Pathophysiology of Critical Ill Patients: Focus on Critical Oxygen Delivery

Arif Mansjoer*, Yohanes W.H. George**

ABSTRACT

Critical ill patients experience acute physiological changes because the body cannot fulfill the oxygen demand to perform normal aerobic metabolism. Factors determining oxygen delivery include cardiac output, hemoglobin, and oxygen saturation. Incapability to fulfill adequate oxygen of the body to produce adenosine triphosphate (ATP) may occur due to decreased oxygen delivery and/or increased oxygen consumption. A condition in which oxygen consumption becomes very dependent on oxygen delivery is called critical oxygen delivery. *Parameters to evaluate the adequate oxygen delivery to meet the oxygen consumption are central vein oxygen saturation (SvO2), serum lactate, oxygen extraction ratio (O_2ER). A comprehension about oxygen delivery and consumption is very important to overcome tissue hypoxia and various factors in critical ill patients.*

Key words: oxygen delivery, oxygen consumption, critical oxygen delivery, critical ill patient, tissue hypoxia.

INTRODUCTION

Critical ill patients are patients who have acute physiological problem. Their previous condition may be healthy or having an underlying disease. Such critical illness can be reversible when it is treated promptly and appropriately. Delay in diagnosis and treatment will lead to morbidity or even mortality.

An acute physiological change that may lead to mortality is decreased oxygen supply, which may result as tissue hypoxia since there is decreased oxygen delivery so that it cannot fulfill the normal oxygen consumption or increasing normal oxygen consumption without adequate increase of oxygen delivery. Further imbalance between oxygen delivery and oxygen consumption will cause the body to become unable to compensate and to maintain the aerobic metabolism, which then turn into anaerobic metabolism. Such condition is known as a critical oxygen delivery (critical DO_2). In this article, we will discuss about oxygen delivery (DO_2) based on physiological and pathophysiological aspects as well as clinical implementation.
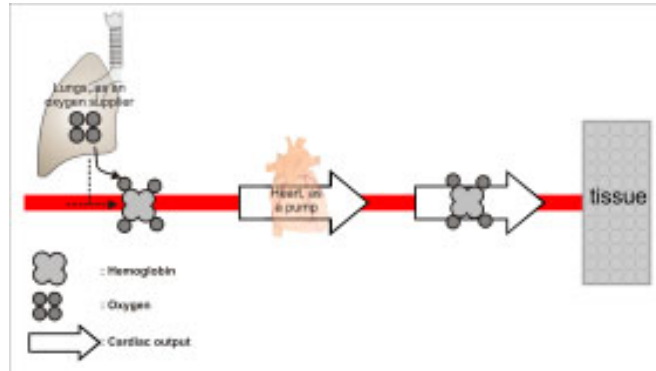
In normal conditions, oxygen is taken from the environment through the airway into alveoli by pulmonary ventilation. Oxygen in alveoli will diffuse into pulmonary capillaries and mostly will be bound to hemoglobin of red blood cells. Subsequently, it will be pumped by the heart and distributed to capillaries all over the body. Then, oxygen is released from the hemoglobin and diffuses into cell entering the mitochondria.[1-3]

In the mitochondria, oxygen is utilized in the aerobic metabolism, i.e. an oxidative phosphorilation process producing adenosine triphosphate (ATP). ATP is an energy resource to support various activities of the body. Disturbance in oxygen supply, from the environment up to mitochondria will cause disruption of ATP production.[1]

* Department of Internal Medicine, Faculty of Medicine, University of Indonesia-dr. Cipto Mangunkusumo Hospital. Jalan Diponegoro no. 71, Jakarta. E-mail: arif.mansjoer@gmail.com. ** Head of Emergency and Intensive Care Unit, Pondok Indah Hospital, Jakarta.
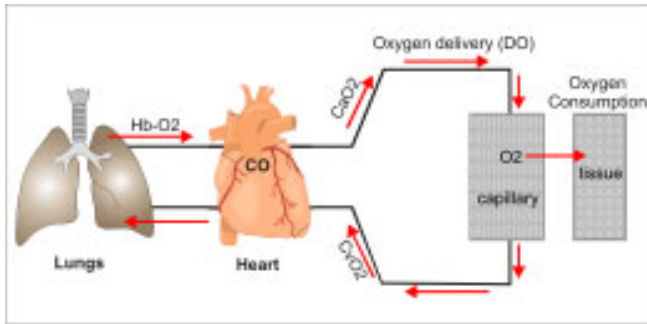
Figure 1. A schematic representation of pulmonary oxygen transportation. The oxygen is bound to hemoglobin, pumped by the heart, and extracted by tissues. The rest of oxygen, which is not taken by the tissues, are then delivered back to the heart/lung. The arrow describes hemoglobin. The size of bold arrow indicates oxygen volume. O_2: oxygen, CO: cardiac output, CaO_2: oxygen level in the arteries, $Cv\dot{O}_2$: oxygen level in veins; Hb.

