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Review Article

ECPella: Concept, Physiology and Clinical Applications

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Addition of Impella on top of venoarterial extracorporeal membrane oxygenation (VA-ECMO) has gained wide interest as it might portend improved outcomes in patients with cardiogenic shock. This has been consistently reported in retrospective propensity-matched studies, case series, and meta-analyses.

The pathophysiologic background is based on the mitigation of ECMO-related side effects and the additive benefit of myocardial unloading. In this perspective, thorough knowledge of these mechanisms is required to optimize the management of mechanical circulatory support with this approach and introduce best practices, as the interplay between the two devices and the implantation-explantation strategies are key for success.

Key Words: VA ECLS; impella; ecpella; cardiogenic shock; physiology

VENOARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION (VA-ECMO) commonly is used to support patients with refractory cardiac arrest or cardiogenic shock,[1–3] mainly via percutaneous cannulation.[4] This strategy may cause left ventricle (LV) distention that compromises myocardial recovery.[5] Direct LV unloading provided by Impella was associated with lower mortality in patients with cardiogenic shock supported with VA-ECMO in a recent international multicenter study.[6]

The present paper has a specific purpose to provide a complete overview of this strategy, starting from a solid pathophysiologic approach. Then, the rationale for unloading the LV and the related available techniques is discussed. Finally, the combined configuration of VA-ECMO and Impella (ECPella) is fully treated, providing its significant clinical applications.

Pathophysiologic Background

Left Ventricle Pressure-Volume Loop

The mechanical and hemodynamic properties of the heart are shown by the ventricular pressure-volume loop (PVL). The PVL describes the four phases of the cardiac cycle, respectively: (1) isovolumic contraction, (2) ejection, (3) isovolumic relaxation, and (4) filling.

Typically, the PVL is characterized by the intrinsic (ventricular) properties of the myocardium and by the influence of the extrinsic vascular conditions.

The ventricular intrinsic properties are represented by two lines that inscribe the PVL shape. The end-systolic pressure-volume relationship is linear.[7] On the contrary, the end-diastolic pressure- volume line is a nonlinear relationship and reflects the diastolic properties.[8]

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Differently, the extrinsic conditions mainly are defined by the concepts of preload and afterload. The end-diastolic volume (and, therefore, pressure) indicate the preload, which is a surrogate of the sarcomere length. Differently, the afterload can be depicted on the pressure-volume plane by the "effective arterial elastance" line, influenced by the systemic vascular resistances, the heart rate, and, finally, the preload [9] (see Table 1 and Figure 1).

Finally, the PVL defines the determinants of myocardial oxygen consumption.[8] The most important determinant is the pressure-volume area (PVA). The PVA is the sum of the external stroke work and the potential energy, which represents the residual energy stored in the myofilaments at the end of systole. Myocardial oxygen consumption (MVO_2) is linearly related to ventricular PVA; therefore, any increase in PVA corresponds to a linear increase in MVO_2 [10] (see Figure 2).

Pressure-Volume Loop on Peripheral VA-ECMO

During cardiogenic shock, VA-ECMO primarily alleviates the hemometabolic shock associated with low-output state, supporting the cardiopulmonary system and secondarily reducing the heart's preload, by drawing blood from the right atrium.

However, a direct hemodynamic consequence after peripheral VA-ECMO implantation is the increase of LV afterload, moving the arterial elastance line to the right. In this condition, only the LV volume increase allows overcoming the high generated afterload through the Starling's Law. As a result, the subsequent LV distention leads to increased LV end-diastolic pressure, left atrial pressure and pulmonary capillary wedge pressure that may cause pulmonary edema. Indeed, this mechanism is particularly unfavorable because slight LV volume increases may cause large increases in end-diastolic pressure. The global effect is the shift of PVL rightward and upward along the end-diastolic pressure-volume relationship, becoming progressively narrow and taller (see Figure 3). Translating these changes in hemodynamic terms: PVA increases despite the stroke- volume reduction. Therefore, the poorly oxygenated blood due to pulmonary edema and the increased myocardial oxygen demand might further worsen the LV function.[7]

Table 1
Main Pressure-Volume Loop Features Related to Figure 1.

