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Managing drainage insufficiency during ECLS – clinical implications of P1 monitoring

Extracorporeal life support (ECLS), including extracorporeal membrane oxygenation (ECMO), temporarily supports heart and/or lung function during acute severe cardiopulmonary failure, particularly in patients at high risk of mortality ($\geq 50\%$) despite conventional therapy.^{1,2} The number of adult ECMO cases has risen substantially over recent decades, with more than 5,000 respiratory and over 8,000 cardiac ECMO cases in 2024, according to the Extracorporeal Life Support Organization (ELSO) registry.³ Nevertheless, ECMO remains a complex and high-risk procedure associated with significant complications, including mechanical (e.g., cannula, circuit, blood pump) or patient-related issues (e.g., hemorrhage, kidney failure, infection, or hemolysis).¹⁻⁴

From 2020 to 2024, data from the ELSO registry showed cannula problems in approximately 3-7% of adult ECMO runs. Clots and air emboli occurred in 0.2-0.4%, and severe hemolysis in approximately 3%.³ Venous insufficiency can be a significant contributor to such complications.

Etiology of drainage insufficiency during ECMO

Multiple clinical situations can lead to drainage insufficiency (Figure 1). Centrifugal blood pumps are preload-dependent, and any drainage insufficiency can result in reduced blood flow, thus putting the patient at risk for inadequate oxygenation supply during therapy.⁵⁻⁷ In extreme conditions, drainage insufficiency often presents as “chattering” or “chugging” of the venous drainage line, which refers to the visible shaking or vibration of the venous tubing due to inconsistent, nonlaminar blood flow.^{5,7,8} This is primarily caused by excessive negative drainage (or suction) pressure and an insufficient venous capacity.^{5,7,8} The negative drainage pressure, measured as pump inlet pressure by P1 sensor, is mainly caused by the suction of the blood pump.^{2,9} However, if the suction exceeds venous capacity, vessel collapse around the cannula can obstruct the drainage

ports.^{2,7,8} As blood reaccumulates, the blockage intermittently releases, creating a repeating cycle of obstruction and release that produces noticeable tubing chatter.⁷ This phenomenon is referred to as “drainage insufficiency”⁷ and can be exacerbated by insufficient venous capacities caused by inflow obstruction, inadequate or malpositioned drainage cannulas, vasodilatation, hypovolemia, or increased intrathoracic pressure (e.g., pneumothorax, Valsalva maneuver), intra-abdominal pressure (e.g., intra-abdominal hypertension), especially if drainage from the inferior vena cava is affected.^{5,7} Also sepsis, elevated cardiac output, or patient agitation due to reduced sedation may be considered as underlying causes when the effect is seen later in the course of ECMO.^{5,7}

