iVAC 2L Product Presentation

PulseCath

V112022_001

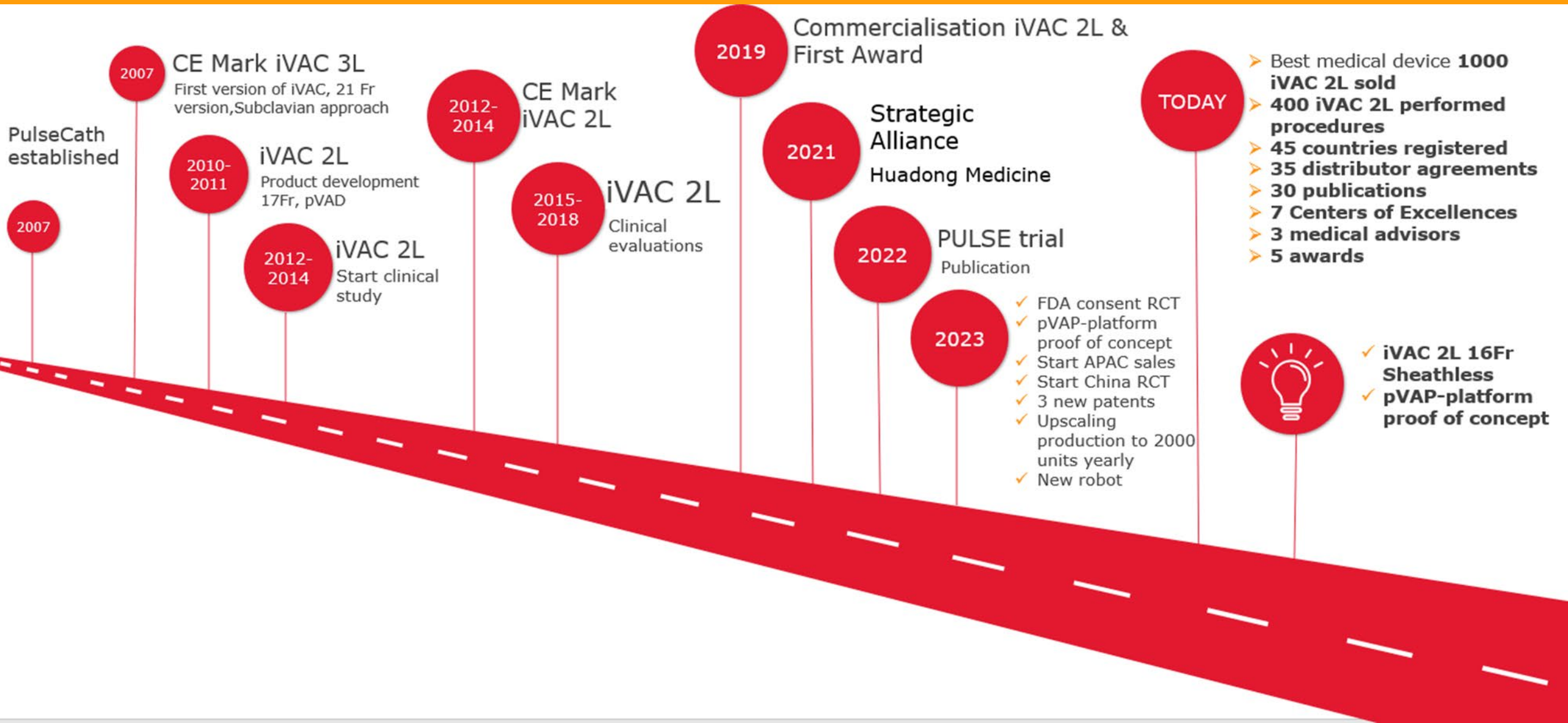
PulseCath

A Netherlands based medical device company that develops, manufactures and markets mechanical circulatory support (MCS) system.

Our Mission

To provide effective circulatory support systems to the cardiologist and the cardiac surgeon that address a wide range of patients through novel solutions that reduce healthcare costs and improve patient outcomes.