Intrinsic Properties	
ESPVR	The linear relationship is defined by 2 main features[7]: - the slope is the end-systolic elastance *(Ees),* a load-independent LV contractility parameter. Therefore, different loading conditions lead to distinct PVLs which move along the same ESPVR line defined by identical *Ees*. - the volume−axis intercept *Vo*
EDPVR	The nonlinear relationship defines only the *passive diastolic properties* of the ventricle and represents diastolic stiffness. These properties are influenced by pressure and required sophisticated engineering assumptions. Consequentially, diastolic properties are difficult to apply in practice.[8]
Extrinsic Properties	
Ved	The end diastolic volume (*Ved*) defines the pre-load which is strongly determined by the venous return.[9]
Ea	The arterial elastance (*Ea*) connects the *Ved* with the end systolic pressure volume. The Ea line slope is defined by the ratio between *systemic vascular resistance (SVR)* and the duration of the heartbeat. Therefore, Ea is influenced by the *SVR*, the *heart rate* and the preload (*Ved*).[9]
Others	
SV	The stroke volume (*SV)* is the width of the loop. The product between SV and heart rate is the cardiac output.
Pes	The *Pes* (ventricular end-systolic pressure) represents the height of the loop

Venting the Left Ventricle

Rationale of LV Venting

LV overload caused by peripheral VA-ECMO is a crucial concern for LV recovery. The detrimental effect of retrograde flow in the aorta that might lead to LV dilatation, increased left atrial pressure, and pulmonary edema is prominent. Moreover, it jeopardizes ventricular recovery, particularly in the presence of ischemia-induced myocardial impairment. In case of extreme overload and severe LV dysfunction, the aortic valve may remain closed, even during systole, causing blood stasis in the LV and increasing the risk of thrombus formation.[11]

LV Venting Techniques

When the pharmacologic LV venting, through the modulation of LV contractility and systemic vascular resistance (SVR), is insufficient, mechanical strategies should be utilized to decompress the left ventricle. The first step considered usually was intra-aortic balloon pump (IABP) counterpulsation, which unloads the LV by afterload reduction.[12] Nevertheless, more sophisticated approaches are required in order to overcome significant ventricular overload. These include surgical techniques or percutaneous techniques.

A review paper showed an increased use of percutaneous techniques, confirming the growing attention to noninvasive approaches.[13] The percutaneous approach might consist of placing a venting cannula in the pulmonary artery or in the left side through the transaortic or transseptal approach. Furthermore, different percutaneous assist devices, such as Impella or Tandem Heart, may be useful for avoiding or reducing the LV overload.[11] The most common locations of unloading were the left atrium (31%), followed by the aorta/IABP (27%) and transaortic (27%).[11] As a matter of fact, the optimal technique and the target patient population who actually will benefit from venting procedures are still under investigation.

ECPella

Among percutaneous devices, Impella (Abiomed, Danvers, MA) represents the most extensively validated solution. The Impella is a catheter-mounted microaxial flow pump capable of drawing from 2.5-to- 6.0 L/min of blood from the LV into the aortic root, across the aortic valve. The current use of

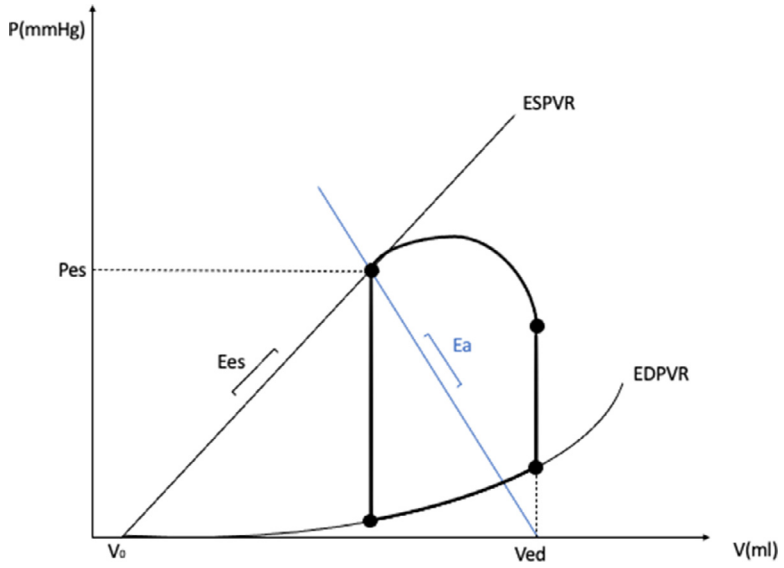

Fig 1. Pressure volume loop. Pressure volume loop is bounded by the end-systolic pressure-volume relationship (ESPVR) and end-diastolic pressure-volume relationship (EDPVR).