OXYGEN DELIVERY

The function of oxygen supply is called *oxygen delivery* (DO_2), which is determined by oxygen saturation of arterial blood, hemoglobin, and cardiac output.[2-7] After entering the body through the airway by ventilation process and diffuses through the alveolus, most of the oxygen will be bound to hemoglobin and some of them (1.5%) will be dissociated in blood. Oxygen saturation of arterial blood (SaO_2) is a ratio of hemoglobin containing oxygen (g/dL) and total hemoglobin (g/dL). The amount of hemoglobin dissociated in blood is so small ($0.003 \times pO_2$) that it is usually eliminated from the calculation. One gram of hemoglobin is able to bind 13.4mL of oxygen. The oxygen content bound to hemoglobin of arterial blood (CaO_2) may be calculated as follows:

$$\mathbf{CaO_2} = 1.34 \times Hb \times SaO_2 \text{ mL/dL}$$

The blood volume pumped by the heart to the whole body every minute is called cardiac output (mL/min) which is determined by stroke volume (mL) and heart rate (/min). Stroke volume is affected by preload, contractility, and afterload. The amount of oxygen delivered per minute is called oxygen delivery (DO_2) and may be calculated as follow:

$$\mathbf{DO_2} = CO \times 1.34 \times Hb \times SaO_2 \times 10 \text{ mL/min}$$
$$= 13.4 \times CO \times Hb \times SO_2 \text{ mL/min}$$

(**Note:** The value of 10 is a multiplying factor for altered unit, i.e. 1 L into 10 dL).

Figure 2. The schematic representation of oxygen delivery and its determining factors, i.e. hemoglobin, oxygen saturation, and saturated oxygen, and cardiac output.

For example, in patient with Hb 15 g/dL, 97% SaO_2, and cardiac output of 5 L/min, there will be CaO_2 of 194.97 mL/L. It means that the patient has 194.97 of oxygen bound to hemoglobin in every 1 L of blood. The DO_2 of such patient is 974.85 mL/min which means that in every minute the tissues receive 974.85 mL oxygen delivery.

OXYGEN CONSUMPTION

When blood flow from the heart has reached the capillaries, oxygen bound to hemoglobin will be dissociated and moves into cells through the tissues. In normal condition, 20-25% of oxygen is consumed by the tissues. The remained oxygen, which is not taken by the tissues will be returned to circulation system and finally to the heart.[4-8]
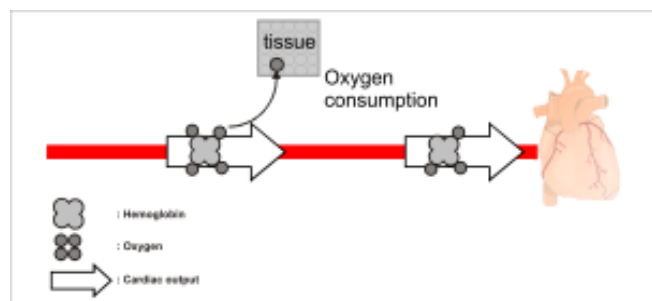
Figure 3. Schematic representation of oxygen consumption

Since oxygen is not stored in tissues, the oxygen uptake is also a measure of the oxygen consumption of the tissues (mL/minute). The oxygen consumption (VO_2) can be calculated as the difference between the amount of oxygen delivered per minute and the amount of

oxygen that returned to the heart:

VO2 = [13.4 x CO x Hb x SaO_2] – [13.4 x CO x Hb x SvO_2]

= 13.4 x CO x Hb x (SaO_2 – SvO_2) mL/min

The above equation is called *reverse Fick method*, i.e. CO = VO_2 / (CaO_2 – CvO_2), where the CaO_2 is defined as 13.4 x Hb x SaO_2 and CvO_2 is 13.4 x Hb x SaO_2. Evaluation of VO_2 by such method of Fick actually does not represent VO_2 of the whole body since it does not include oxygen consumption by the lungs. In normal condition, the oxygen consumption by lungs is less than 5% of whole-body oxygen consumption, but in inflammatory condition, it may rise to 20%. It is important regarding to overaggressive management to increase the VO_2.

SvO_2 is a value of oxygen saturation of central vein. Ideally, the blood is taken from vessels before entering lungs, i.e. the pulmonary artery by using Swan-Ganz pulmonary artery catheter. The blood saturation of pulmonary artery is called mixed vein saturation (SvO_2) and the saturation value is approximately 5% less than blood saturation of vena cava. For more practical reason in our practice, the blood samples to validate saturation of central vein is taken from vena cava and it is called oxygen saturation of vena cava ($ScvO_2$). In normal condition, the $ScvO_2$ is 5% less than SvO_2 since there is mixed blood in pulmonary artery which contains blood from superior and inferior vena cava as well as blood of *sinus venosus*, i.e. blood of coronary veins.

