

Commentary

The International Sepsis Forum's frontiers in sepsis: high cardiac output should be maintained in severe sepsis

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Abstract

Despite a usually normal or high cardiac output, severe sepsis is associated with inadequate tissue oxygenation, leading to organ failure and death. Some authors have suggested that raising cardiac output and oxygen delivery to predetermined supranormal values may be associated with improved survival. While this may be of benefit in certain patients, bringing all patients to similar, supranormal values, is simplistic. It is much preferable to titrate therapy according to the needs of each individual patient. A combination of variables should be used for this purpose, in addition to a careful clinical evaluation, including not only cardiac output but also the mixed venous oxygen saturation and the blood lactate concentrations. The concept is to assess the adequacy of the cardiac output in patients with severe sepsis, enabling management strategies aimed at optimizing cardiac output to be tailored to the individual patient.

Keywords mixed venous oxygen, oxygen delivery, oxygen uptake, saturation

Introduction

Sepsis is associated with systemic, mediator-induced alterations in oxygen utilization, including increased oxygen demand, altered oxygen extraction, and decreased myocardial contractility (Fig. 1). Hence, despite a normal or high cardiac output, severe sepsis and septic shock are characterized by an inadequate organ oxygenation, leading ultimately to multiple organ failure and death. Almost 20 years ago, Abraham and colleagues [1] noted that survivors from septic shock had significantly higher cardiac indexes prior to the shock episode than did nonsurvivors, leading to the suggestion that pushing patients to reach high and even 'supranormal' levels of cardiac output could be beneficial. This early hypothesis has fueled an ongoing debate regarding the potential benefit or harm of this strategy in the patient with septic shock.

The 'supranormal' studies

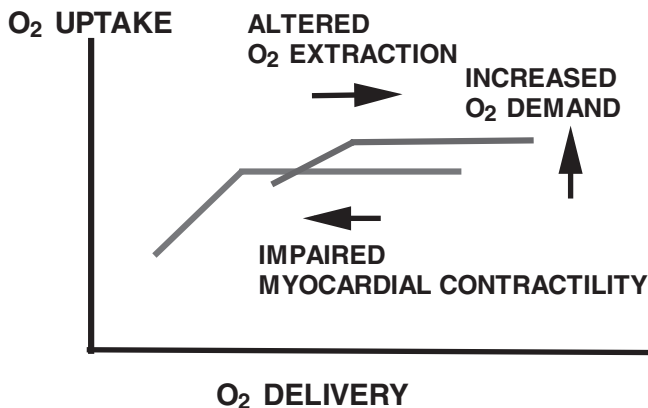
Several groups have indicated increased survival in various groups of patients treated with a strategy to increase cardiac output or oxygen delivery (DO_2) to so-called 'supranormal' values (cardiac index ≥ 4.5 l/min per m^2 , $DO_2 < 600$ ml/min

per m^2 and oxygen consumption [VO_2] > 170 ml/min per m^2) [2–9]. However, two notable studies conducted in mixed groups of critically ill patients by Hayes and coworkers [10] and Gattinoni and coworkers [11] showed that supranormal DO_2 values do not result in improved outcomes. A possible explanation for those findings is that, unlike many of the other studies in this field, the heterogeneity of the critically ill patients included in the studies influenced the results. Thus, although some individuals might well have benefited from the trial strategy, these positive results may have been negated by harmful effects in other patients who perhaps had already been adequately resuscitated and therefore received excessive doses of vasopressor agents or fluids. There is little doubt that, in certain patients, achieving and maintaining high levels of cardiac output is associated with improved outcomes; the difficulty lies in identifying those patients.

Should we maintain adequate cardiac output in all patients with septic shock?

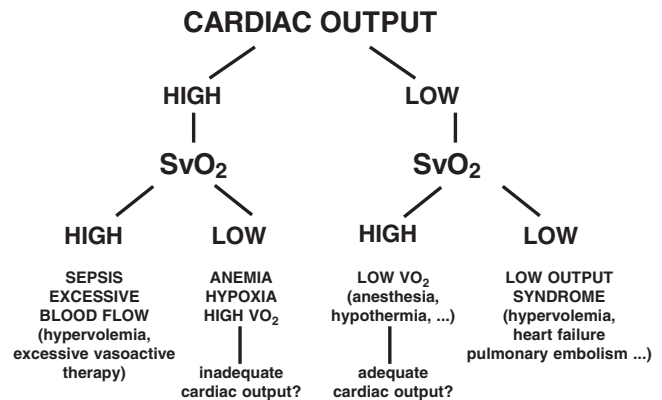
The available studies suggest that rather than protocolize all patients to increased cardiac output and DO_2 , this strategy should be tailored to the individual patient. Hayes and

Figure 1



Influence of sepsis mediators on the relationship between oxygen uptake and delivery.