Ea, arterial elastance; Ees, end-systolic elastance; P, pressure; Pes, end-systolic pressure; V, volume; Ved, end-diastolic volume.

Impella and VA-ECMO is called "ECPella" and is an efficient technique to unload the LV.[6]

Hemodynamics of ECPella

As previously discussed, VA-ECMO support in cardiogenic shock leads to a significant afterload increase, which shifts the PVL upward and rightwards. The overall effects consist of higher end-diastolic volume, stroke work rise, and MVO_2 increase. This overload condition might be followed by increased left atrial and capillary wedge pressures and pulmonary oedema.[14]

The hemodynamic effects generated by Impella may be summarized in three main concepts analyzing the single role of this device: (1) increasing cardiac power output, (2) increasing oxygen supply, and (3) decreasing oxygen demand.

First of all, the Impella's outflow, placed in the aortic root, provides an active flow that depends on the pump support setting (P level) and the aorta-LV pressure gradient. The combination between P level setting and pressure gradient, as a consequence of VA-ECMO support and afterload, results in a forward flow that is significantly increased by Impella.[15,16]

Second, Impella is able to raise oxygen supply. The flow through the coronary arteries is influenced by the pressure gradient across the artery and vascular resistance. Assuming the venous pressure and the primary artery tract resistance as fixed, the flow depends on the microvascular resistance and aortic pressure. In addition to the increased ascending aortic

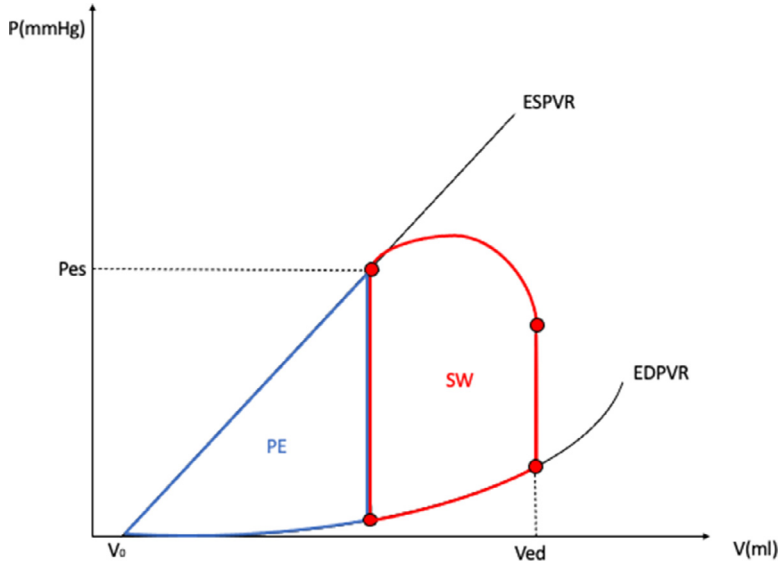

Fig 2. Left ventricular energetics. The sum of the stroke work (SW) and potential energy (PE) is called pressure-volume area (PVA).

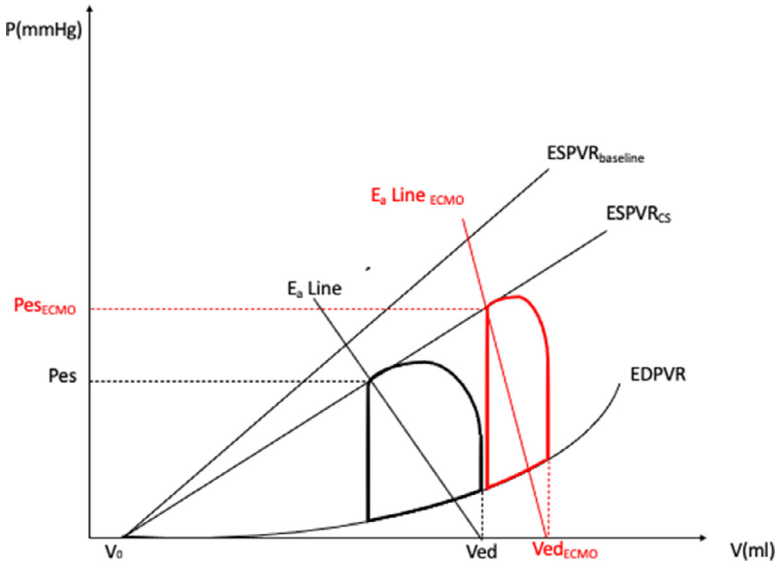

Fig 3. Pressure-volume loop changes in venoarterial extracorporeal membrane oxygenator support during cardiogenic shock. The pressure-volume loop moves rightward and becomes narrow.

