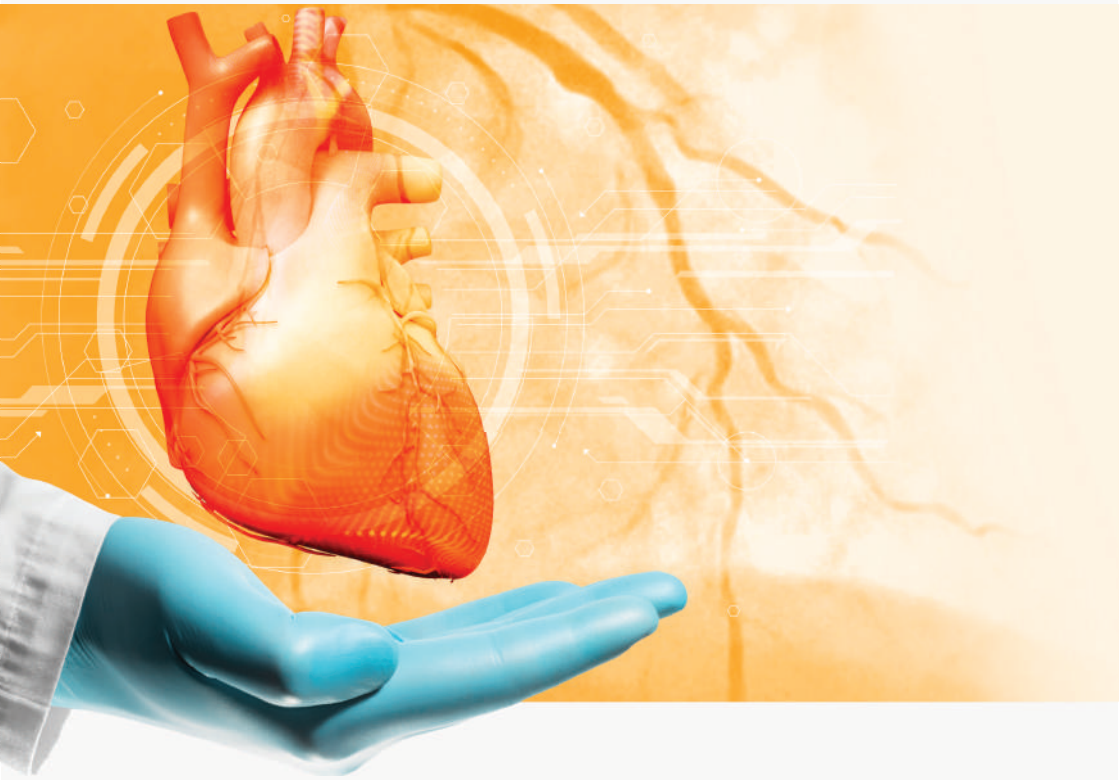
Clinical summary iVAC 2L pVAD

Percutaneous Left Ventricular Assist Device



General Context

Today, Percutaneous Mechanical Circulatory Support (MCS) can be used to facilitate High-risk Percutaneous Coronary Interventions (HR-PCIs).
The in-hospital mortality rate of high-risk PCI patients is higher than usual, and may reach up to 28% after 30 days. Against this, the increasing use of prophylactic MCS in this setting aims to provide a backup to the circulatory system from the very first minutes of the intervention. This may reduce the risk of hemodynamic instability or circulatory collapse during manipulation of the coronary arteries and provide sufficient time to achieve optimal and complete revascularization[1],

The main goals of Left Ventricular (LV) short-term MCS include:

- ✓ LV unloading
- ✓ Reduction in Myocardial Oxygen Consumption (MVO_2)
- ✓ Reduction in LV afterload
- ✓ Optimization of coronary flow and end-organ perfusion

Purpose of protected High-Risk PCI with pVAD

With prophylactic MCS in HR-PCI, operators can expect a reduction in major adverse events.