The VO_2 can be measured directly by measuring the rate of oxygen disappearance inhaled and exhaled by the lungs. This can be performed with an instruments equipped to the proximal airway (usually in intubated patients) and to measure the O_2 concentration in inhaled and exhaled gas by the lungs. The VO_2 is calculated from minute ventilation (MV) and differences between fractional oxygen of inhaled and exhaled gas:

$$VO_2 = MV \text{ x } (FiO_2 – FeO_2)$$

The other parameter of oxygen consumption is the ratio of oxygen taken up into the tissues and delivered oxygen which is called oxygen extraction ratio (O_2ER), that is :

O_2ER = VO_2 : DO_2

= [SaO_2 – SvO_2] / SaO_2 x 100%

The O_2ER is normally about 0.25 (range = 0.2–0.3). This ratio can be multiplied by 100 and expressed as a percentage. It means that only 25% of oxygen delivered to systemic capillaries is taken up into and used by the

tissues. Although O_2 extraction is normally low, but it is adjustable and can be increased when oxygen delivery to the tissues is decreased.

For example, a patient with Hb 15 g/dL, 97% SaO2, and cardiac output of 5 L/min is found to have 75% saturation of central veins. Based on those data, the oxygen consumption rate (VO_2) is 221.1 mL/min. It means that 221.1 mL oxygen per minute is consumed by the body. The oxygen ratio extracted by the body (O_2ER) is 22%, i.e. 22% of the oxygen delivered by circulation system is used by the tissues, and the rest, 78% is returned back to the heart.

Tabel 1. A normal value of parameters for oxygen delivery and oxygen consumption[2]

| Parameters	Absolute value	Normal value based on BSA
Cardiac output	5 – 6 L/m	2.4 – 4.0 L/min/m^2
Oxygen delivery (DO_2)	900 -1,100 mL/min	520 – 600 mL/min/m^2
Oxygen consumption (VO_2)	200 – 270 mL/min	110 – 160 mL/min/m^2
Oxygen extraction ratio	0.2–0.3 (20% – 30%)	

BSA : Body Surface Area

PATHOPHYSIOLOGICAL ASPECTS

In patients with critical illnesses, there are physiological changes of DO_2 and VO_2. The relationship of DO_2 and VO_2 is shown on DO_2 - VO_2 curve. Initially, decreased DO_2 is relatively not followed by decreased VO_2. For instance, for the decreased DO_2 from 1000 mL/min to 500 mL/min, the 250 mL of VO_2 is not equally decreased. However, further decreases from 500 mL/min will be followed by decreased VO_2. The decreasing point when VO_2 starts to decrease is called the critical DO_2.[9]

Thus, the critical DO_2 is the lowest DO_2 that is capable of having full role in aerobic metabolism. The shift of DO_2 over the critical DO_2 indicates pathologic condition that is anaerobic metabolism has occurred. Unlike the aerobic, anaerobic metabolism will produce 2 ATP and lactate acid for each mol of glucose.[6]

Although it is able to identify the anaerobic metabolism threshold, the critical DO_2 has a limited clinical value. First, the critical DO_2 has varied widely in studies of patients with critical illness and it is not possible to predict the critical DO_2 in any individual patient in the ICU. Second, the DO_2-VO_2 curve can be curvilinear (i.e. without a single transition point from constant VO_2 to decreased VO_2), and in this cases, it is impossible to determine the critical VO_2.[6]
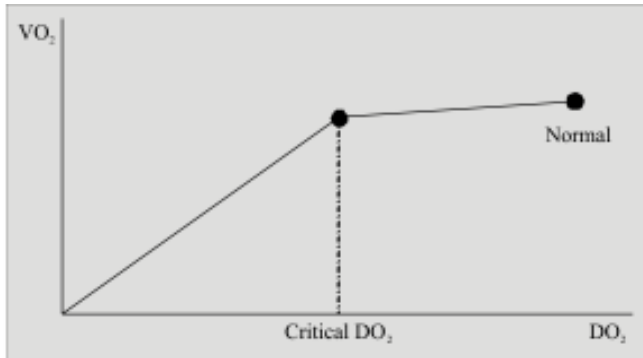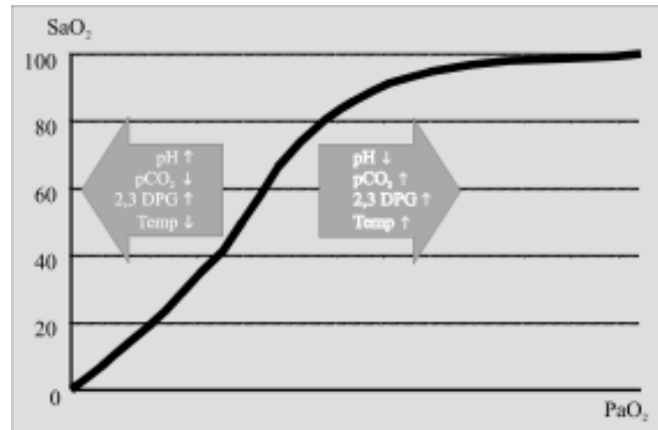
Figure 4. The normal relationship between oxygen delivery and oxygen consumption. Oxygen delivery (DO2) is determined by several components, i.e. Hb, VO2, and cardiac output. Alteration of such components will affect the DO2. Decreased DO2 is initially not accompanied by significant decrease of VO2.