ESPVR, end-systolic pressure-volume relationship; EDPVR, end-diastolic pressure–volume relationship; Ea, arterial elastance; Ees, end-systolic elastance; P, pressure; Pes, end-systolic pressure; V, volume; Ved, end-diastolic volume.

pressure, the unloading of the LV, reducing end-diastolic pressure and volume, causes reductions of wall tension and microvascular resistance, according to Laplace's Law.[7]

These assumptions are supported by different investigations: Sauren et al reported a maximum 47% increase in coronary flow with Impella in animals,[17] and Remmelink et al reported this augmentation in humans.[18] The microvascular effects were studied by Aqel et al using a perfusion imaging technique; this experience showed the improvement of myocardial perfusion with Impella support, explained by the augmentation of the blood flow through the collateral pathways. Finally, the total result of the combination between these factors leads to the myocardial oxygen supply's increase.[19] Third, the Impella's inflow drainage reduces ventricular end-diastolic volume and pressure, left atrial and wedge pressures, drawing blood directly from the ventricle.[15] Sauren et al showed a significant reduction from baseline in mechanical work and end-diastolic pressure-volume with Impella[17] in an acute animal model, further confirmed by Valgimigli et al.[18] As a consequence of reducing mechanical work and decreasing myocardial wall tension, the myocardial oxygen demand is lowered.[20–22]

Overall, the total balance of myocardial oxygen demand and supply becomes favorable.[15,17] Reesink et al, considering only the kinetic work, demonstrated a 36% improvement with Impella compared with an 18% improvement with IABP.[15] Differently, Sauren et al took into consideration the potential energy component, reporting a 69% improvement with Impella compared with 15% with IABP.[17]

Pressure-Volume Loops of ECPella

To summarize, the hemodynamic effects of Impella in combination with VA-ECMO may be identified as direct or indirect (see Figure 4):

1. **Direct**: the first direct impact is the loss of isovolumic periods, caused by continuous pumping of blood from the LV to the aorta, independently of the phase of the cardiac cycle. The lack of these components modifies the PVL from its normal trapezoidal shape to a triangular shape. LV results in progressive unloading, shifting the PVL leftward.[23]

2. **Indirect**: all of these changes cause reductions in PVA and MVO_2, improving blood oxygenation, systemic pressure, and perfusion, leading to beneficial secondary changes in LV contractility and SVR.[24] Furthermore, Impella, as an unloading strategy in combination with VA-ECMO, has relevant effects on the pulmonary and systemic hemodynamics.[25] First, total blood flow increases, and pulmonary artery wedge pressure decreases. Second, the increase in pulmonary artery capacitance exceeds the reduction in pulmonary vascular resistance; thus, increasing the pulmonary artery time constant, being the product of pulmonary artery capacitance and pulmonary vascular resistance. The increase in pulmonary artery capacitance is particularly relevant, being a measure of pulsatile right ventricle (RV) afterload.[26] Therefore, the global result should be the reduction of RV afterload, increasing right stroke volume and reducing arterial CO_2 pressure − end-tidal CO_2 gradient, caused by the reduction of alveolar deadspace ventilation. Importantly, this reduced arterial CO_2 pressure-end-tidal CO_2 gradient remains abnormal, and indicates residual ventilation-perfusion abnormalities, which, in combination with increased LV output, might induce delivery of poorly oxygenated blood into the systemic circulation, as confirmed by the reduction in right radial arterial oxygen saturation. This phenomenon might be particularly evident in the upper half of the body and depends either on the residual gas exchange abnormalities in the lungs or the anteroretrograde balance of blood flow, generated between LV output and the extra-corporeal life support arterial cannula and warrants continuous