Body of Evidence

The efficacy of MCS has been suggested by multiple comparative studies:

- The Protect II trial is the largest randomized controlled trial comparing MCS with IABP in high-risk percutaneous coronary interventions. The results show a significant reduction in Major Adverse Events after 90 days in the MCS group compared to the IABP group[1].
- An analysis of 198 high-risk patients undergoing mechanically assisted HR-PCI at the Erasmus Medical Center (Rotterdam, NL) showed that MCS improved survival and reduced adverse events when compared with standard-of-care only[2].
- The PULSE trial shows LV unloading, increased mean arterial pressure (MAP) and lower myocardial oxygen consumption (MVO_2) with the use of iVAC 2L in high-risk PCI[3, 4].
- A recently published expert consensus recommends that MCS may be considered in highly selected patients undergoing HR-PCI in case of acceptable femoral access (> 6 mm in diameter of the common femoral artery with no severe tortuosity) and should be preferred instead of IABP and VA-ECMO[5].

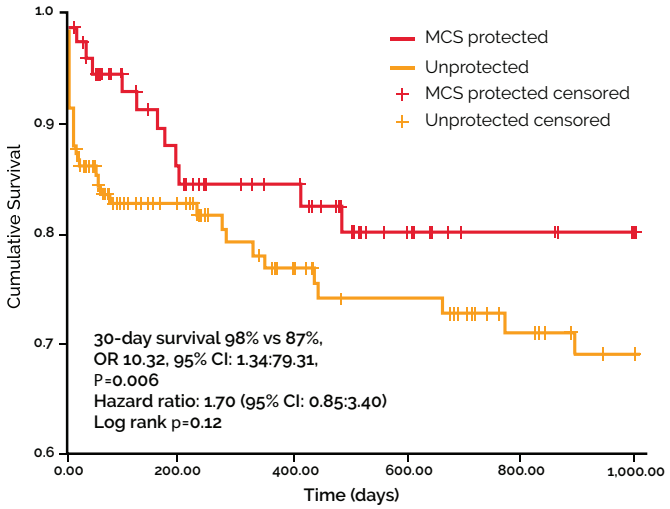


Figure 1. *Kaplan-Meyer survival curves showing that mechanically-assisted HR-PCI may have better survival compared to HR-PCI with no mechanical support. Adapted from Ameloot et Al, 2018.*

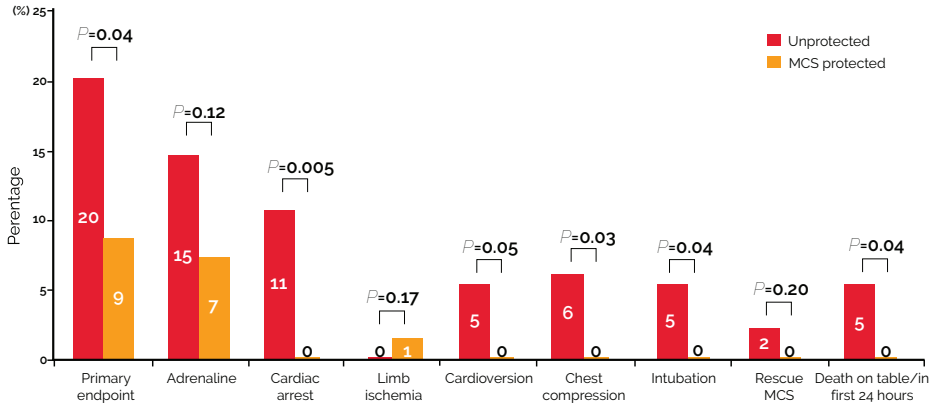


Figure 2. *Severe procedural adverse events related with the use of mechanical support during HR-PCI. The primary endpoint of the study (composite of cardiac arrest requiring resuscitation, hypotension with need for vasopressor support, need for rescue MCS, limb ischaemia with need for surgery and need for endotracheal intubation) occurred in 20% of the unprotected patients and in 9% of the MCS protected patients (OR: 0.38, 95%CI: 0.15-0.97, p = 0.04). Adapted from Ameloot et al, 2018.*

PULSE Trial[3]

- Design: prospective single-arm two center prospective cohort.
- Study population: patients undergoing HR-PCI with MCS.
- Objective: to understand the hemodynamic changes produced by iVAC 2L.
- Primary endpoint: change in pressure-volume area (PVA).
- Secondary endpoints: clinical endpoints at 30 days.

Investigators: Prof Nicolas Van Mieghem MD PhD (PI)[1], Dr M. B. Bastos MD MHSc[1], Dr J. Daemen MD PhD[1], Dr J. Schreuder MD PhD[1] and Dr S. Redwood, MD, PhD[2].