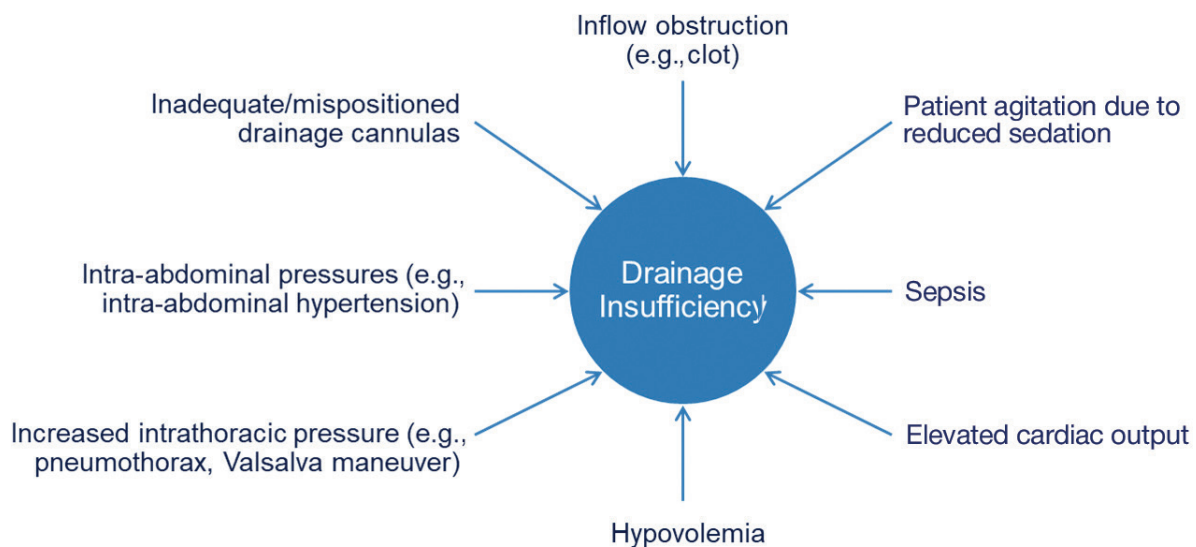


Figure 1: Overview of the etiologies of drainage insufficiency.

Potential consequences of drainage insufficiency

Drainage insufficiency can lead to progressive hypoxemia due to reduced blood flow through the ECMO circuit.⁷ The reduced flow may prompt inexperienced clinicians to increase the pump speed, which worsens the issue by further increasing negative drainage pressure.⁶ Excessive negative pressures can damage the vessel intima and cause cavitation, thereby amplifying hemolysis, especially when these pressures occur as pressure swings^{1,2,5-7} or air entrance.

When blood is exposed to pressures below -650 mmHg, cavitation occurs, meaning the pressure drops below the vapor pressure of blood, leading to vaporization and the formation of gaseous microbubbles.^{6,10,11} Centrifugal pumps, which are state-of-the-art technology for ECMO blood pumps, can generate pressures of -700 mmHg or even more negative pressure in certain parts of the system if the venous line is occluded or experiences chattering.⁶ The cavitation bubbles can collapse once blood flow carries them to areas of the circuit with higher pressures, such as the impeller.^{2,11} This process can lead to physical damage to blood cells such as hemolysis.^{2,6,11,12}

Hemolysis is the premature disruption of erythrocytes due to enhanced mechanical stress or other factors.^{2,12,13}

Among other causes (e.g., toxins, heat, osmosis),^{12,14} hemolysis can result from negative pressure, either from high-pressure jets (Bernoulli effect) or from suction.⁶ As a result, the erythrocyte's content, mainly hemoglobin and its heme and iron components, are released into the bloodstream, where they can promote inflammation, coagulation, deterioration of microcirculation, and ultimately organ dysfunction.^{2,12,13,15} The incidence of hemolysis during ECMO varies (0-41%) and is influenced by mechanical and patient factors.^{2,16-18} Hemolysis risk can be affected by factors like blood flow rates and the patient's condition.^{2,16-18}

As free plasma hemoglobin is mainly filtered by the kidneys, they are strongly exposed to its harmful effects.¹⁵ Single-center cohort studies reported an association of increased plasma-free hemoglobin during pediatric ECMO with the occurrence of acute kidney injury or renal replacement therapy.^{19,20}

Hemolysis has been shown to affect mortality rates in ECMO patients.^{16,21} To reduce these consequences of drainage insufficiency, preventive and management measures have been established.

Management of drainage insufficiency

The management of drainage insufficiency (Figure 2) and the prevention of its consequences begins with early recognition.

Besides the visible chattering, the inability to increase the blood flow with increasing pump speed may also be an indicator.^{5,7} Some authors suggest that there is no "safe level" of P1 and propose to maintain it as high as possible.²² ELSO recommends using blood pumps with "inlet pressure control" and to maintain the inlet pressure above -100 mmHg to avoid chattering.^{1,2}

In case of occluded inlet lines, ELSO recommends avoiding inlet pressures more negative than -300 mmHg either by inherent pump design or a servocontrolled sensor for the inlet pressure.¹ As the pump inlet pressure is also affected by the size and length of the drainage

cannula, the choice of an adequate cannula size may contribute to the prevention of drainage insufficiency.^{7,9,22,23}