Figure 5. The Hb-O2 dissociation curve. The curve can shift to the right due to acidosis, increased pCO2, 2-3 DPG, and temperature. This condition means that the oxygen binding is easily released and dissociated into the tissues, and vice versa.

Decreased Oxygen Delivery

A decrease of oxygen delivery may occur due to decreased oxygen level from the air, diffusion disturbance of alveoli-capillary membrane, decreased hemoglobin concentration, and decreased cardiac output, problems in distributing diffusion from capillary to cellular tissues, cells, and mitochondria. In general, there are three components that may cause decreased oxygen delivery namely oxygen saturation (SaO_2), hemoglobin concentration (Hb), and the cardiac output (CO).[2,3,11-13]

Oxygen is taken up into the body and the process is affected by airway condition, ventilation, and oxygen diffusion. Oxygen saturation of arterial blood (SaO_2) is determined by pO_2, pCO_2, pH, temperature, and 2-3 DPG as shown on curve of dissociation. The pO_2 is influenced by FiO_2 and PEEP; the pCO_2 is affected by minute ventilation, i.e. tidal volume and respiratory rate and death space; the pH is affected by pCO_2, strong ion different (SID), and weak anions. Inadequate oxygen transportation of the lung until being bound by hemoglobin is frequently caused by hypoxemia (PaO_2 is less than 60 mmHg). This condition is attacked by the hypoxic hypoxia (hypoxemic, hypoxia).[3,10,12] The other factors are intoxication of carbon monoxide and methemoglobinemia.

Cardiac output is determined by stroke volume and heart rate. The stroke volume is affected by preload, contractility, and afterload. The heart rate includes frequency and regularity. Inadequate blood circulation results in reduced blood volume that delivers both systemic and regional oxygen. Such condition is called ischemic hypoxia. There are several causes of reduced systemic blood flow including severe heart failure and various types of shock. The regional cause involves obstruction of blood vessels, such a coronary or cerebral thrombosis.[3,12]

Severe anemia is considered as deficiency of hemoglobin molecules which may be caused by bleeding, nutrient deficiency, and hematopoetic disorder (anemia aplastic and leukemia). Such a condition is named as anemic hypoxia.[3,11-12]

Pathophysiology of The Oxygen Consumption

Increased oxygen demand in the tissues may result due to increasing metabolism (hypermetabolism) induced by long and hard exercise, systemic inflammatory response syndrome or sepsis, cramp, thyroid crisis, high fever, and malignant hyperthermia.[3]

Table 2. Sample of calculation for decreased oxygen delivery in someacute clinical conditions[7]

	Normal	Hypoxemia	Anemia	Heart failure
Oxygen saturation of arterial blood (SaO_2) - %	98%	**70%**	98%	98%
Hemoglobin concentration (Hb) – g/dL	15	15	**8**	15
Cardiac index (CI) – L/min/m2	3	5	3	**1.6**
Oxygen delivery (DO2) – mL/min/m²	590.94	422.1	315.17	315.17

Tabel 3. Factors causing changes of oxygen consumption[3]

Variables	% increase
Condition that increases VO$_2$	
Minor surgery	7
Fever (each 1oC)	10
Bone fracture	10
Agitation	16
Increasing work of breathing	40
Severe infection	60
Severe infection	60
Chest trauma	20-80
Multiple organ failure	50-100
Shivering	100
Burns	50-100
Sepsis	50-100
Head injuries, sedated	89
Head injuries, not sedated	138
Medication that increases (VO$_2$)	
Norepinephrine (0.10-0.31 ug/kg/min)	10-21
Dopamin (5 ug/kg/min)	6
Dopamin (10 ug/kg/min)	15
Dobutamine	19
Epinephrine (0.10 ug/kg/min)	23-29
Procedures/activities that increase VO$_2$	
Dressing change	10
Nursing assessment	12
Electrocardiogram	16
Physical examination	20
Visitors	22
Bath	23
Chest X-ray	25
Endotracheal suctioning	27
Turn	31
Chest physiotherapy	35
Weight on sling scale	36
Getting out of bed	39
Nasal intubation	25-40
Factors that decrease VO$_2$	
Hypothermia (each 1oC)	10
Morphine sulfate IV push (0.5 mg/kg)	9-21
Morphine sulfate IV (0.2-0.5 mg/kg/hr)	21
Anesthesia	25
Anesthesia in burnt patients	50
Assist/control ventilation	30
Propranolol in head injury	32
Neuromuscular blockade	Abolishing the increase in VO$_2$ incurred by shivering

In addition to the abovementioned factors, reduced oxygen consumption by cells may occur due to: (1). incapability of cells to take up or use the oxygen, for example in patients with sepsis or intoxication of cyanide or ethanol, which result in a condition known as cytopathic hypoxia or toxic hypoxia; (2). disturbance of oxygen uptake at capillaries level due to by alkalosis, hypocarbia, massive consumption of blood supply, interstitial edema, and systemic arterio-venous shunting

(sepsis, cirrhosis). Factors that affect the oxygen uptake from capillary into the cells are factors that also affected diffusion (pressure gradient, and range of diffusion).