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Main results

- LV unloading with reduction in pressures and volumes in the LV chamber.
- Significant reduction in MVO_2 as demonstrated by a fall in PVA.
- Reduction in LV afterload.
- Decrease in mechanical dyssynchrony.
- Increase in MAP.

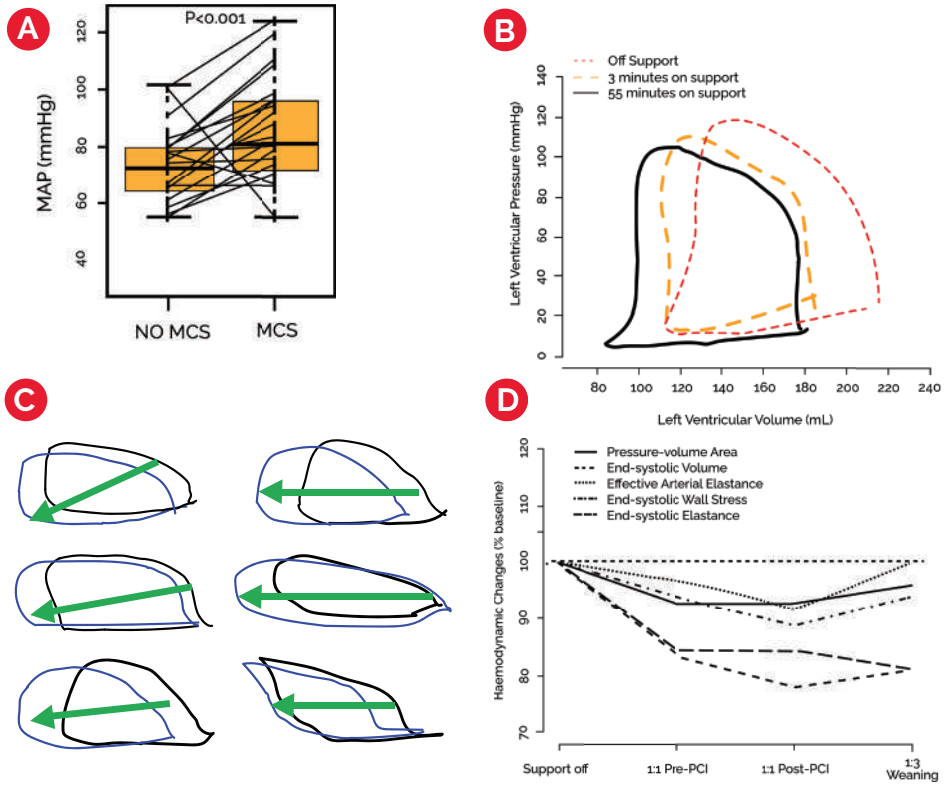

Figure 3. *(A) MCS with iVAC 2L significantly increased the mean arterial pressure (MAP) when activated. (B) Pressure-volume loops show progressive unloading of the left ventricle during the period iVAC 2L is active. (C) Pressure-volume loops from separate individuals showing left ventricular unloading with iVAC 2L activated (blue loops) as opposed to baseline (black loops) with iVAC 2L in stand-by. (D) Progression of hemodynamic markers during use of iVAC 2L show a gradual reduction in the Pressure-volume Area (MVO_2), Effective arterial elastance (afterload), wall stress and in chamber volumes. Additionally, a partial return to baseline levels can be observed at weaning.*

Conclusion

The efficacy of iVAC 2L is demonstrated by the following features:

- Unloaded the LV
- Increased the Mean Arterial Pressure by 17%
- Reduced the Afterload also by 17%
- Increased the Cardiac Power Output by 23%
- Reduced MVO_2 by 7 to 8%
- 30-day mortality (6.9%) comparable to PROTECT II (6.9%)
- Low rates of intraprocedural hemodynamical instability
- Low rates of major bleeding if operated by qualified hands

PulseCath iVAC 2L Post-Market Surveillance Registry

PulseCath maintains retrospective registry that includes data from patients receiving iVAC 2L-assisted interventions with a variety of indications. The data derives from published studies, medical records and from reports provided by PulseCath.

The current version of the registry includes data from 214 cases that originate from 67 different centers across 24 different countries in Europe, South America and Asia. The results show low rates of Major Adverse Events in elective cases of HR-PCI than observed with Impella 2.5 in other studies. iVAC 2L also improved hemodynamics in stable and shocked patients. However, more data on 30-days endpoints is needed in order to validate these findings.