PulseCath Milestones



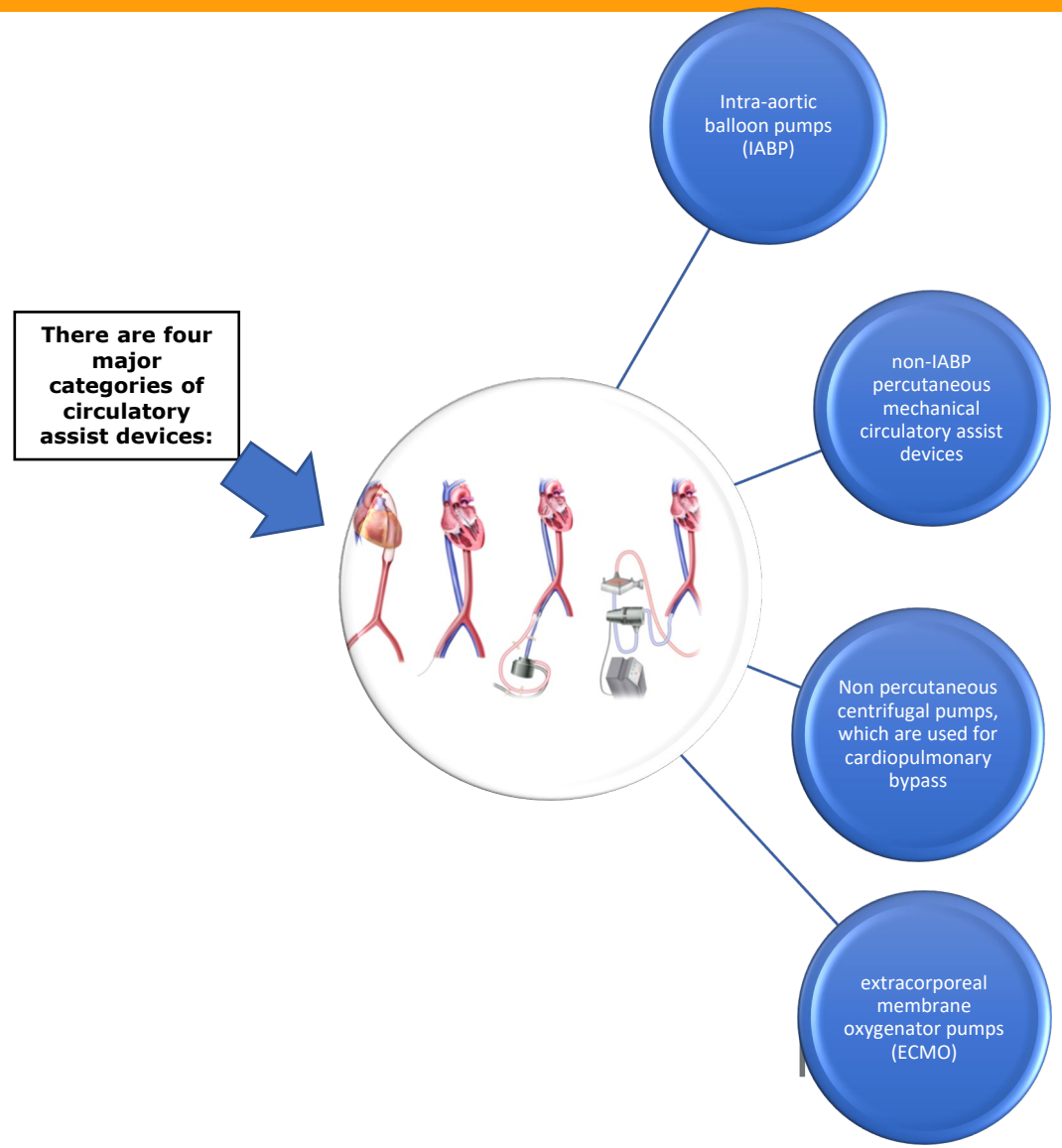
Background to Short Term Mechanical Circulatory Devices

Short-term mechanical circulatory assist devices are designed to provide hemodynamic support for a wide range of clinical conditions

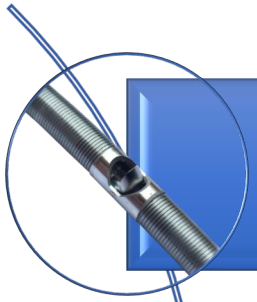
- prophylactic insertion for high-risk invasive coronary artery procedures to the management of cardiogenic shock
- acute decompensated heart failure
- or cardiopulmonary arrest

These devices provides circulatory support by performing work for a failing left or right ventricle or both

There has been a significant increase in the use of short-term percutaneous ventricular assist devices (pVADs) as acute circulatory support in cardiogenic shock and to provide hemodynamic support during interventional procedures, including high-risk PCI