The Critical DO$_2$

Decreased aerobic metabolism (VO$_2$) following the critical DO$_2$ indicates that the production of energy substrates, adenosine triphosphate (ATP) will be reduced, resulting in cell dysfunction and cell death. The process of aerobic metabolism will be altered to anaerobic metabolism that produces lactate.[12]
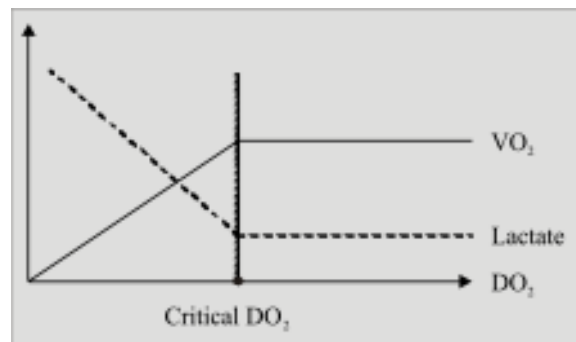
Figure 6. Graph showing analysis of changes that occur in critical oxygen delivery. Decreased DO$_2$ after critical point will be followed by the decreased VO$_2$ and increased lactate concentration

The graph on figure 6 shows that increased lactate concentration after the oxygen delivery has reached the critical point. Other parameters that appear after the critical DO$_2$ has been completed are decreased MAP, reduced HCO$_3$, lower production of CO, and smaller cardiac index.

Mechanism of Acute Compensation

At condition of oxygen deficiency, the body mechanism will maintain tissue oxygenation and normal organ function. In acute condition, the mechanisms involved are increased cardiac output and increased oxygen extraction from the tissue hemoglobin. Both mechanisms of acute compensation occur in critical patient; therefore, the patient becomes more susceptible to hypoxia. Another mechanism is an increased hemoglobin level (polycytemia) after several weeks. Polycytemia usually occurs in patients with chronic hypoxia condition, i.e. patients with chronic pulmonary disease, patients or those who live in high altitude.

Early physiological response to satisfy the increased oxygen demand is by increasing cardiac output in order to increase oxygen delivery. Such mechanism appears in patients with anemia, acute hypoxemia, and increased oxygen consumption in the tissues. A normal heart is

able to increase its cardiac output up to 15-25 L per minute.
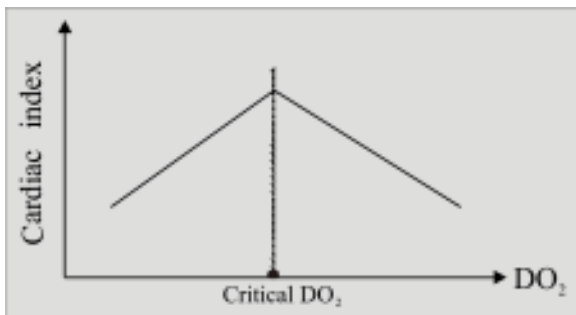
Figure 7. The graph showing analysis on altered cardiac output index that occurs in critical oxygen delivery. Saar DO2 has decreased before critical point, cardiac output raised as a compensation to maintain oxygen delivery. However, the cardiac output will decrease after passing the critical point.[12]

Increased of oxygen extraction from blood capillaries may occur in two conditions. First, in patients with increased metabolic rate (such as induced by exercise, fever, shivering, seizure), decreased PO_2 in tissues will increase the gradient of diffusion the tissues and capillaries; thus, oxygen extraction to the tissues will have more increase and become more rapid. Second, it may occur in patients with normal metabolic rate but decreased oxygen delivery due to reduced cardiac output, anemia, or hypoxemia. In both conditions, the tissues will still take up the oxygen on normal rate so that the oxygen extraction is relatively increasing.[2,3]

CLINICAL IMPLEMENTATION

Early Goal-directed Therapy

In terms of management for patients with critical illness, a protocol by River (2001) has been used as a guidance to maintain oxygen delivery, i.e. the Early Goal-Directed Therapy (EGDT).[14] The protocol has become the initial part of recommendation of the sepsis management guidelines, the Surviving Sepsis Campaign 2008.[15] The first part of protocol discusses about assuring the oxygen consumption to the respiration system by supplying oxygen and ventilator when necessary. The next step is about giving solution (crystalloid or colloid) until adequate central venous pressure (CVP) target of 8-12 mmHg has been reached. The following step is about administering vasopressor agents (dopamine or norepinephrine) with target mean arterial pressure (MAP) between 65-90 mmHg. The measurement is monitoring oxygen saturation of central veins, in this case the blood of edge vein of vena cava at the right atrium ($ScvO_2$) with the target of measurement

