Optimizing the Delivery of Ultrafiltration in Critically Ill Patients

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ABSTRACT

Extracorporeal ultrafiltration (UF) has been proposed to treat fluid overload in patients who do not respond to diuretic therapy. However, because rapid UF may induce a decrease in intravascular volume, it is susceptible to create hemodynamic instability. To prevent this potential side effect, the impact of UF on plasma volume and hemodynamics should be carefully monitored and UF rates should be individualized. When the UF rate exceeds the plasma refill rate, UF may induce a decrease in plasma volume that can be detected by a rise in hematocrit (Hct). When UF is responsible for a decrease in plasma volume, cardiac filing (or preload) decreases, and it may be responsible for a decrease in stroke volume (SV), cardiac output (CO) and ultimately in blood pressure. In this respect, continuous monitoring of SV and CO may be useful for the early detection of UF-induced hemodynamic instability. However, a limited number of patients undergoing UF are equipped with a CO monitor. An alternative to CO monitoring is venous oxygen saturation (SvO_2) monitoring. A UF-induced decrease in SvO_2 strongly suggests a concomitant decrease in CO. Therefore, we propose a rational approach for safe and effective UF based on the simultaneous monitoring of Hct and SvO_2.

The burden of fluid overload

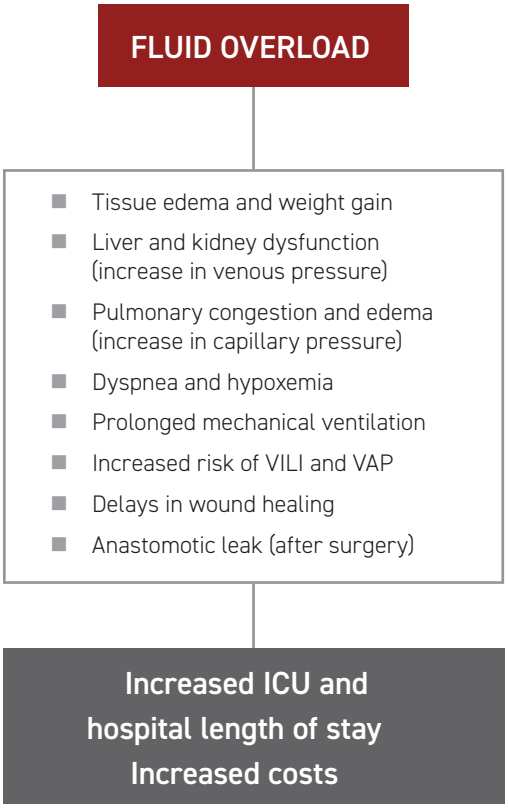
Fluid overload remains the primary issue for patients with chronic heart failure (CHF)[1]. It is responsible for weight gain and tissue edema, and sometimes for dyspnea (orthopnea) in case of pulmonary congestion. This is a common cause for hospital admission and readmission in patients with CHF, with a dramatic economic impact.

As a result of aggressive fluid resuscitation and increased capillary permeability, fluid overload and tissue edema are also frequently observed in high-risk surgical patients, as well as during sepsis and septic shock. In surgical patients, tissue edema may hamper wound healing[2].

Both in surgical and septic patients, pulmonary edema may prolong the duration of mechanical ventilation and increase the risk of ventilator-induced lung injury (VILI) and ventilator-associated pneumonia (VAP).

The main clinical consequences of fluid overload and tissue edema are summarized in **figure 1**.

Figure 1. The clinical consequences of fluid overload and tissue edema.



VILI = ventilator-induced lung injury, VAP = ventilator-associated pneumonia

Extracorporeal ultrafiltration

Extracorporeal ultrafiltration (UF) has been proposed to treat fluid overload in patients who do not respond to diuretic therapy[3]. This method does not induce electrolyte changes (e.g. hyponatremia and hypokalemia) and enables the precise control of fluid loss[4]. In patients with CHF, UF has potential to improve outcomes and decrease hospital readmissions and costs[5].

