Perspective

Veno-arterial extracorporeal membrane oxygenation (VA ECMO) in postcardiotomy cardiogenic shock: how much pump flow is enough?

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Abstract: Post-cardiotomy cardiogenic shock (PCCS) is a complication of heart surgery associated with a poor prognosis: veno-arterial extracorporeal membrane oxygenation (VA ECMO) ensures end-organ perfusion while fully replacing heart and lung function, though it is associated with unsatisfactory results. Few studies have identified reliable predictors of poor prognosis early in the course of extracorporeal support. A recent study showed the strong prognostic power of urine output in the first 24 hours of VA ECMO in predicting early and late mortality of PCCS. Urine output is a commonly collected parameter in all intensive care units (ICU) and has a defined role in the diagnosis of acute kidney injury (AKI) and is inexpensive. These findings offer the possibility to summarize some aspects regarding the adequacy of extracorporeal support early in the course of cardiogenic shock and to shed light about cardio-renal interactions in ECMO patients. Finally, it is our opinion that a timely implantation of mechanical circulatory support in post cardiotomy shock should be considered if systemic perfusion is not ensured by low or medium dose inotropic support and intra-aortic balloon counterpulsation.

Keywords: Extracorporeal membrane oxygenation (ECMO); cardiac surgery; cardiogenic shock; multiple organ failure

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Post-cardiotomy cardiogenic shock (PCCS) is a complication of heart surgery with an incidence of 0.5–6%, associated with a poor prognosis and mortality rates exceeding 60%, without a significant reduction in the last decade, notwithstanding undeniable technical progresses in mechanical circulatory support (MCS) (1).

Veno-arterial extracorporeal membrane oxygenation (VA ECMO) aims to fully replace heart and lung function, ensuring end-organ perfusion and allowing time for possible heart recovery.

When recovery of heart function does not take place, VA ECMO may bridge patients to durable left ventricular assist device (LVAD)/total artificial heart (TAH) or heart transplantation.

The recent study by Distelmaier *et al.* (2) analysed a cohort of 205 patients requiring VA ECMO for cardiogenic shock following cardiovascular surgery, with the aim to evaluate the predictive value of urinary output (UO) in the first 24 hours after extracorporeal support initiation.

Mortality rate of patients was 64% during a median follow-up of 35 months.

They reported that the UO in the first 24-hour after VA ECMO support for PCCS is a strong predictor of early and late mortality.

Furthermore, the addition of 24-hour UO to the widely used intensive care units (ICU) scores such as the Simplified Acute Physiology Score-3 (SAPS-3) and Sequential Organ Function Assessment (SOFA) score increased their

discriminatory power.

The first question arising from the results of this study is: which parameters have to be considered to evaluate that the level of extracorporeal support in patients on VA ECMO is adequate?

In other words, how much pump flow is enough?

The regulation of ECMO flow is an awkward process in which the need to ensure an adequate end-organ perfusion, especially during the first phase of resuscitation and stabilization, could conflict with the inherent risks of increased left ventricular afterload (3): indeed, the attempt to maximise end-organ perfusion during the immediate post implantation phase with high VA ECMO flows is not without risk.

On an haemodynamic base, the inadequate drainage of the right heart by the inflow cannula, the bronchial circulation and the increased afterload caused by the flow from the outflow cannula in the aorta may cause serious consequences on LV performance (4,5); this is particularly true when the native cardiac function is completely abolished. The need to LV venting may be unavoidable if overt pulmonary oedema overcomes. As a matter of fact, LV distension, by increasing myocardial oxygen consumption (VO_2), reduces the possibility of recovery (5). An experimental study on a porcine model of cardiogenic shock showed a marked decrease in haemodynamic indexes of LV performances at high ECMO flow (6), whereas, in humans, Aissaoui *et al.* demonstrated that LV ejection fraction (LVEF) and aortic velocity-time integral (VTI) are reduced at the highest VA ECMO flow (7).