above 70%. If it appears low value and there is also hematocrite of less than 30%, then patient should be indicated to get transfusion. But provided that the hematocrite is higher than 30%, then administering dobutamine as an inotropic agents would become an option.
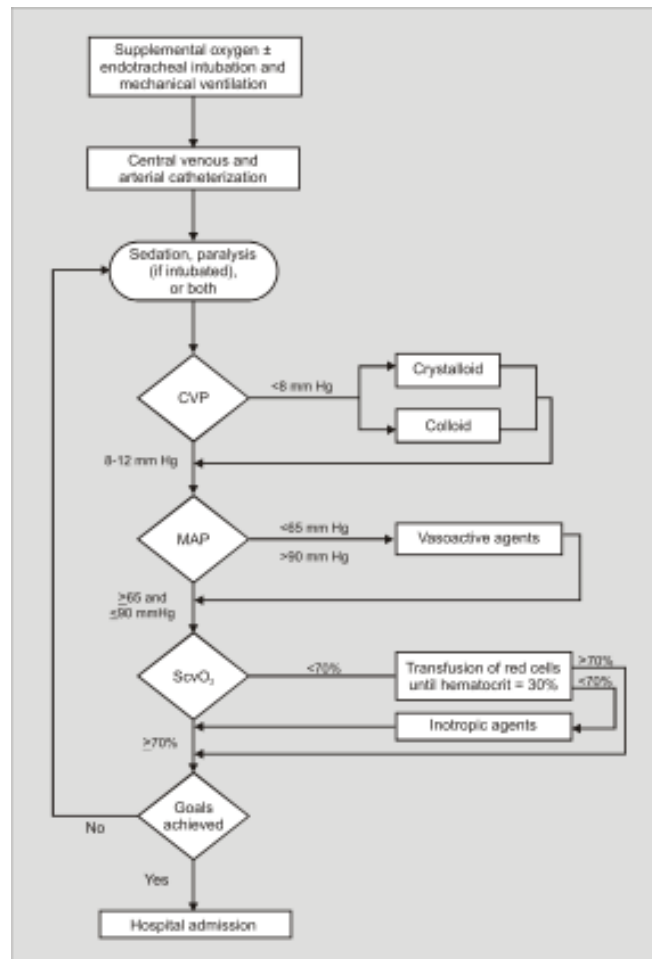
Figure 8. Protocol of early goal-directed therapy(EGDT) by Rivers et al. (2001)

In the protocol, we could see that the components of oxygen delivery, i.e. oxygen saturation, hemoglobin, and cardiac output, have been optimized. The oxygen saturation is assured by supplying oxygen and ventilator management when necessary. The adequate cardiac output has been maintained, either on the aspects of preload (target CVP 8-12 mmHg), afterload (target MAP 65-90 mmHg), and contractility (administering dobutamine when the hematocrit is less than 30%). The parameter used in this protocol to evaluate the effectiveness of oxygen delivery is the $ScvO_2$. $ScvO_2$ less than 70% indicated that oxygen delivery is getting down toward the critical DO_2.

Based on the equation of : $VO_2 = 13.4$ x CO x Hb x $(SaO_2–SvO_2)$, then the value of SvO2 depends on VO_2, cardiac output (CO), hemoglobin concentration (Hb), and oxygen saturation of arterial blood. If the SaO2 and Hb are normal, then the SvO2 can be used as a reference of adequate cardiac output to comply with metabolic needs. For example, there is low cardiac output (2 L/min/m²) but the SvO2 is normal (70%), then it can be said that the global oxygen delivery function is adequate enough. In contrast, when the cardiac output is high but the SvO2 is low (50%) then the global oxygen delivery function is inadequate.

However, in a certain condition, the abovementioned condition does not occur since the SvO2 does not measure the adequacy of tissue oxygenation. For example, the extensive vasodilatation in systemic inflammatory response syndrome (SIRS) may open the *arteriovenous cutaneus* shunt. Meanwhile, at the same time, the microcirculation is reduced. In this condition, the arterial blood that rich of oxygen will pass through the tissues and it will not be taken up by the tissues. In this case, the examination of SvO2 may reveal normal or increasing result in spite of severe hypoxemia in the body.