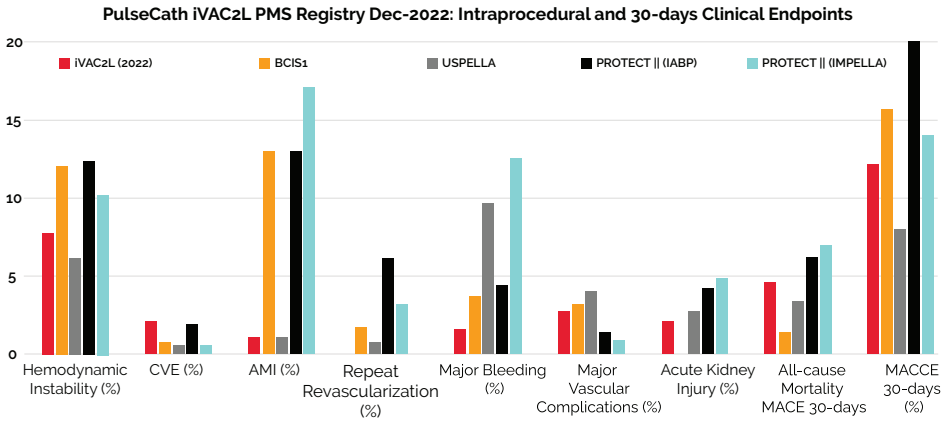

Figure 4. *Rates of major adverse events on the use of PulseCath iVAC 2L at 30 days suggest equivalent results compared to other relevant studies on short-term mechanical circulatory support.*

IVAC 2L overview

iVAC 2L is a short term, fully percutaneous, 17Fr transfemoral LVAD that effectively generates blood flow up to 2 L/min. By actively unloading the LV, the iVAC 2L provides critical haemodynamic support during high-risk revascularization procedures, in cases of acute myocardial infarction and in cardiogenic shock. [4, 6-8]

What is the labeled indication for the iVAC 2L system?

iVAC 2L is intended for use in patients with impaired LV function which require LV MCS for up to 24 hours. This includes LV support in the following situations:

- Elective or emergent HR-PCIs for Coronary Heart Disease
- Cardiogenic shock of various etiologies
- Acute Decompensated Heart failure
- High-risk electrophysiological procedures