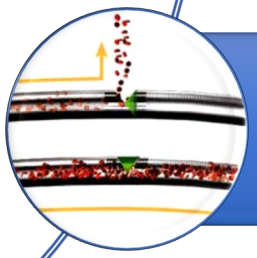


iVAC 2L



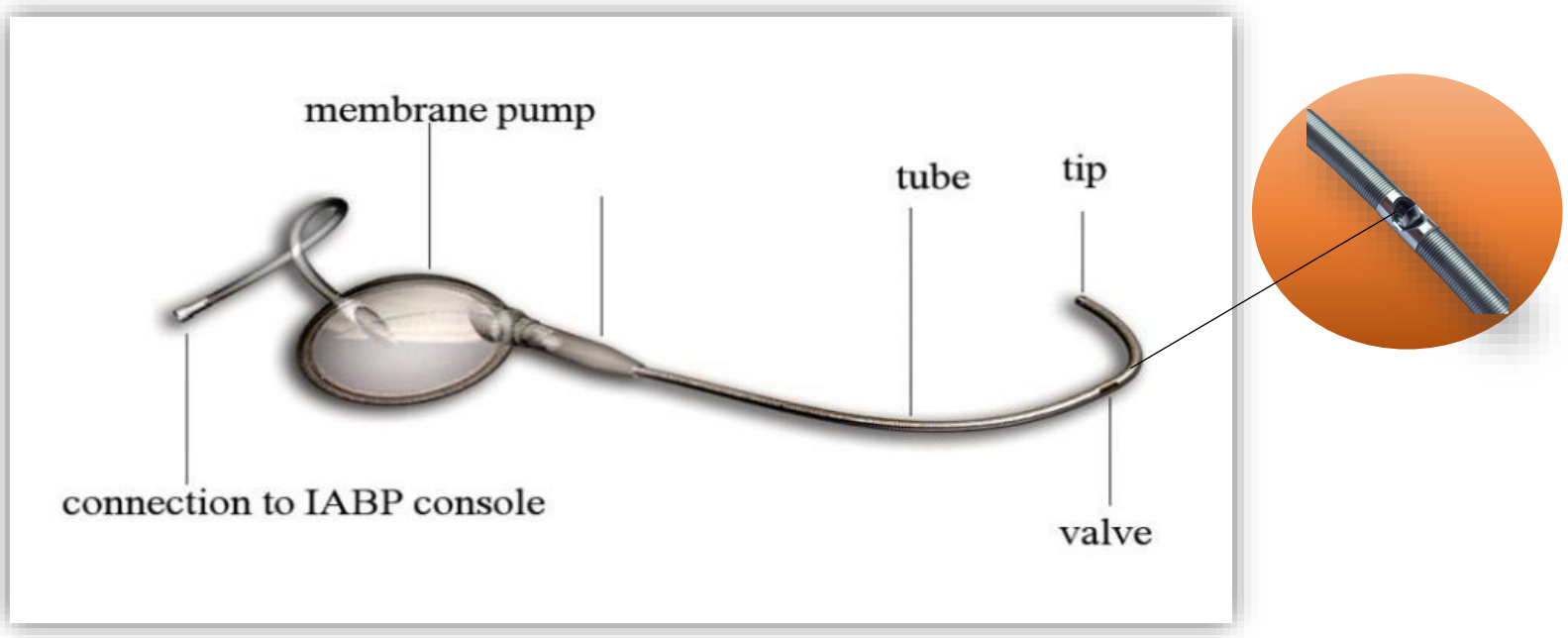
iVAC 2L is a short term Pulsatile Mechanical Circulatory Support System in the form of a pVAD (Percutaneous Ventricular Assist Device) that effectively generates blood flow of up to 1.5 liters per minute

It works by actively unloading the left ventricle to provide critical hemodynamic support for patients being treated for acute myocardial infarction and cardiogenic shock



Its application as hemodynamical backup may also result in more extensive treatment of the coronary lesions and improved long-term clinical outcomes and improve myocardial perfusion and optimize the cardiac workload, thus reducing the likelihood of peri- and post-procedural adverse events

What does it consist of?



- 17Fr flexible thin-walled catheter
- Bi-directional valve
- Single port 40cc membrane pump
- Delivered via 18Fr braided, hydrophilic delivery sheath
- Run by an IABP console

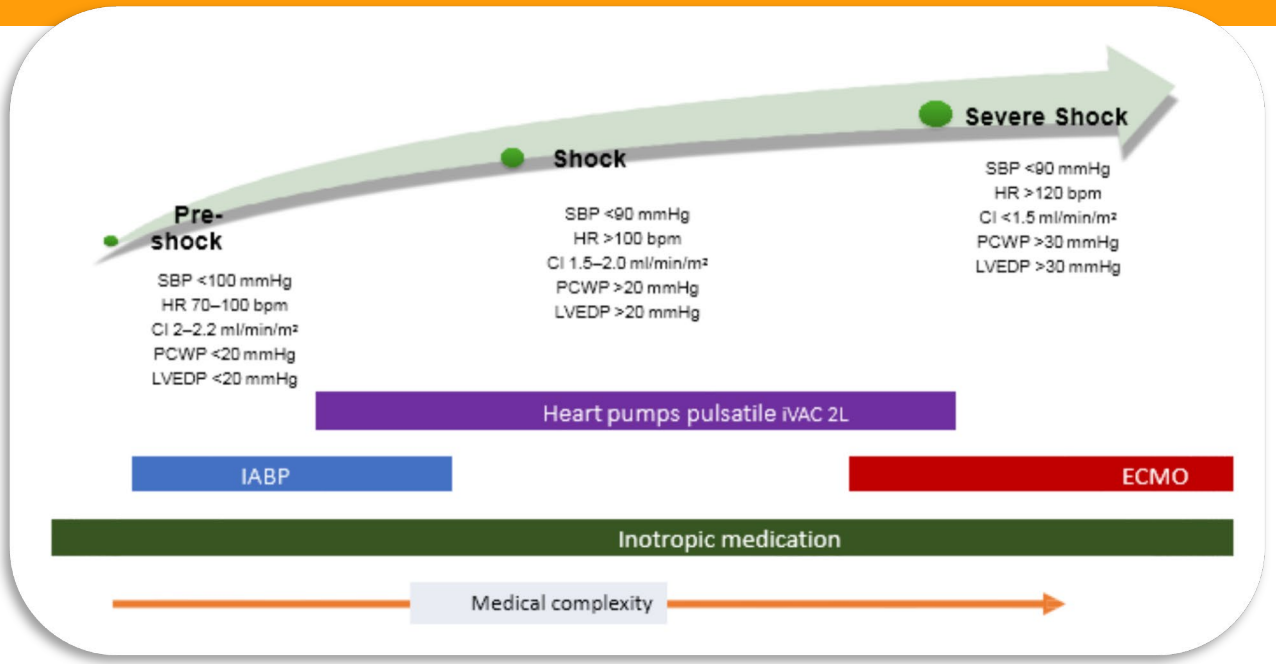
Bastos, Marcelo B et al. “PulseCath iVAC2L: next-generation pulsatile mechanical circulatory support.” Future cardiology vol. 16,2 (2020): 103-112.

Where can it be used?