Figure 2



Interpretation of cardiac output according to mixed venous oxygen saturation (SvO₂) values. VO₂, oxygen consumption.

coworkers [6] suggested that survivors from septic shock are characterized by an ability to increase DO₂ and VO₂, whereas nonsurvivors do not have sufficient physiologic reserve to do this, and in such patients excessive doses of vasopressors or fluids worsen an already bad situation. Rather than making attempts to target cardiac output and DO₂ randomly in all patients, our approach should rather be to try to restore hemodynamic stability, which will necessitate different approaches in different patients. Indeed, no one would dispute the need for clinical interventions to enhance DO₂ and support the circulation where tissue perfusion is clearly inadequate. The problem lies in identifying those patients in whom tissue hypoxia is less overt, who may in fact have 'normal' hemodynamic parameters, and augmenting DO₂ in such patients may necessitate reaching 'supranormal' values.

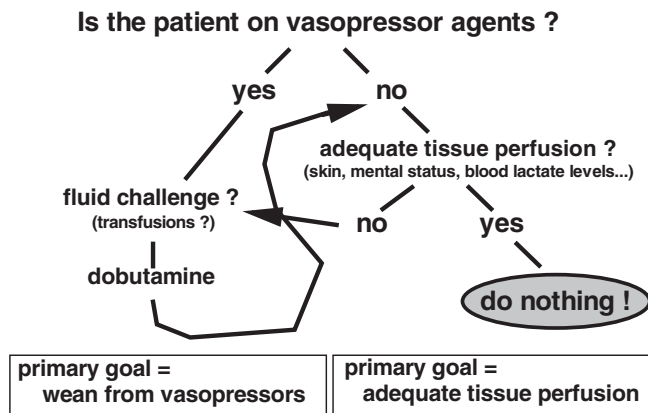
So, how can we determine which patients require what therapy? Perhaps the mixed venous oxygen saturation (SvO₂) is the most important parameter to follow. SvO₂ provides an indication of the degree of oxygen extracted by the organs before the blood returns to the right heart and hence gives a measure of the balance between DO₂ and VO₂, thus providing an indication of the ability of the cardiac output to meet the individual's oxygenation needs. Admittedly, SvO₂ is a global parameter and gives no specific regional information, but neither does cardiac output; in fact, it may be interesting to combine SvO₂ and cardiac output (Fig. 2). Indeed, this is one of the problems with the less invasive methods of measuring cardiac output; we are all agreed that 'less invasive' is the way to go, but how does one interpret cardiac output values without knowledge of the SvO₂? Some may say that SvO₂ monitoring is useless in sepsis or septic shock because, in sepsis, SvO₂ may be normal or high despite regional tissue hypoxia, because of altered tissue oxygen extraction. However, clinical evidence shows that SvO₂ does

fluctuate in patients with sepsis or septic shock [12], and there are two major arguments in support of the value of SvO₂ monitoring in sepsis. First, Ronco and coworkers [13] noted that patients who are about to die may still have high oxygen extraction capabilities. Hence, in septic shock, a high or normal SvO₂ does not necessarily mean that oxygen extraction cannot increase further. Second, Rivers and coworkers [14] showed, in a patient population treated in an emergency department, that the initial central venous oxygen saturation (measured as a substitute for SvO₂) was only $48.6 \pm 11.2\%$. Hence, it is only after initial resuscitation that central venous oxygen saturation (or SvO₂) may reach normal (or supranormal) values. Conversely, it may decrease again if there is hypovolemia or myocardial depression.

Importantly, it is not necessary to calculate DO₂. Moreover, the relationship between VO₂ and DO₂ is subject to mathematical coupling of data. In complex cases, the relation between cardiac index and oxygen extraction ratio may be helpful, especially in anemia [15,16]. Finally, blood lactate levels may help to identify the patient who requires a higher cardiac output because survivors from septic shock have significantly lower initial blood lactate levels and their blood lactate levels are raised for shorter periods of time [17].

Another important feature may be the timing of optimization. In the early studies conducted by Shoemaker and coworkers [2] that showed improved outcome in surgical patients, optimization was commenced before the surgical procedure. Rivers and coworkers [14] recently showed the beneficial effects of early goal-directed therapy, within 6 hours of diagnosis of septic shock, over standard therapy. The methods for increasing cardiac output or DO₂ (e.g. fluids, inotropes, and blood transfusions) may also impact on results.

Figure 3



Schematic showing the combination of variables involved in the assessment of the patient with septic shock.

Conclusion

More important than achieving supranormal DO_2 and, hence, oxygen consumption in those patients who may benefit from this strategy is achieving optimal hemodynamic status in all patients (Fig. 3). If augmentation of DO_2 is associated with a reduction in serum lactate levels and improved target organ perfusion, then these interventions may be continued. Each patient must be assessed according to their clinical (urine output, skin perfusion, mental status), hemodynamic (arterial pressure, cardiac output), and oxygenation (Svo_2 , blood lactate) parameters. Practising good medicine is never simple, and applying protocols to reach supranormal DO_2 in all patients is naïve. The challenge is to identify which approach is needed in which patient so that all patients receive optimal care.

Competing interests

None declared.

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