If drainage insufficiency occurs despite these measures, the initial response is to reduce the pump speed in order to prevent further increases in negative pressure and to maintain a steady blood flow.⁵⁻⁸ The above-mentioned underlying etiologies like intra-abdominal or intrathoracic pressure increases, patient agitation, hypovolemia, as well as cannula malpositioning or occlusions should be evaluated and corrected appropriately.^{5,7}

If the drainage insufficiency is still persistent, the fluid responsiveness of the patient should be evaluated.^{5,7} Trendelenburg position may be an option for fluid-responsive patients prior to fluid resuscitation.^{5,7}

Once a volume replete state is reached, fluid administration should be terminated.⁵ If, despite these interventions, drainage insufficiency persists, physicians should consider the use of an additional drainage cannula to meet the blood flow requirements.^{5,7}

The flowchart below (Figure 2) summarizes the management of drainage insufficiency, as suggested by different clinical groups.^{5,7}

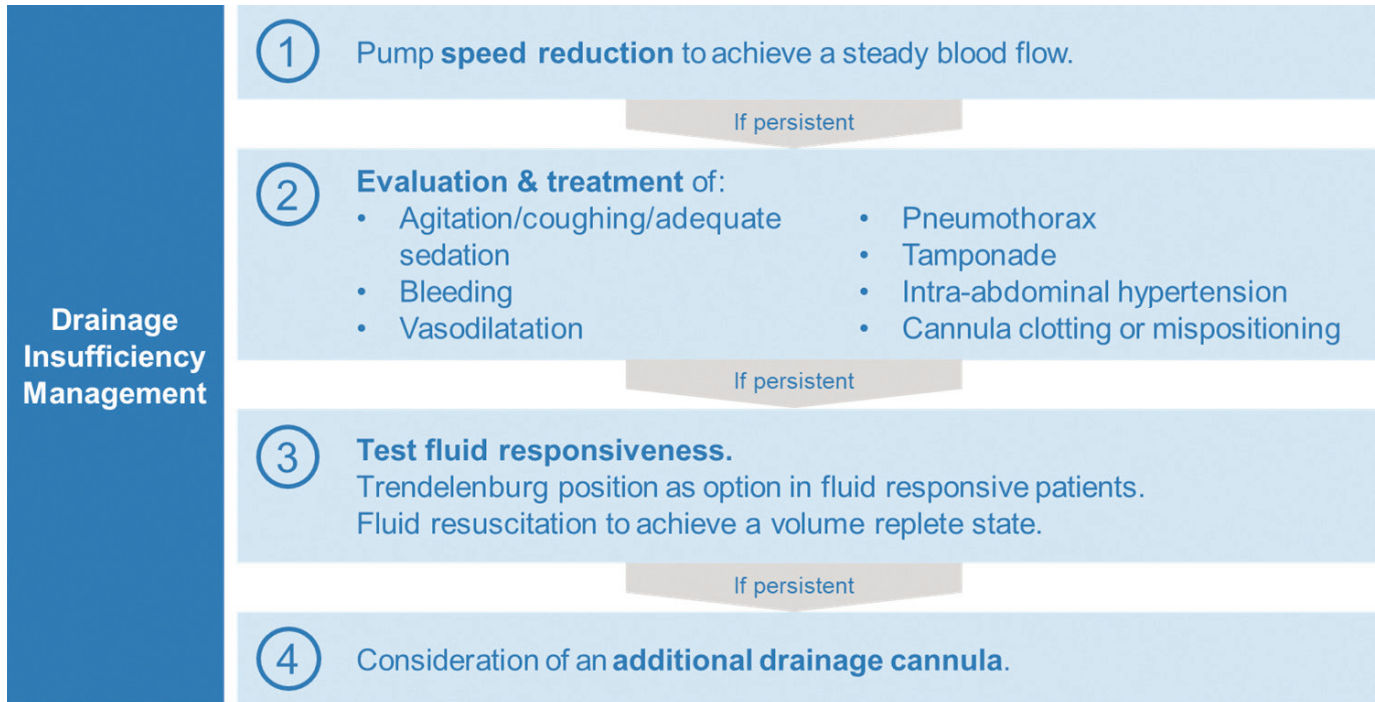


Figure 2: Flowchart for Managing Drainage Insufficiency. Measures to correct drainage insufficiency modified from Zakhary et al. and Krishnamurthy and Karanth.^{5,7}