Indications

Protected high-risk PCI*

Cardiogenic shock - In patients where IABP isn't enough and ECMO is too severe



*

1 Clinical characteristic + 1 Angiographic characteristic

Clinical Characteristic	Angiographic Characteristic
• LVEF < 35%	• Diffuse CAD
• Hemodynamic Instability	• Multivessel Disease
• Diabetes Mellitus	• Unprotected LM involving bifurcation
• Acute Coronary Syndrome	• Severe Coronary Total Occlusion
• Previous Cardiac Surgery	• Rotational Atherectomy
• Chronic Kidney Disease	• Late Patent Conduit

Contra indications include*: Femoral artery diameter <6mm, Severe Aortic stenosis, Thrombus in LV, Presence of a mechanical aortic valve

*please check the PulseCath iVAC 2L Instructions for Use for other contra indications

Arri, Satpal S et al. "Myocardial revascularisation in high-risk subjects." Heart (British Cardiac Society) vol. 104,2 (2018): 166-179.

Bastos, Marcelo B et al. "PulseCath iVAC2L: next-generation pulsatile mechanical circulatory support." Future cardiology vol. 16,2 (2020): 103-112.

J Am Coll Cardiol. 2015 May 19;65(19):e7-e26

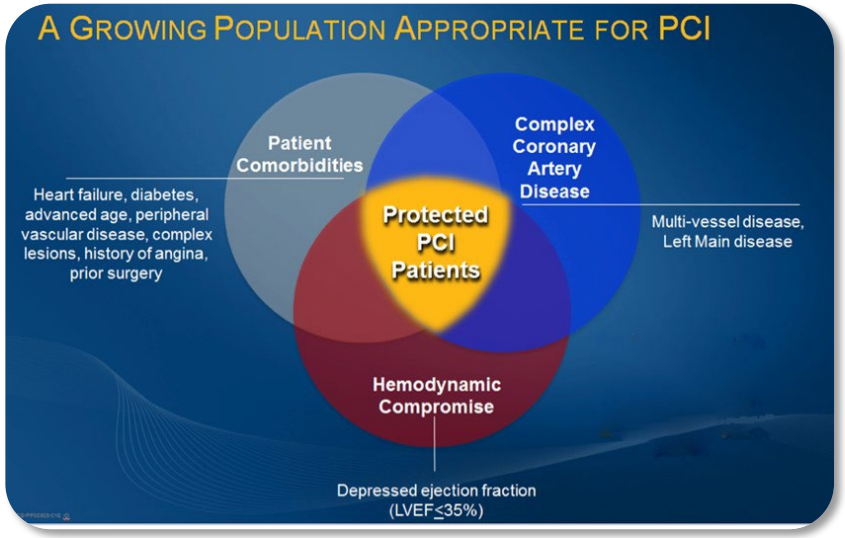
Percutaneous Coronary Intervention

- Percutaneous coronary intervention (PCI) is a non-surgical procedure used to treat narrowing of the coronary arteries of the heart found in coronary artery disease

- Indications for PCI include the following: Acute ST-elevation myocardial infarction (STEMI) Non–ST-elevation acute coronary syndrome (NSTE-ACS) Unstable angina

- More than 600 000 (PCIs) are performed in the United States each year, accounting for over $12 billion in healthcare spending.

- The number of PCI centers has grown 21.2% over the last 8 years
  - 39% of all hospitals having interventional cardiology capabilities