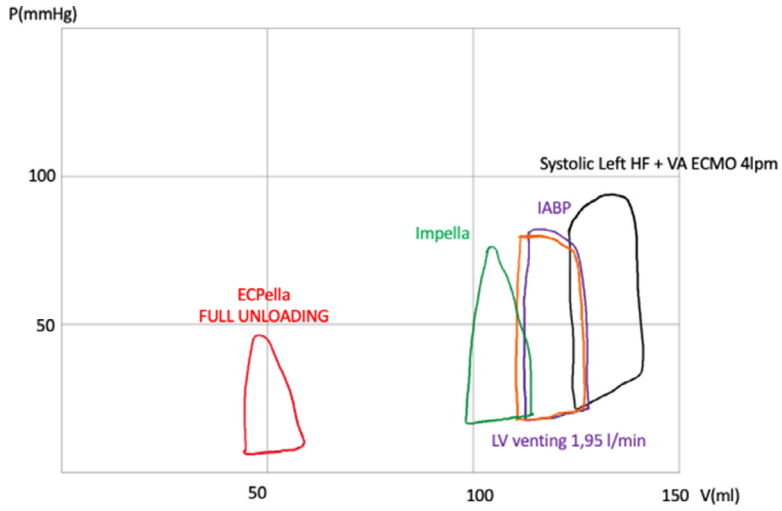

Fig 4. LV venting techniques and related pressure-volume loops. In case of cardiac failure (shock or arrest), ECPella provides full left ventricle unloading. In ECPella configuration, the pressure-volume loop moves leftward and becomes triangular.

monitoring, especially in the early phases until pulmonary edema is resolved and gas exchange is improved.[22]

ECPella Evidences

After a preliminary case series,[27] Pappalardo et al showed that patients supported with the ECPella strategy not only had improved outcomes but also showed a trend toward higher left ventricular ejection fraction after weaning. This experience investigated 34 ECPella support: after propensity score matching, the ECPella group presented significantly lower in-hospital mortality (47% *v* 80%, $p < 0.001$) and a higher rate of successful bridging to either recovery or further therapy (68% *v* 28%, $p < 0.001$), as compared with VA-ECMO alone patients.[28]

Patel et al showed similar results with 30-day mortality significantly lower in the ECPella cohort (57 *v* 78%; hazard ratio 0.51[0.28-0.94], log rank $p = 0.02$); moreover, the inotropic score was greater in the VA-ECMO group by day two (11 *v* 0; $p = 0.001$). Bridge to recovery, although not statistically significant, was numerically almost double in the ECPella cohort (40% *v* 22%; $p = 0.18$); bridge to left ventricular assist device (LVAD) was more prevalent in the ECPella group as well (33 *v* 13%; $p = 0.60$). No statistically significant differences in terms of hemolysis, bleeding, renal failure, and stroke were observed.[29] This was further corroborated by the work of Truby et al, which showed that myocardial recovery was higher in patients without left ventricular distention, prompting the need for LV venting.[30] They also identified extracorporeal cardiopulmonary resuscitation as the clinical scenario with higher need for decompression. Interestingly, these figures were independent from the site of arterial cannulation (femoral, central or axillary) and were reported in a group of patients receiving an average ECMO flow of 3.6 L/min.[30]

Finally, Schrage et al recently reported the most important evidence on the combined use of Impella and VA-ECMO. In this international, multicenter cohort study, 255 propensity-matched patients supported with ECPella were compared with 255 patients supported with only VA-ECMO. Left ventricular unloading was associated with lower mortality in patients with cardiogenic shock treated with VA-ECMO, despite higher complication rates.[6]

Clinical Applications

Different Models and Different Placement

The Impella devices are commercially available in different models, characterized by their capacity to guarantee different support [31] (ranging from 2.5-to-6 L/min):

- the Impella 2.5 (maximum flow rate 2.5 L/min): percutaneous insertion with a 12-Fr sheath in the femoral artery
- the Impella CP (3.0-4.0 L/min): percutaneous insertion with a 14-Fr sheath in the femoral artery
- the Impella 5.0 (5.0 L/min): surgical cut-down insertion with a 21-Fr sheath; axillary artery is the preferred site of placement, facilitating ambulation and a longer period of support
- the Impella 5.5 (up to 6.0 L/min): surgical cut-down insertion with a 21-Fr-sheath; axillary artery or directly to the ascending aorta, facilitating long-term use and full LV unloading

The Impella 2.5/CP is FDA-approved to provide circulatory support for up to five days and the Impella 5.0 is approved for up to ten days.[32] The new Impella 5.5 with ceramic bearings is intended for prolonged use, up to 30 days.

Contraindications

ECPella has the same contraindications as isolated Impella support: LV thrombus, mechanical aortic valve, and significant aortic regurgitation. In these scenarios, other venting strategies should be pursued. For instance, IABP may be the less-invasive approach compared with a cannula connected to the drainage side of the VA-ECMO circuit, which might be more

elaborate. Furthermore, significant arterial disease should be systematically investigated in order to quantify the risk of navigating through an atherosclerotic aorta.[33]

Device Selection, Timing, and Targets

The adequate Impella device should be chosen according to the amount of required support[34–36] and the severity of hemodynamic compromise.