Scarce data are available on the specific question of ECMO flow setting. Extracorporeal Life Support Organization (ELSO) guidelines (8) report that VA ECMO flow for cardiac support should be set at 60 mL/kg/min, with a value corresponding on average to the normal calculated cardiac output of the patient.

One can suggest that this issue may be faced by regulating the ECMO flow on the basis of haemodynamic stabilisation and the reduction of signs of hypoperfusion. This approach is not straightforward.

Arterial blood gases, lactates, mixed venous oxygen saturation (SvO_2) are all used to monitor the systemic perfusion in VA ECMO patients (9). Some of these parameters have demonstrated a prognostic value, but not a single system of monitoring is per se sufficient to rule out a state of systemic hypoperfusion during extracorporeal support.

During VA ECMO, monitoring of SvO_2 is a more reliable marker of whole balance between oxygen delivery (DO_2) and VO_2 than during veno-venous (VV) ECMO, but a true SvO_2 through pulmonary artery catheter (PAC) cannot be measured, as the venous return is split between the native and ECMO circulation (10).

Furthermore, several studies in shock patients have questioned the concept that a normal (>65%) SvO_2 rules out the presence of hypoperfusion (11).

Lactates have a recognized prognostic role in adult cardiac surgical patients (12): a study on PCCS patients supported with VA ECMO showed that early lactates dynamics is strongly associated with mortality (13). However, recent studies raised doubts about the absolute values of lactates as an index of anaerobic metabolism in shock patients (14), above all when hepatic hypoperfusion is possible, as during shock or on-pump cardiac surgery (15).

Adding an easy, inexpensive, widely diffuse parameter—the UO—could be useful to integrate the above-cited methods.

The study of Distelmaier *et al.* (2) offers the opportunity to spend some considerations about cardio-renal interactions in ECMO patients.

Interpreting urine output in critically ill patients is a complex issue, as it results from many interacting factors (16).

The lack of diuresis recovery after ECMO implantation and haemodynamic stabilization represents a clinical dilemma, because it is of paramount importance to clarify if this situation is secondary to ongoing kidney hypoperfusion due to inadequate extracorporeal support, acute oliguric renal failure or a physiological antidiuretic and antinatriuretic adaptation to the reduction of effective blood volume.

Cardiogenic shock is a leading cause in determining type-1 cardio-renal syndrome (CRS-1), which can be defined as the development of acute kidney injury (AKI) as a consequence of an acute heart disorder, such as PCCS (17).

The prognostic effect of AKI in ECMO patients is remarkable, with a 4-fold increase in mortality (18) and a very poor prognosis when renal replacement therapy (RRT) is required (19).

Oliguria after 24–48 hours after ECMO weaning has been recognized as an independent predictors of mortality (20) and the subsequent need of use of loop diuretics to treat fluid overload is associated with worsening of renal function in CRS-1 (21).

In patients on VA ECMO, many factors contribute to the development of AKI, and the final result is determined by the complex interaction between factor promoting

renal protection—the increased renal perfusion through the extracorporeal support—and factors potentially causing renal function impairment (22). In particular, the continuous flow generated by ECMO has been associated in animal models to an unfavourable distribution of renal regional perfusion compared to pulsatile flow devices (23). Hormonal changes, ECMO-induced systemic inflammation, ischemia-reperfusion injury and acute left ventricular distension as a consequence of high ECMO flow and concomitant profound cardiac depression, are all factors potentially implicated in renal impairment during VA ECMO (22).

Acute Kidney Injury Network (AKIN) (24) and RIFLE criteria (25) include the reduction of UO and the increase in serum creatinine in AKI definition. Oliguria is an early marker of renal failure, but requires a careful evaluation because, during shock states, mechanisms other than renal failure may sustain a decrease in UO, representing a physiologic renal adaptation to restore blood volume or maintain electrolyte homeostasis (16).

Furthermore, oliguria in the early postoperative phase of cardiac surgery is a common finding that not necessarily implies a functional renal impairment.