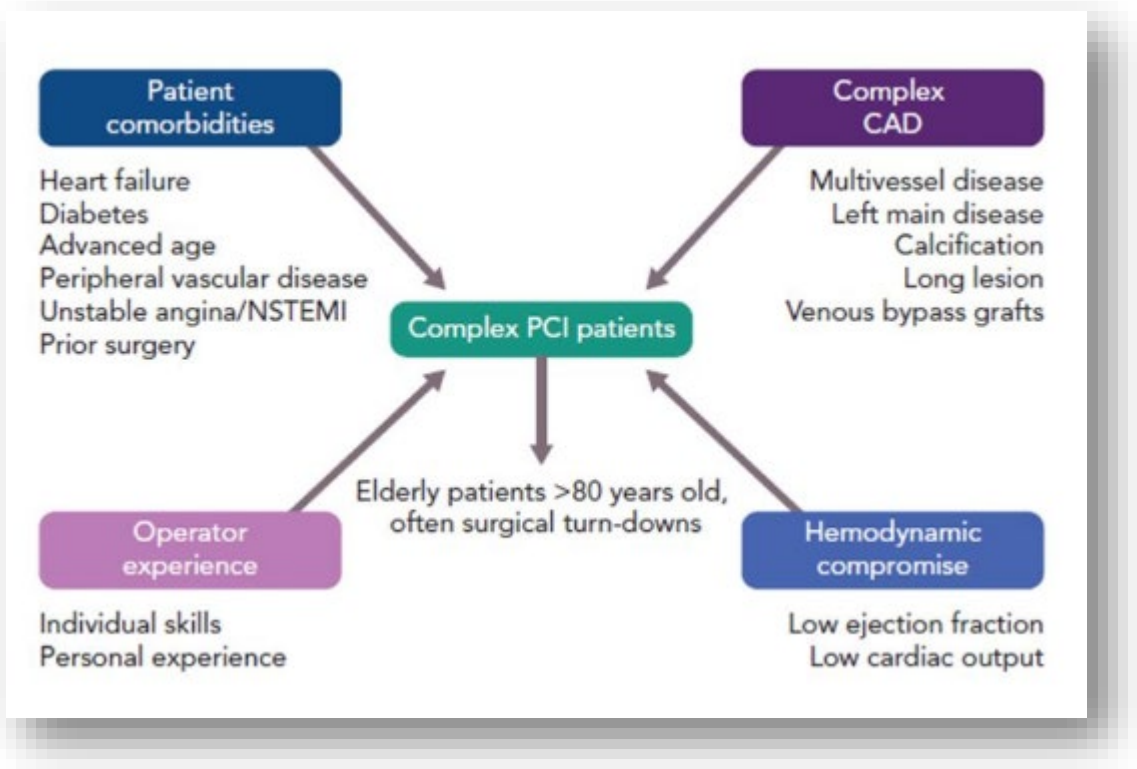


Theodore Bass, MD, from University of Florida College of Medicine

Appropriateness of Percutaneous Coronary Intervention
Paul S. Chan

Types of PCI and what constitutes high-risk PCI?

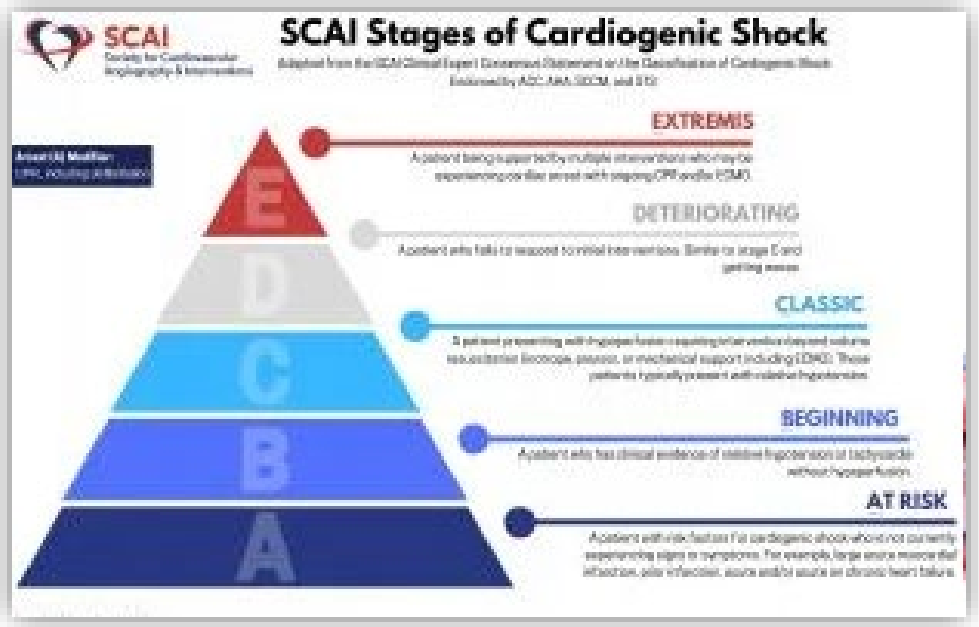
- Balloon angioplasty
- Laser angioplasty
- Rotational atherectomy
- Angioplasty with a stent
- MCS-supported PCI



*Arri, Satpal S et al. "Myocardial revascularisation in high-risk subjects." Heart (British Cardiac Society) vol. 104,2 (2018): 166-179.

Cardiogenic Shock

- Cardiogenic shock remains a challenging condition with mortality rates of approx 50%
- Cardiogenic shock is essentially circulatory failure, as a consequence of left, right or biventricular dysfunction
- The heart in unable to sufficiently pump enough blood to meet needs of the body
- Heart problems that cause cardiogenic shock include:
  - Unstable angina
  - Heart attack/myocardial infarction
  - Certain abnormal heart rhythms
  - Heart failure
  - Heart defects



Challenges in the conduct of randomised controlled trials in cardiogenic shock complicating acute myocardial infarction
Anne Freund