Application of P1 limiter to prevent drainage insufficiency with the Xenios 2.0

Due to the connection between excessive negative pressures in the blood circuit and the risk of vessel damage, hemolysis, and cavitation, several safety features have been integrated into Xenios 2.0.

One such feature is the P1 limiter, which is a protection function intended to avoid blood damage caused by high negative pressures, as recommended by ELSO.^{1,2,24} When activated, the system automatically reduces the pump speed when the pressure in the system reaches the limit value set by the user, to prevent further pressure drops. When the P1 limiter is active, it is not possible to manually increase the speed. The P1 limiter can only be activated if the lower limit for flow has been set and the alarm is enabled.²⁴

To limit the risk of hypoxemia associated with reduced blood flow, the P1 limiter aims to increase the blood flow automatically once the negative pressure has normalized again.²⁴ As a result, negative pressure episodes can be reduced, helping to provide more consistent blood flow and, thus, oxygenation support (see Figure 3).²⁴

To avoid continuous rapid speed restrictions and accelerations, hysteresis for speed control is implemented, while P1 limiter function intervenes. This way, when the P1 limiter actively regulates the flow, an alarm is triggered (see Figure 3).

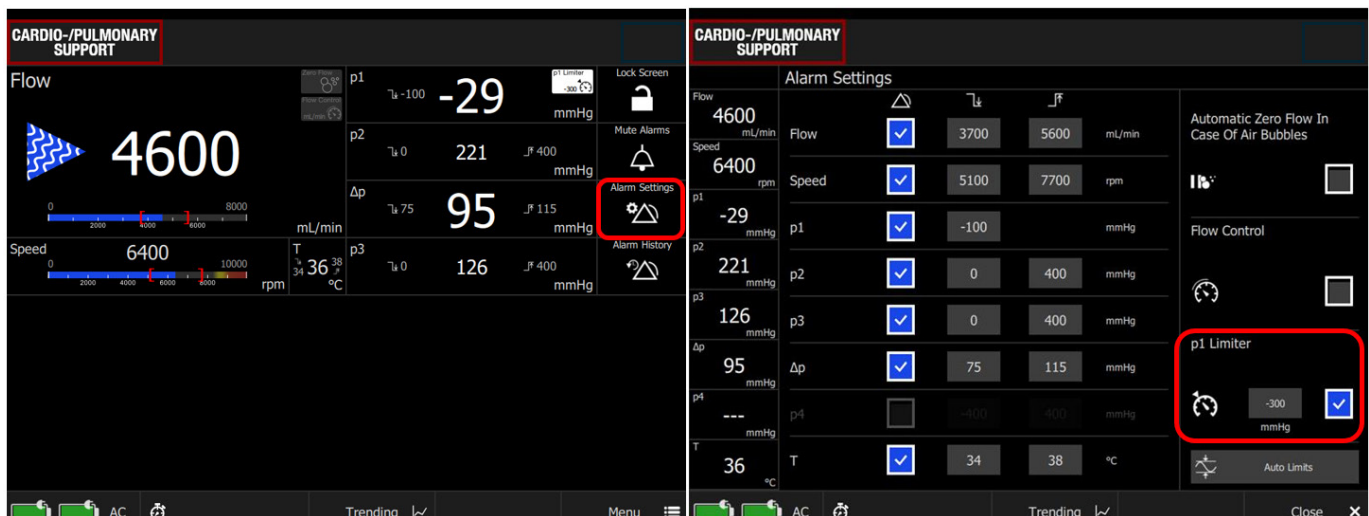


Figure 3: Graphical user interface of the Xenios 2.0 showing where to find the overview on alarm settings (left) with detailed alarm settings and the activated P1 limiter (right).