In VA-ECMO and concomitant Impella support, the total cardiac output is not simply the sum of the preinsertion cardiac output and the flow generated by the Impella. Since the LV should be fully or partially unloaded by the Impella device, the native heart contribution subsequentially decreases.[18]

The Impella's performance should be set in order to provide sufficient LV unloading and adequate hemodynamic support, avoiding excessive suction. This might be particularly demanding over the first hours of support. In fact, the full venous drainage and the aortic valve closure lead to frequent LV size changes over this first period of time.

Although there were clinical reports proving the effectiveness of Impella and IABP combination,[37,38] a European expert user group did not recommend the systematic simultaneous use of the Impella device with IABP. First, Impella forward flow might be attenuated by IABP during diastole. Second, this combination might lead to misinterpretation of alarms, potential position issues, and, finally, increased risk of hemolysis and thrombosis.[13]

The necessity to unload the LV ventricle during VA-ECMO support might be summarized in four main scenarios, each of which has specific features and goals that are described in the following table (see Table 2).

Access Site, Impella Placement and Monitoring

The selection and management of the access site should consider the patient's anatomy and the operator's experience. The advisable site for the percutaneous placement is the common femoral artery, while the axillary artery is suitable in the surgical approach. The appropriate access management techniques should guarantee low risk of arterial complications such as local bleeding and access site-related ischemia.[44,45] However, considering the concomitant VA-ECMO support, the risk of complications might be lower, as limb ischemia can be managed by reperfusion via the ECMO circuit.[33] On the other hand, the ECMO-induced coagulopathy might be responsible for a higher incidence of bleeding complications.

The positioning of the Impella device should prevent migration into the LV and avoid hemolysis, suction episodes, and inadequate hemodynamic support; in particular, for long-term support. The placement can be performed in the catheterization laboratory or operating room, but also at the bedside, which is particularly attractive for patients who are critically unstable on VA-ECMO.[19] The inlet should be placed approximately 3.5 cm (Impella 2.5, CP, and 5.0) or 5.0 cm (Impella 5.5) distal to the aortic valve without being close to the mitral subvalvular apparatus or interfering with the anterior mitral leaflet and papillary muscles. Bedside echocardiography should be available, possibly transthoracic, to evaluate the correct placement, in addition to right ventricular function and volume status[13] (see Figure 5).

The ECPella monitoring requires a right radial arterial line for oxygenation monitoring, a daily x-ray to assess pulmonary edema, and regular echocardiographic studies, especially in case of an abnormal positioning signal on the console monitor. Echocardiography should be able to check the Impella position, to exclude pericardial effusion, to evaluate cardiac chamber loading, and to examine valvular function.[46]

However, decision-making during ECPella support might be extremely demanding and requires direct and reliable hemodynamic information. Therefore, advanced hemodynamic monitoring with a pulmonary artery catheter is strongly recommended.[47] These measurements help to better

Table 2
Clinical Scenarios and Detailed ECPella Configurations.

	Stone heart (after eCPR)[39]	Acute Severe Myocardial Dysfunction (AMI[40], Myocarditis[41])	Chronic Severe Myocardial Dysfunction[42] (End Stage Chronic HF)	Myocardial Dysfunction in Post-Cardiotomy Patients[43]
Configuration	peripheral VA ECMO	peripheral VA ECMO	peripheral VA ECMO	central VA ECMO
Expected duration	days	days	days to weeks	2-15 days
Timing	Early LV distension	Early LV distension	Early and delayed LV distension	Early LV distension
Device	*Impella 2.5 or CP*[*]	*Impella 2.5 or CP*[*]	*Impella 5.0*[*], *5.5*	*Impella 2.5, CP or 5.0.5.5* based on the clinical situation[*]
Impella Insertion	13-Fr or 14-Fr sheath Femoral Artery	13-Fr or 14-Fr sheath Femoral Artery	Surgical cut-down insertion through 8-10mm Dacron graft anastomosed to the axillary artery	13-Fr or 14-Fr sheets or surgical cut-down insertion through 8-10mm Dacron graft anastomosed to the axillary artery or directly in the ascending aorta.
Goal	BTD, De-escalation, Myocardial Recovery	De-escalation, Myocardial Recovery	BTT, BTD or Bridge to LVAD implantation	Myocardial Recovery

AMI, acute myocardial infarction; BTD, bridge to decision; BTT, bridge to transplant; HF, heart failure.
[*] In combination with Impella RP in case of RV dysfunction.