Cardiogenic Shock

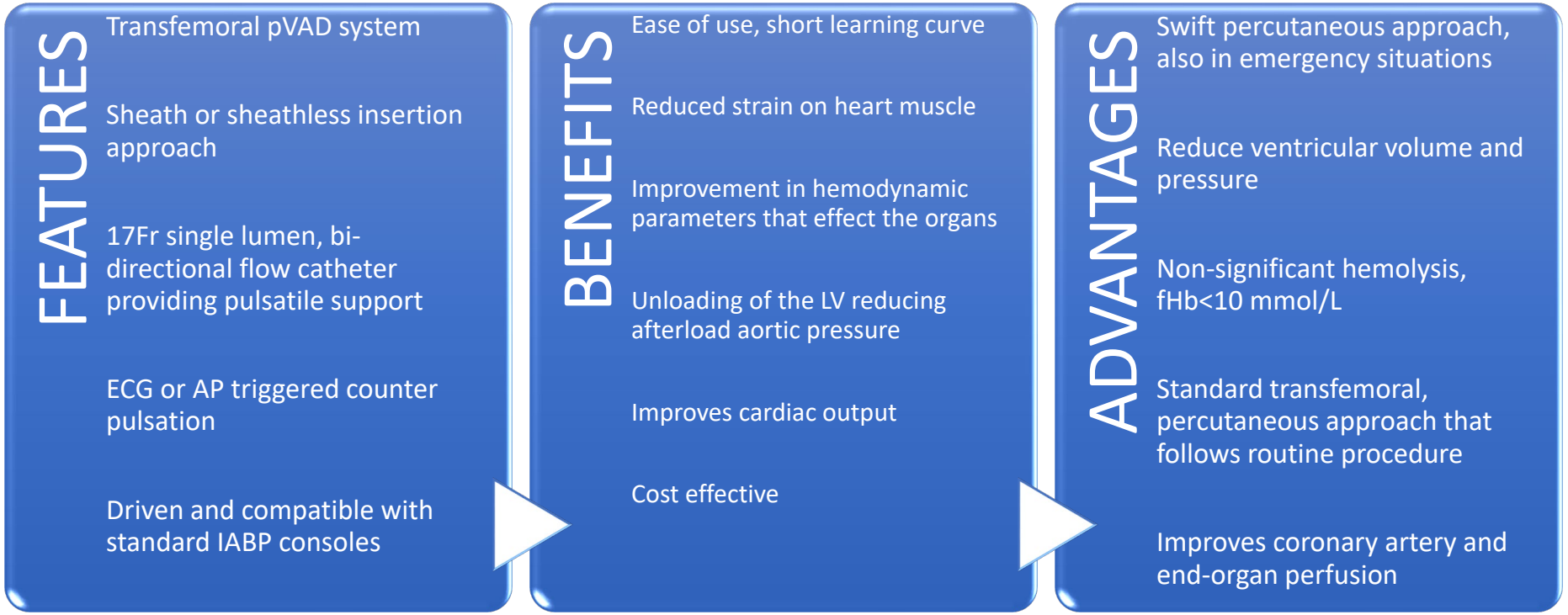
- Cardiogenic shock is not only decreases cardiac contractile function, but is responsible for multiorgan dysfunction syndrome involving the entire circulatory system

- Cardiogenic shock is managed by early diagnosis and directed therapy to optimize oxygen delivery and tissue perfusion

- The field of temporary mechanical circulatory support to manage patients with cardiogenic shock has advanced in the last decade

- Early intervention with adequate selection of the most appropriate mechanical circulatory support device may improve outcomes

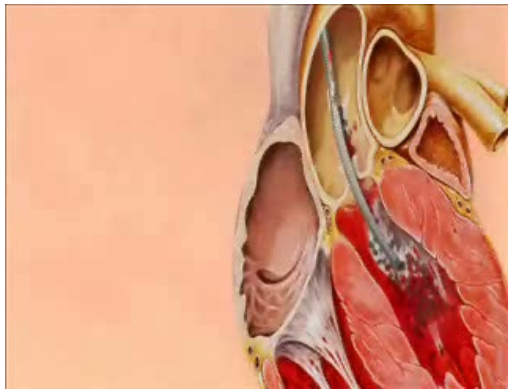
iVAC 2L: Features – Benefits - Advantages



How does it work?

- The iVAC 2L is activated by standard IABP console that is triggered by ECG /AP

- The helium from IABP console is “pushing and pulling” the iVAC 2L membrane pump synchronized with heart beats

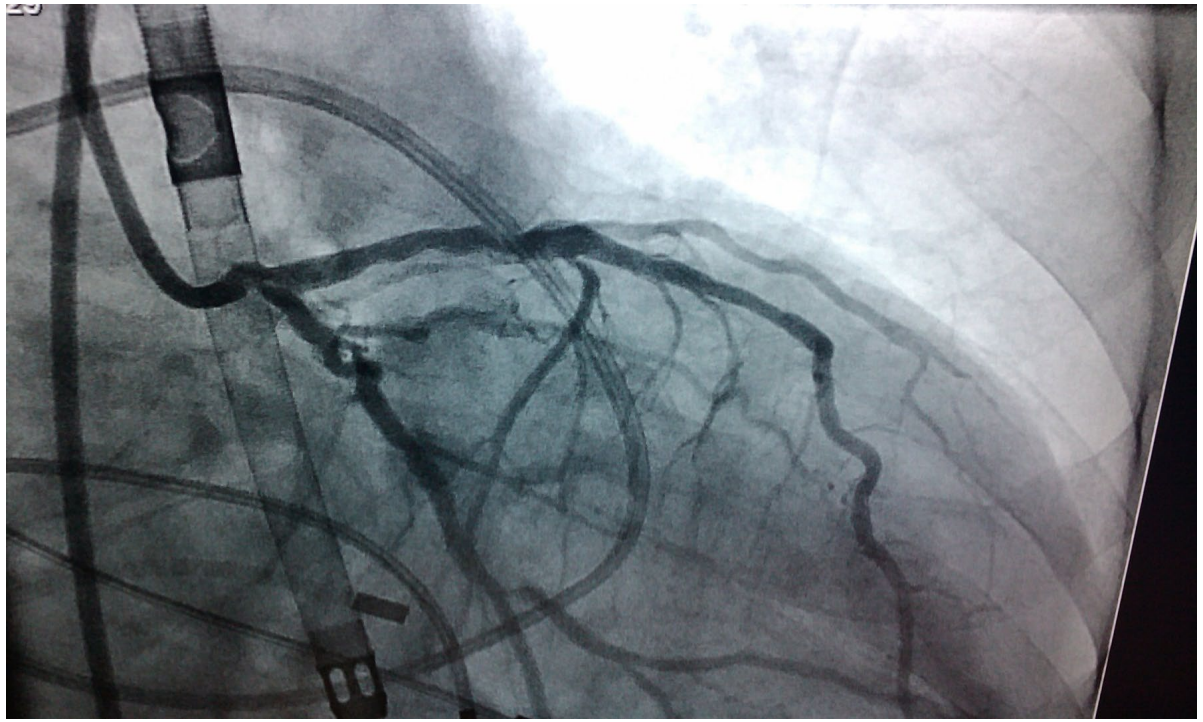


- During systole, blood enters the catheter through its tip located at the left ventricular and is aspirated into the membrane pump