However, because rapid UF may induce a decrease in intravascular volume, it is susceptible to create hemodynamic instability[6] [7]. To prevent this potential side effect, the impact of UF on plasma volume and hemodynamics should be carefully monitored and UF rates should be individualized[8] [9].

Hematocrit (or plasma volume) monitoring during ultrafiltration

When the UF rate exceeds the plasma refill rate, UF may induce a decrease in plasma volume[6]. When starting UF, the plasma refill rate may vary from one patient to the other. Maybe more importantly, because of the UF-induced decrease in hydrostatic pressure gradients between the extravascular and the intravascular space, plasma refill rate progressively decreases in any given patient. In other words, if UF does not always induce a significant decrease in plasma volume when initiating the treatment, it may do so after a few hours or a few days. Unfortunately, it remains technically challenging to continuously monitor plasma volume at the bedside[10].

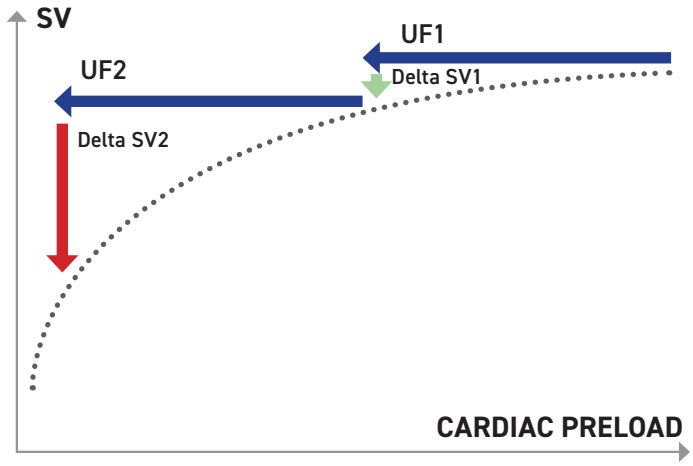
Therefore, it has been proposed to use hematocrit (Hct) as a surrogate[11]. Indeed, any decrease in plasma volume is associated with a concomitant increase in Hct (aka hemoconcentration). Monitoring venous Hct on the UF extracorporeal circuit is now technically possible. Ensuring hematocrit does not change significantly during UF is a simple way to ensure that UF does not induce any significant changes in plasma volume[12] [13].

SvO_2 (or cardiac output) monitoring during ultrafiltration

When the UF rate exceeds the plasma refill rate, UF is responsible for a decrease in plasma volume and in cardiac filling (or preload) that may ultimately be responsible for a decrease in stroke volume (SV), cardiac output (CO) and blood pressure.

The impact of any decrease in cardiac preload on SV depends on the position on the Frank-Starling curve[14]. If the heart is operating on the flat part of the curve – which is usually the case when initiating fluid depletion in CHF patients - a decrease in preload will not induce any significant decrease in SV. As a result, UF will be well tolerated from a hemodynamic standpoint. In contrast, as soon as the steep portion of the curve is reached, any further decrease in preload will induce a significant decrease in SV **(figure 2)**.

Figure 2. Franck-Starling (curvilinear) relationship between cardiac preload and stroke volume (SV).



Because of fluid overload, most CHF patients operate on the plateau of the curve. Decreasing preload with ultrafiltration (UF) has no significant impact on SV (DeltaSV1 during UF1). At some point, patients may reach the steep portion of the curve. Then, their SV becomes dependent on cardiac preload and additional UF (UF2) would induce hemodynamic instability.

The impact of any decrease in SV on CO depends on simultaneous changes in heart rate (HR). When SV decreases, HR may theoretically increase to maintain CO (CO = HR x SV). However, in patients with CHF, the heart rate reserve is often limited, either because they are already tachycardic at baseline, or because they receive medications to prevent tachycardia (e.g. beta-blockers). As a result, any decrease in SV is usually associated with a decrease in CO.

Mean arterial pressure (MAP) depends on CO and systemic vascular resistance (SVR). MAP is a regulated physiologic variable. Facing a decrease in CO, vascular tone (or SVR) will increase to maintain MAP. As a result, a decrease in MAP is only observed at a late stage, when the SVR increase is not sufficient to compensate for the UF-induced decrease in CO.