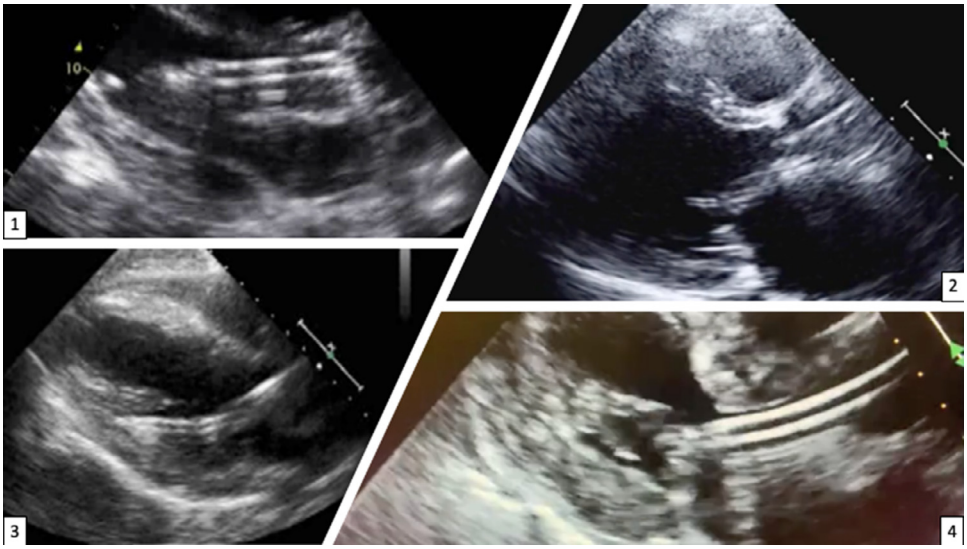

Fig 5. Impella positioning. (1) Normal Impella position in parasternal long axis (3.5 cm from the aortic valve plane). (2) Impella position in aorta. (3) Impella position too far in left ventricle. (4) Impella pigtail caught in papillary muscle.

understand the complex changes in order to adjust device flows, medical therapy and volume management.

Clinical Remarks

Firstly, clinical decisions basically should be guided by carefully weighing potential therapeutic benefits and risks in every individual patient, including the intended goal and expected length of the bridging strategy under VA-ECMO. Left ventricular overload at any time during VA-ECMO may develop in up to 70% of patients,[48] however, an urgent decompression is undertaken in only roughly 10% of cases, whereas an additional 20% of cases might need an unloading intervention at a later stage.[30] Notably, recent literature suggests improved outcomes when adjunct unloading strategies are employed.[6] In routine clinical practice, patients under high-flow VA-ECMO support (>4 L/min) and exhibiting a dilated LV in the virtual absence of native left ventricular contractility, should be considered at a very high risk for significant LV overload.

Secondly, the right-left ventricular interaction is of paramount importance, as sustained right ventricular contractility may actually contribute to mechanical overload, which negatively impacts on the failing left ventricular myocardium.[23] In this setting, despite right ventricular drainage, it still may be able to eject enough blood via the left atrium into the failing LV that is facing an increased afterload as mediated by the retrogradely-directed extracorporeal flow in the aorta toward the LV. Therefore, paradoxically, preserved right ventricular function is a critical additional risk factor for significantly overloading a failing LV under VA-ECMO support.

Thirdly, Impella automated controller algorithms may detect suction at the device inflow in case of full LV unloading. In fact, the suction alarm may be triggered by constant high aorta-LV differential pressures and low pulsatility on the aortic pressure waveform.

Finally, the patients who have worsening lung function supported with VA-ECMO may demonstrate the "Harlequin syndrome."[49] Impella seems to be the most effective method, allowing earlier and expeditious weaning from VA-ECMO.[50] This would focus not only on LV unloading, but also on the respiratory system, which should be protected from injurious mechanical ventilation.

Weaning

Patients treated with ECPella should be supported until hemodynamics are stable with resolution of shock.

The de-escalating process should start by first removing inotropes. Thereafter, VA-ECMO reduction should be pursued. At this time, the focus should be on the right ventricle, as this is the major limitation for de-escalating from biventricular to univentricular support. If biventricular failure is predominant, despite successful hemodynamic optimization, evaluation for heart transplantation or biventricular support is warranted; if left ventricular support only is required, de-escalation to an axillary approach for a prolonged attempt at heart recovery should be pursued. The axillary approach encompasses the use of the Impella 5.0 and/or 5.5 regardless of the residual function of the LV, in light of its dedicated tools for axillary surgery that allow ambulation, better hemocompatibility, and a longer pump duration.[51] A total percutaneous approach with the Impella implanted in the axillary artery may be envisioned in the future in patients who are of small size and, therefore, require lower flow.