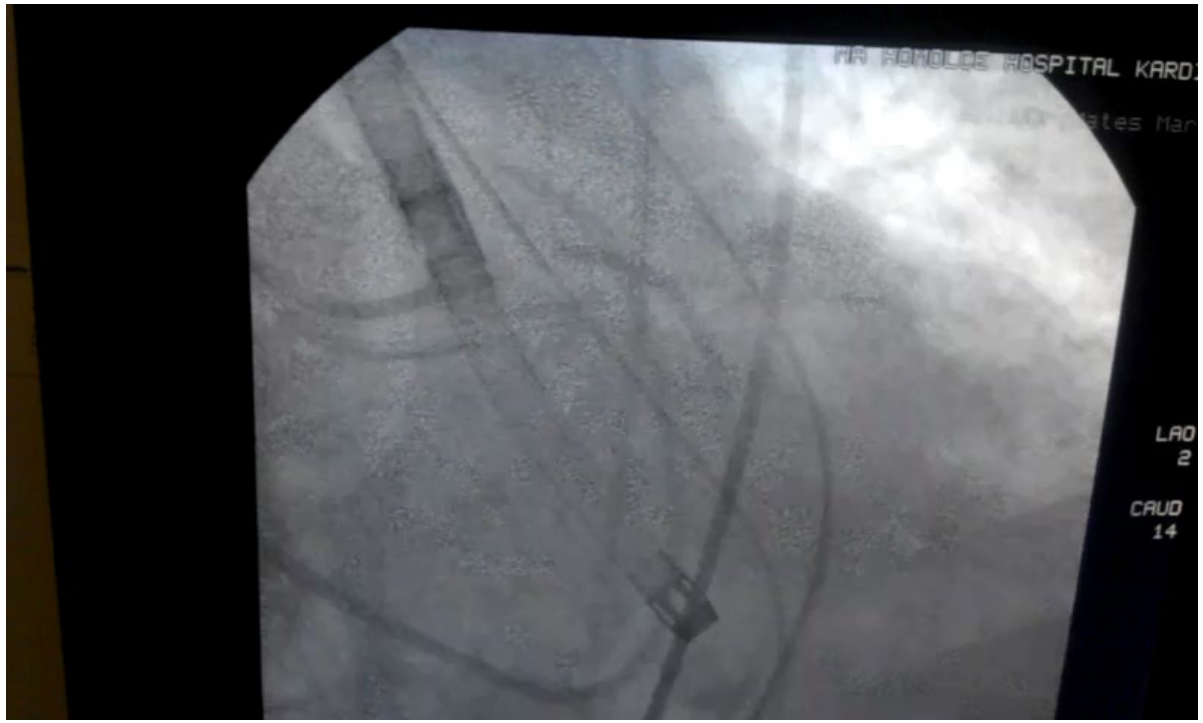
- The membrane pump pushes the blood back in the catheter, the valve at the side hole opens, and ejects the blood out sideways to aorta during diastole