Continuous monitoring of CO may therefore be very useful for the early detection of UF-induced hemodynamic instability[15]. However, a limited number of patients undergoing UF are equipped with a CO monitor. An alternative to CO monitoring is venous oxygen saturation (SvO_2) monitoring.

Arterial oxygen saturation (SaO_2), hemoglobin (Hb), oxygen consumption (VO_2), and CO are the four main physiologic determinants of SvO_2 [16]. Assuming that SaO_2, Hb and VO_2 are constant, any decrease in SvO_2 indicates a decrease in CO.

SvO_2 values depend on the site of measurement. In patients undergoing UF, SvO_2 is usually measured in a central vein or in the basilic or brachial vein. Absolute values are different from measurements in the pulmonary artery (mixed venous oxygen saturation), but changes in SvO_2 remain correlated with changes in CO.

Of note, the relationship between CO and SvO_2 is not linear. When SvO_2 is low (typically in CHF patients), changes in CO induce significant changes in SvO_2 and it makes sense to track changes in SvO_2 to detect changes in CO. In contrast, when SvO_2 is high (typically in septic shock where peripheral oxygen extraction is impaired), changes in CO are responsible for small changes in SvO_2. Therefore, in this context, it is recommended to directly monitor SV and CO to ensure a timely detection of hemodynamic deterioration.

During UF, assuming the patient is resting in bed or in the sitting position, VO_2 should remain constant. However, UF may induce hemoconcentration, as well as an increase in SaO_2 in hypoxemic patients with pulmonary congestion. Therefore, if a stable SvO_2 does not always mean that CO is stable as well, a UF-induced decrease in SvO_2 strongly suggests a concomitant decrease in CO[17].

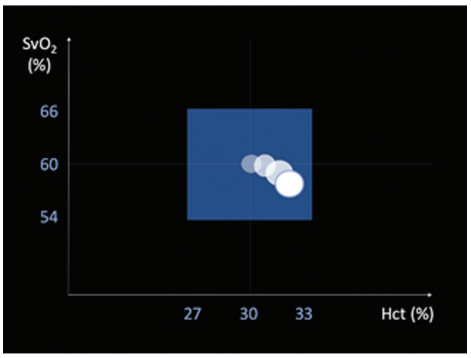
Several clinical conditions are responsible for an increase in VO_2 that would induce a decrease in SvO_2, despite hemodynamic stability. They include agitation, ambulation, fever, and the initiation, interruption or modification of a treatment by catecholamines (e.g. dobutamine infusion in patients with right or left ventricular systolic dysfunction). In these clinical situations, it is not recommended to use SvO_2 monitoring as a surrogate for CO monitoring.

Practical considerations

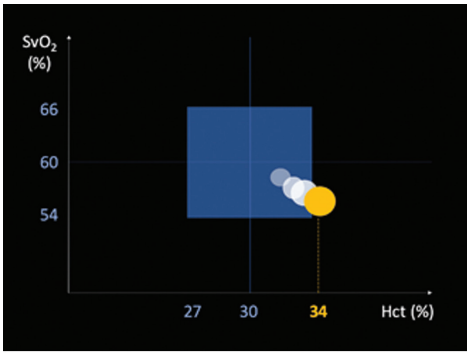
In practice, it is not recommended to start UF in patients with a low MAP or clinical and biological signs of circulatory shock (e.g. mottling, increase in blood lactates or serum creatinine).

In hemodynamically stable patients, it may be useful to define target ranges both for Hct and SvO_2, on the basis of values recorded at the beginning of the UF session. For example, a 10% variation from baseline may be tolerated, defining safety limits, as illustrated in **figure 3**.

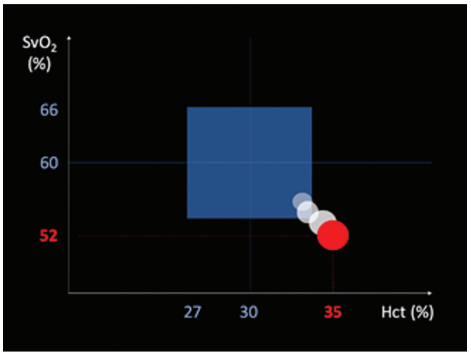
Figure 3. Examples of target screens.