This bridge-to-bridge strategy has proven very effective in improving results in patients requiring a durable LVAD, as it is associated with lower complications compared with the direct transition from VA-ECMO to LVAD. Indeed, from the hemodynamic standpoint, this is an 'LVAD test' that challenges the right ventricle and avoid futile implants.[52]

ECPella Advantages

The ECPella approach has some valuable advantages. ECPella approach results are extremely attractive, since the treatment of cardiogenic shock should be effective within a short time frame after initiation of mechanical circulatory support. In fact, significant reduction of lactates[53] and of the inotropic score[54] should be an important achievement within 24 hours. Impella provides additional flow to the ECMO and overcomes the limitation of ECMO performance driven by the cannula size. According to the size of the cannula usually selected for femoro-femoral cannulation (21-29 Fr venous 15-19 Fr arterial), the VA-ECMO pump would not provide more than 5 L/min of flow. An associated LV pump provides an additional flow that has to be viewed in a double perspective. On the one hand, Impella is a 'resuscitative' flow, and on the other hand, the device allows smoother weaning from mechanical circulatory support.[55] Indeed, ECMO removal is a complex issue: patients will recover aortic pulsatility and normal cardiac output, although echocardiography usually shows a low ejection fraction, and this translates into a consistent number of patients who are weaned from ECMO but eventually will die before hospital discharge.[56,57]

Furthermore, the ECPella approach guarantees the chance for shorter duration of the extracorporeal support that is associated with more side effects in each patient.[58] However, this approach may prolong the total time when the patient is on a pump. If it is assumed that medical treatment is the target for the management of heart failure after the acute failure, the LV pump might avoid the use of inotropes[59] during weaning and might facilitate the titration of ACE inhibitors and beta blockers under progressive lower levels of Impella support.

ECPella Shortcomings

The major ECPella shortcomings are bleeding complications, hemolysis, and ischemic complications.

Recently, Schrage et al showed higher rates of severe bleeding (38.4% *v* 17.9%) and hemolysis (33.6% *v* 22.4%) in ECPella support compared with VA-ECMO alone. Furthermore, the association between ECPella use and a higher likelihood of interventions because of access site-related ischemia was consistent. In fact, interventions because of access site-related ischemia occurred in 21.6% of patients treated with ECPella versus 12.3% of patients treated with VA-ECMO. Furthermore, laparotomies because of abdominal compartment syndrome were seen in 9.4% of patients treated with ECPella, compared with only 3.7% of patients treated with VA-ECMO. However, no differences were found in ischemic strokes or bowel ischemia.[6]

On the one hand, the presence of two devices and related arterial access may increase the likelihood of bleeding/ischemic complications.[60] On the other hand, these complications might be explained by the relatively large vascular access required (12/14-French for the Impella 2.5/CP).[61] Furthermore, Impella leads to a high shear stress on blood elements and is associated with increased hemolysis.[62]

Interestingly, Pappalardo et al found a higher rate of need for continuous veno-venous hemofiltration in patients supported with ECPella compared with those with VA-ECMO alone.[28] This was confirmed by Schrage et al in a large multicenter study.[6] Obviously, survivorship bias might, to a certain degree, explain higher need for renal replacement therapy. However, this association should be investigated by further study. Finally, another critical and not negligible issue is represented by the cost of this combined configuration.

Conclusions

Up to now, the ECPella strategy has been discussed as a primary configuration. However, it is to be acknowledged that this is far from the 'real world'. Many patients are salvaged by Impella implantation in combination with VA-ECMO because complications related to LV distention have ensued. Furthermore, Impella patients escalate to ECMO because the severity of shock has progressed, mostly due to concomitant right heart failure or inadequate pump selection. This might be overcome by the implementation of new concepts in the management of cardiogenic shock patients: (1) systematic LV venting, (2) assessment of the severity of shock by the inotropic score and mechanical support strategy to avoid toxic catecholamine levels, and (3) right ventricular 'sensitivity' and early application of biventricular support. Further studies are needed to face this demanding medical condition.

Conflict of Interest

Prof. Lorusso is consultant for Medtronic and LivaNova and member of the Advisory Board for Eurosets and PulseCath. The other authors declare that they have no conflicts of interest.

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