Based on this study, the trigger transfusion to maintain tissue perfusion is the low SvO2 and hematocrit level less than 30% after target CVP and MAP have been reached.[14] It is different from the study by Herbert (1999) which compared the strategy of restricted transfusion (triggered transfusion was given when Hb level was less than 7 g/dL and it was maintained at 7-9 g/dL) with the strategy of liberal transfusion strategy (triggered transfusion was given when Hb level was less than 10 g/dL and it was maintained at 10-12 g/dL).[16]

In that study, the restricted strategy may decrease mortality when compared to the liberal strategy, except for myocardium infarct and unstable angina.[16] A study by River (2001) demonstrated the trigger transfusion with hematocrit level less than 30% and the SvO2 less than 70% which indicated that there is decreased oxygen delivery due to reduced hemoglobin level.[14] By enhancing the treatment with packed red cell and targeting hematocrite level more than 30%, then the oxygen delivery will be adequate. If the SvO2 remained low then the oxygen delivery is enhanced through increased cardiac output by administering inotropic agents.
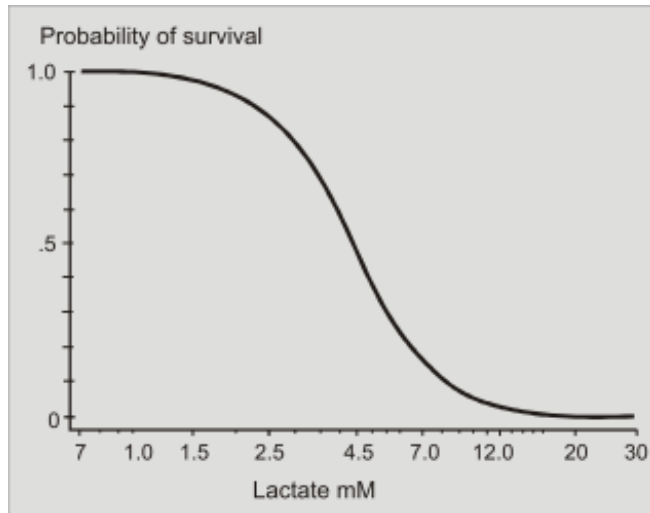
Lactate

The Institute for Health Care Improvement has published the Sepsis Bundle, i.e. a group of intervention on patients with sepsis that when managed simultaneously, it will have good result compared to separate management. The sepsis bundle consists of two parts, which are the Sepsis Resuscitation Bundle and Sepsis Management Bundle.[17] The Sepsis Resuscitation Bundle consists of :

1. Serum Lactate Measured
2. Blood Cultures Obtained Prior to Antibiotic Administration
3. Improve Time to Broad-Spectrum Antibiotics
4. Treat Hypotension and/or Elevated Lactate with Fluids
5. Apply Vasopressors agents for Ongoing Hypotension
6. Maintain Adequate Central Venous Pressure
7. Maintain Adequate Central Venous Oxygen Saturation

Table 4. Mechanism of lactate acidosis[20]

Type	Mechanism	Etiology
Type A: hypoxic	Global ischemia	Shock Severe anemia Severe hypoxemia
	Focal Ischemia	Mesenteric Infarct Ischemia of extremities
Type B : non-hypoxic	Reduced lactate clearance	Liver failure or renal failure
	Dysfunction of Piruvate dehydrogenase	Sepsis, high catecholamine level, thiamine deficiency
	Uncoupling of oxidative phsophosphorylation	Protein degradation, severe catabolism
	Glycolysis acceleration	Sepsis, seizure, malignancy, parenteral nutrition
	Lactate administration	Replacement Solution containing lactate

Figure 9. Probability of survival compared to lactate level in the arterial blood when the patient was admitted to intensive care unit. The higher lactate level, the lower its survival probability, and vise versa.[18]

It is obvious that the lactate examination has become inseparable from management of sepsis. Increased lactate is induced by anaerobic metabolism due to hypoperfusion in the tissue or in other word, due to decreased oxygen delivery. The level of lactate has been used as a parameter for the patient's prognosis.[18]

A study by Nguyen et al.(2004) found that decreased lactate on the initial examination at early admission to intensive care unit, may become a marker of resolute global tissue hypoxia and it was related to decreased mortality rate. Patients with large decrease of lactate level ($\geq$10%) following 6 hours of intervention at the emergency unit will get better compared to patients with smaller decrease of lactate level (< 10%).[19]
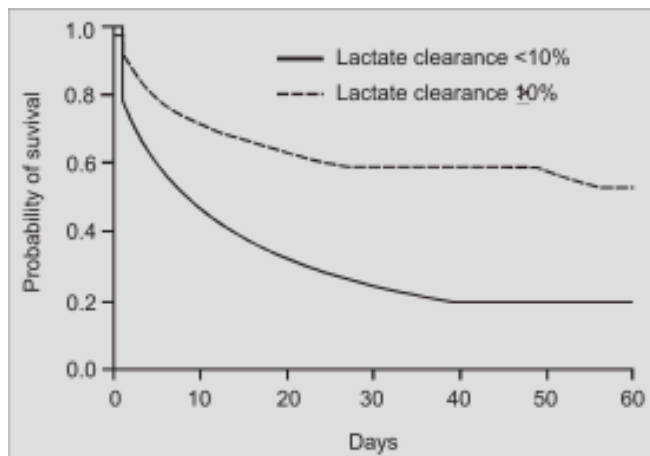

Figure 10. The graph showing analysis on Kaplan-Meier survival between patients with the lactate clearance <10% vs $\geq$10% following 6 hours at the emergency unit[19]