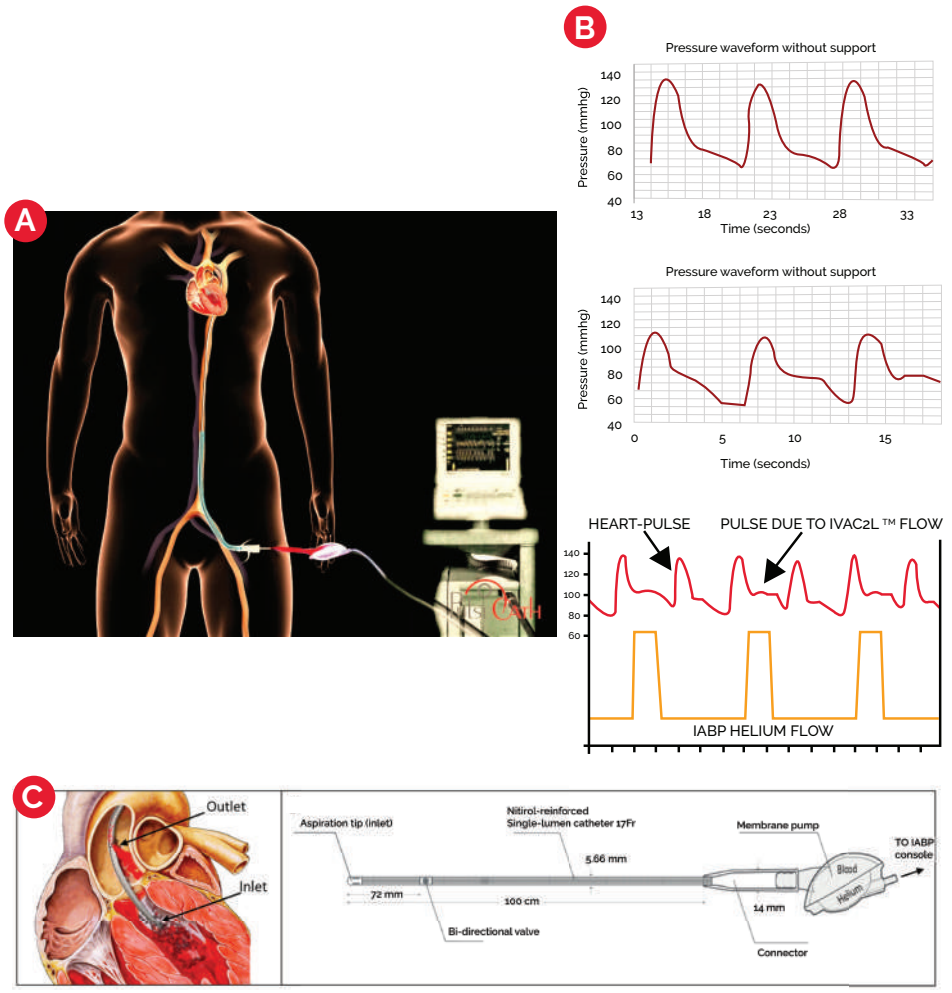

Figure 5. *(A) Implantation of iVAC 2L. The catheter is introduced through the common femoral artery and positioned with the tip inside the LV. The catheter is connected to a membrane pump which is in turn connected to a conventional IABP console. (B) Effect of iVAC 2L on the aortic pressure waveform showing diastolic augmentation and additional pulsatility in the diastolic descent. (C) Schematic view of iVAC 2L showing its main working components.*

General features:

- Trans-aortic short-term LV Assist Device
- Percutaneous insertion
- Actively ejects left ventricular blood into the ascending aorta
- 1.0 to 1.5 L/min (max. observed 2.0 L/min)[6] output to support the native heart
- Counter-pulsation system that creates additional pulsatility during diastole
- Driven by a conventional IABP console

Advantages

- ✓ Natural pulsatile support
- ✓ Fast and easy implementation
- ✓ Fully percutaneous approach
- ✓ Highly flexible catheter
- ✓ Cost effectiveness: iVAC 2L has an universally adaptable design that fully integrates with a standard IABP console

In addition, PulseCath iVAC 2L pumps using Pulsatile flow

There is a difference between pulsatile and continuous flow. Continuous flow reduces the motility of the aortic valve and may increase the aortic impedance. Furthermore, it has been related to worse end-organ perfusion. In contrast, synchronized flow as found in the iVAC 2L system creates additional pulsatility in the systemic vasculature, potentially improving peripheral perfusion. iVAC 2L may also optimize coronary blood flow thus increasing oxygen delivery to the myocardium while sparing it from the additional burden of pumping blood against increased aortic impedance[4].

References

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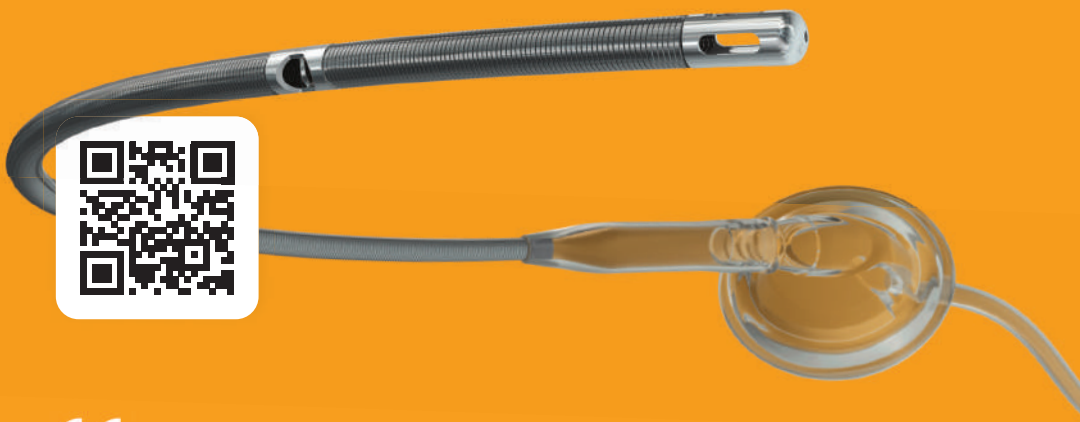
PulseCath



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