The blue zone or target zone is defined using baseline hematocrit (Hct) and venous oxygen saturation (SvO_2) ±10%



A significant rise in Hct (>10% relative increase) indicates a significant decrease in plasma volume.

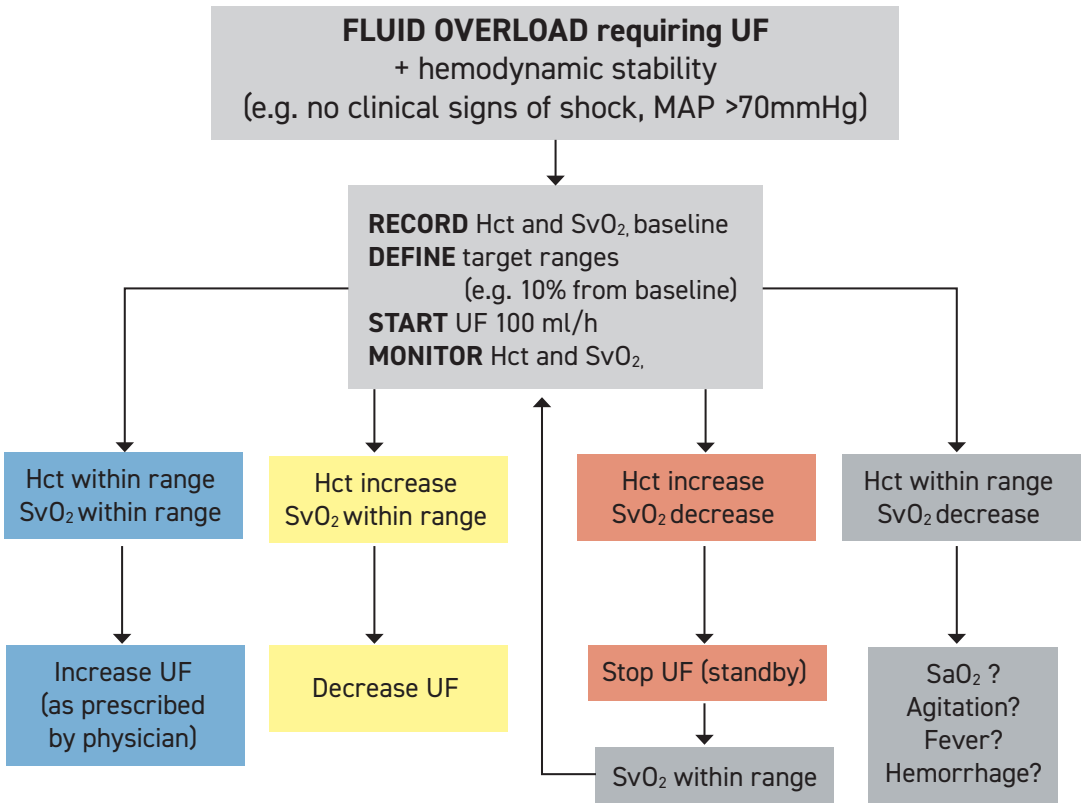


A significant decrease in SvO_2 (>10% relative decrease) suggests a significant decrease in cardiac output.

Conclusion

Ensuring Hct and SvO_2 remain within the target range is a mean to ensure UF does not induce significant changes in blood volume and cardiac output, respectively. In the event that Hct increases beyond the predefined target range, it may be wise to decrease UF in order to prevent hemodynamic deterioration (i.e. a decrease in CO). In the event that Hct increases and SvO_2 decreases beyond their predefined target ranges, it may be wise to stop UF until SvO_2 is back within the target range. In summary, the combination of Hct and SvO_2 monitoring may provide a safe and effective approach to treating critically ill patients with extracorporeal UF **(figure 4)**.

Figure 4. A rational approach to optimal ultrafiltration



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