However, a recent study (26) has evaluated the role of oliguria in diagnosis of AKI in an unselected cohort of ICU patients. Interestingly, the diagnosis of AKI on the basis of isolated oliguria is associated with similar outcomes compared to that diagnosed on the basis of serum creatinine alone. Fluid overload, frequently associated with oliguria, might explain the negative effect on survival and even influence the underestimation of serum creatinine (27).

In clinical practice, it is commonly encountered that patients on VA ECMO, after resolution of cardiogenic shock and haemodynamic stabilisation, experience an oliguric phase lasting 24–48 hours (28), without subsequent evidence of renal failure.

This transient phase of oliguria may result from reduction of effective blood volume secondary to capillary leakage induced by ECMO-related systemic inflammation.

In addition, we can speculate that hormonal mechanisms contribute to oliguria during VA ECMO, as it is associated to contrasting findings in modification of plasma renin activity, whereas several studies showed a reduction of atrial natriuretic peptide levels as a consequence of decreased right atrial distension (28).

Considering all patient population, Distelmaier *et al.* reported a very positive 24-hour fluid balance (FB) of 4,971 mL (IQR, 3,709–7,100 mL), without significant differences for tertiles of UO, together with also elevated central venous pressure (CVP) values (median, 14 mmHg; IQR, 12–18 mmHg) (2).

We agree with the authors that such values may be expression of fluid overload. The relationship between high CVP and renal haemodynamics is well described (29).

A study enrolling cardiovascular patients undergoing right-heart catheterization showed an inverse relationship between CVP values above 6 mmHg and estimated GFR (30): in these patients, no further improvement of cardiac output was observed in response to higher CVP, as higher CVP levels decrease renal perfusion pressure, which will further impair glomerular filtration rate and therefore reduce urine output. Fluid overload may also lead to central venous congestion and decrease of renal perfusion pressure (30), which will promote the development of AKI.

Positive FB is commonly encountered in ECMO patients. The dependence of centrifugal pumps from preload makes sometimes unavoidable, especially in the first 48 hours, the administration of large volumes of intravenous fluid to obtain a stable adequate flow (31).

However, this approach is not without consequences, because an early (from day 3 to day 5) positive FB has been associated with worse 90-day outcomes in a recent retrospective study enrolling cardiac and respiratory ECMO patients (31).

In pediatric patients needing ECMO and continuous renal replacement therapies (CRRT), fluid overload at CRRT initiation is a risk factor for mortality (32). Interestingly, this study showed that fluid overload correction is not associated with improved outcomes, suggesting that an early intervention, prior to the establishment of a significant positive FB, might be desirable.

Furthermore, positive FB is nowadays recognized as a factor leading to excess mortality in various perioperative setting (33,34).

Finally, this study induces some observations about the use of MCS in PCCS.

PCCS, considering an unselcted population of cardiac surgical patient, is a rare complication in its form refractory to inotropes and intra-aortic balloon pump (IABP) (35), but the incidence is higher in patients with a pre-existent cardiac dysfunction.

Analysing the trends in mortality of PCCS in the last decade, the most striking fact is that the prognosis is substantially stagnant and poor despite remarkable technological improvement in mechanical circulatory support.

In a recent editorial (36), Haft wonders which barriers hinder the use of MCS early in the course of shock, before

that an irreversibile end-organ damage makes the patient unsalvageable: fear of complications, inexperience, excessive faith in inotropic drugs, economic considerations are all possible explanations. However, definitive evidence in this field is lacking,

Organizing a prospective randomized trial could be desirable, but undeniable obstacles—ethical concerns, costs, attainment of an adequate sample size to infer mortality have hampered by now its realization (37).

Two single centres studies showed that early initiation of MCS is associated to better outcomes (38,39) and we strongly agree with this approach.

It is our opinion that patients suffering post-cardiotomy shock which is not fixed with low-medium dose inotropic drugs and IABP placement, including the recovery of an adequate diuresis, should promptly receive implementation of full mechanical support to avoid the subsequent irreversible multiple organ failure.

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Footnote

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