated, widely available and (patho)physiologically highly relevant. Despite its great clinical significance, plausibility and practicability, it is not yet used to its full potential. Additional surrogates of impaired oxygen supply to individual organs are promising more conclusive answers to the supply-demand question: micro-circulatory insufficiency or utilisation disturbance? at the mitochondrial level as the final common pathway of O₂-metabolism.

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