P1 is one of three integrated pressure sensors (IPS) placed along the tubing lines to monitor pressure within the extracorporeal circuit (Figure 4). The first IPS (P1) is positioned on the blood inlet tubing before the pump head, the second IPS (P2) is located between the pump head and the oxygenator, and the third IPS (P3) is mounted on the blood outlet tubing after the oxygenator.^{25,26} Each IPS consists of a compact pressure sensor package attached to the tubing line.²⁶ Pressure in

the tubing line is transmitted to a chip via a silicone element that serves as an isolating layer between the blood and the sensor, avoiding direct blood contact.²⁶ The intent of the integrated P1 pressure sensors is to be a safety feature, in that if the measured pressure falls, the speed of the pump is reduced to keep the suction pressure at the set limit.²⁶

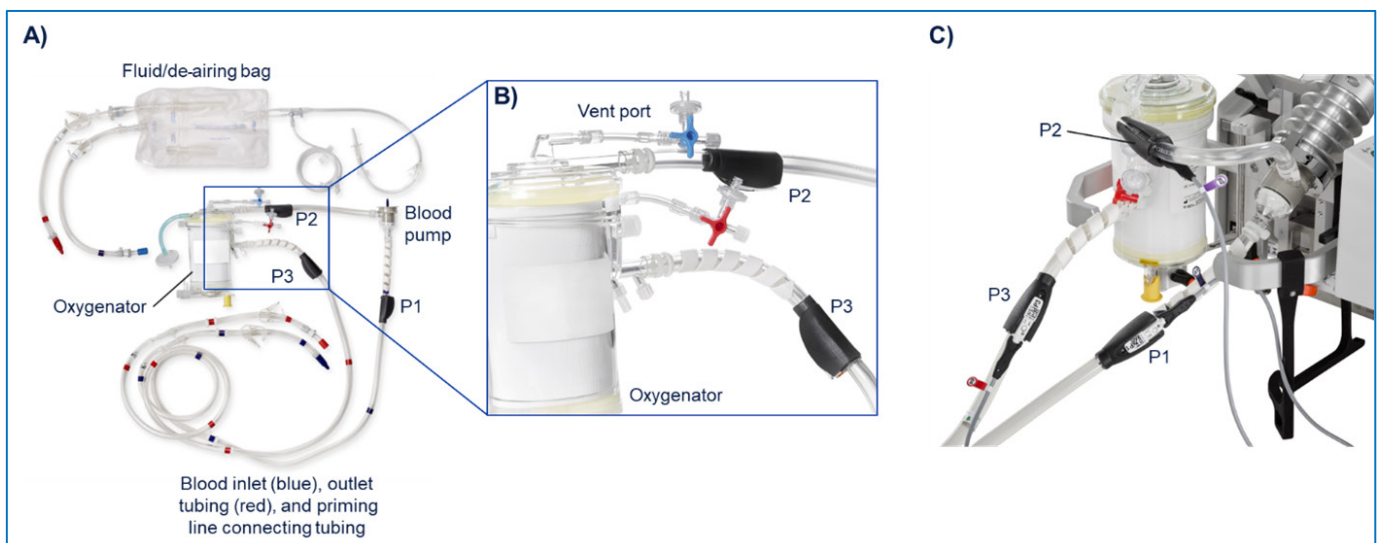


Figure 4: Tubing kit (XLung or Novalung ultimate kit), which are designed for use with Xenios 2.0. A) The tubing kits are equipped with three integrated pressure sensors (IPS) placed along the tubing to monitor pressure within the extracorporeal circuit. The sensors are located before the pump head on the blood inlet line (P1), between the pump head and the oxygenator (P2), and after the oxygenator on the blood outlet tubing (P3).^{25,26} B) Air accumulations inside the kit should be avoided and must be removed per the Instructions for Use. C) The tubing kits can be integrated with Xenios 2.0.^{25,26}

Case report*

Pressure, flow, and pump speed measurements from a COVID-19 patient who was supported with venovenous ECMO are presented in Figure 5. Following initiation of ECMO, the patient stabilized at approximately 4.5 LPM of blood flow for three days. The flow was eventually titrated upward – approximately to 5 LPM on day four.