However, the lactate evaluation should be performed in serial examination and combined with other parameters because lactate can also be elevated in patients with sepsis, although there is no hypoperfusion. In addition, disturbed lactate degradation in the liver of patients with sepsis may also increase the lactate blood level.[20]

Algorithm of Physiological Approach on The Critical DO$_2$

Based on the data of oxygen delivery, shock or inadequate tissue oxygenation may be classified into: quantitative shock (decreasing DO$_2$) and distributive shock (decreasing O$_2$ER). The quantitative shock may be caused by reduced flow (hypovolemic shock and hemorrhagic shock) and decreased total oxygen level in the arterial blood or CaO$_2$ (hemorrhagic shock, acute respiratory failure, and intoxication).[21]
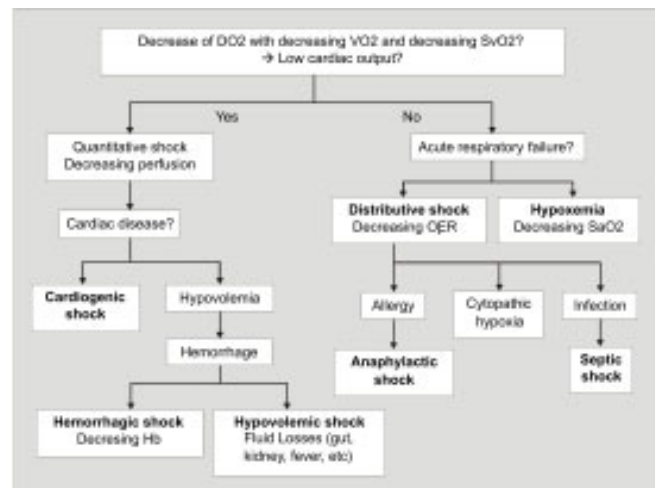
Figure 11. Algorithm of Physiological Approach on the Critical DO[21]

Reduced flow may be caused by reduced volume in the circulation system (absolute or relative hypovolemia) or by pumping failure of the heart. The hypovolemia is defined as 'absolute' when it is resulted from water loss, plasma or blood loss, and it can turn into 'relative' state if the provided solution is not sufficient enough to compensate the decreasing vascular tones, such as in sepsis condition, anaphylactic, or high-dose sedation. Hence, there is imbalance between the volume and vascular capacity. Heart failure may be caused by myocardium damage (induced by infection, virus, or ischemia), resistance of ventricular ejection fraction (increased afterload of the right ventricle, increased resistance of pulmonary vascular, increased afterload of left ventricles, increased resistance of systemic blood

Table 5. Acute clinical conditions in oxygen delivery disorder

Oxygen delivery components	Affecting factors	Examples of clinical conditions
Oxygen saturation in arterial blood	pO_2 Dissociation curve: • pCO_2 • pH • 2,3 DPG • Temperature V/Q mismatch	Acute respiratory distress syndrome Severe acute asthma, COPD exacerbation Acidosis / alkalosis Blood transfusion (banked blood) Fever / hypothermia Pulmonary Atelectasis
Hemoglobin concentration	Production Elimination Loss	Aplastic Anemia hemolytic Anemia Bleeding
Cardiac output	Stroke volume • Preload • Contractility • Afterload Heart Rate • Frequency • Regularity	 Hypovolemic shock, cardiac tamponade Cardiogenic shock Septic shock, anaphylactic, neurogenic shock Bradycardia, tachycardia Atrial fibrillation

vessels) and disturbance in ventricular loading (decreased preload of the right or left ventricle), valve dysfunction, reduced loading time due to tachycardia).

Reduced total oxygen blood level is probably caused by reduced hemoglobin (Hb) level and decreased oxygen level (SaO_2). The decreased Hb is not always associated with hypovolemia (hemodilution may decrease the DO_2). In hypovolemia due to acute bleeding, decreased DO_2 is more likely caused by reduced flow. The Hb capacity to carry oxygen is also decreased in mono-oxyde intoxication caused by competitive binding between CO and O_2 on hemoglobin. In acute respiratory failure, reduced SaO2 will decrease CaO2 and DO2 soon after the cardiac output is not able to compensate it.

The distributive shock may occur due to altered redistribution flow in the organ or tissues (induced by inflammation, anaphylaxis, overdose of sedatives), decreased capillary recruitment induced by vascular reactivity changes, increased intravascular coagulation, enhanced adhesion of red blood cells and, endothelial edema, and abnormal mitochondria function (mitochondria dysfunction or cytopatic hypoxia).

CONCLUSION

A patient will experience critical condition when there is a threat or disturbance in oxygen delivery. In simple terms, the patient's clinical conditions which affect the oxygen delivery is described on the following equation: DO2 = SaO2 x Hb x CO, i.e. oxygen saturation in arterial blood, hemoglobin concentration, and cardiac output. A comprehension on the occurring physiological changes will simplify the diagnosis and treatment of patients with critical illness

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