During this entire period, however, the P1 limiter was enabled and frequently intervened due to intermittent periods of venous insufficiency (e.g., from patient coughing or circuit manipulation). The graph of flow (right panel), in relation to the graph of P1 pressure (left panel), demonstrates that, while there were some very brief periods in which P1 dropped, the P1 limiter functionality

aided in providing consistency of ECMO flow to the patient.

The clinicians disabled the p1 limiter on day six. As seen in the graphs below, the remainder of the patient run was far less stable, with large swings in ECMO flow (frequently reaching near 0 LPM) in relation to excessively low P1 pressures (frequently fluctuating between -300 and below -400 mmHg).

As laid out above, this level of venous pressure, in addition to the prolonged periods of flow disruption, can have profound consequences for the patient.

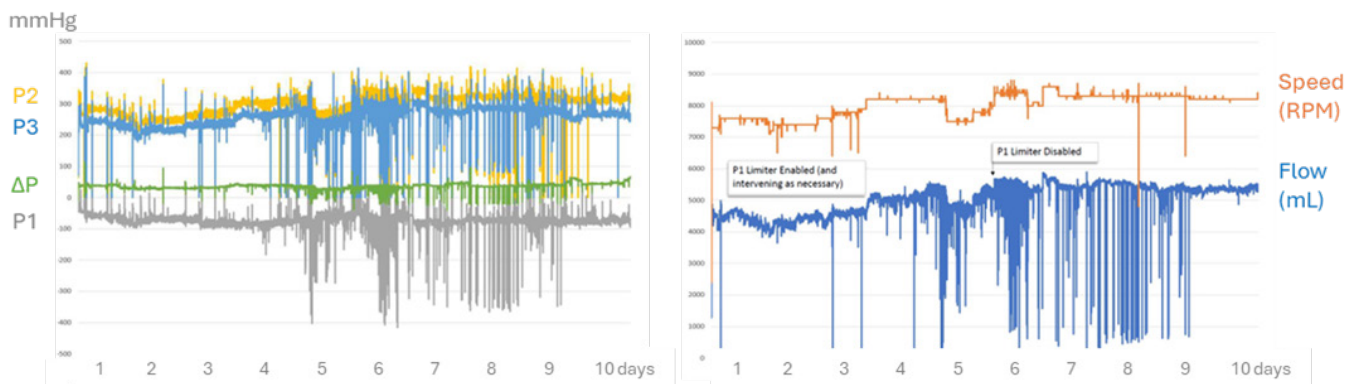


Figure 5: Example of P1 limiter feature minimizing negative pressure episodes. The ECMO console screen plots the pressures P1, P2, P3, and the difference between P3 and P2 (ΔP) as a function of ECMO duration (left panel). Similarly, flow and speed are visualized on the screen (right panel). While the P1 limiter function of the ECMO device was enabled for the first five days of treatment, negative pressure episodes were automatically regulated by adjusting the pump speed, helping to provide a more consistent blood flow compared to when the function was disabled from day six onward.

Summary

Drainage insufficiency is a severe complication of extracorporeal membrane oxygenation, provoked by excessive negative drainage pressure or insufficient venous preload. To prevent its harmful consequences, like vessel injury, hemolysis, or cavitation, lower limits of drainage pressure have been recommended by the Extracorporeal Life Support Organization. The P1 limiter function within Xenios 2.0 is a safety feature designed to maintain non-critical limits and helps prevent excessive negative pressures. If drainage insufficiency occurs despite such preventive measures, a systematic management approach can help to eliminate the root cause and obtain the best possible patient outcomes.

*Data on file with Fresenius Medical Care.

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