View on X-ray

iVAC 2L in position on X-ray

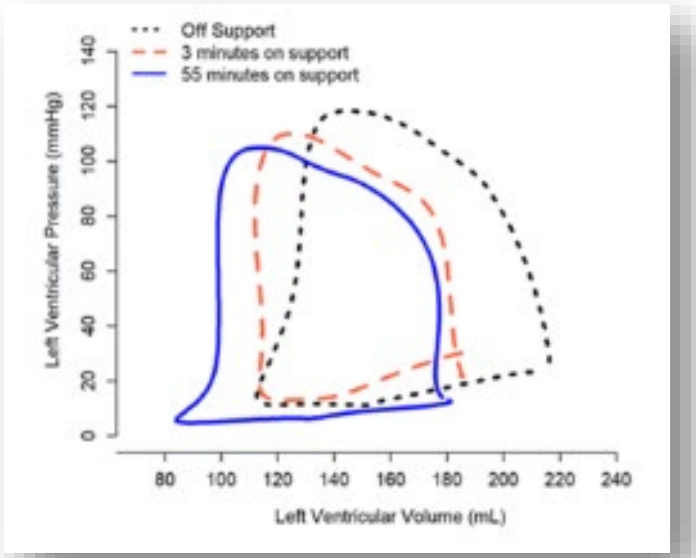


iVAC 2L in action as seen on Fluoroscopy

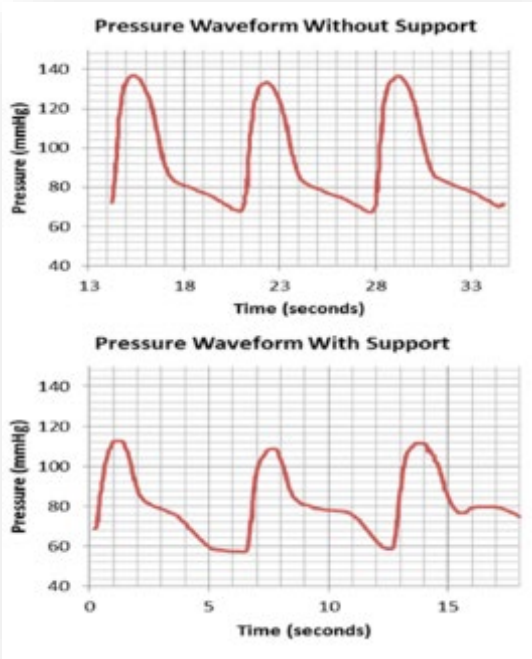


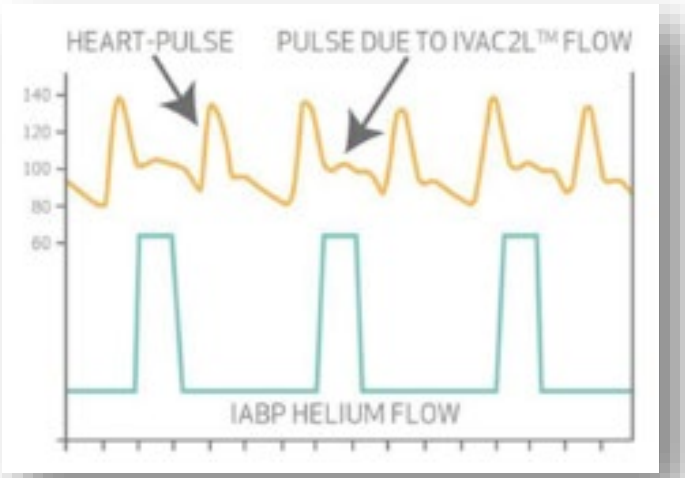
Impact of iVAC 2L as seen on PV Loop and Waveform

A significant shift to the left and south is observed on use of iVAC 2L



iVAC 2L increases pressure diastolic providing additional diastolic flow without taking over LV ejection fraction volume

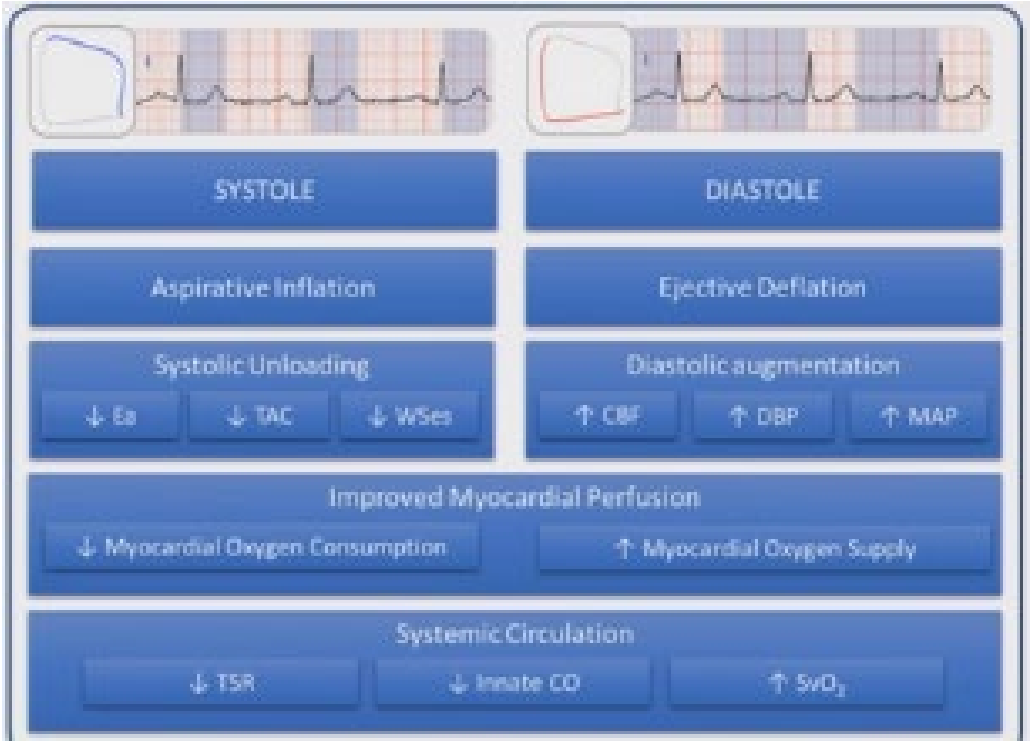




Bastos, Marcelo B et al. “PulseCath iVAC2L: next-generation pulsatile mechanical circulatory support.” Future cardiology vol. 16,2 (2020): 103-112.

iVAC 2L Mechanical Unloading

- Impact of iVAC 2L in heart failure patients
  - Improvement in heart work efficacy
  - Improvement in systematic hemodynamics
- LV volumes and pressure show significant increase
- The Arterial Elastance (Ea), reflecting the forces opposing blood ejection by the LV, is reduced significantly and consistently after activation of iVAC 2L
- Total systemic resistance is significantly reduced after iVAC 2L activation as the blood reaches the peripheral circulation more easily
- The global cycle efficiency is significantly improved



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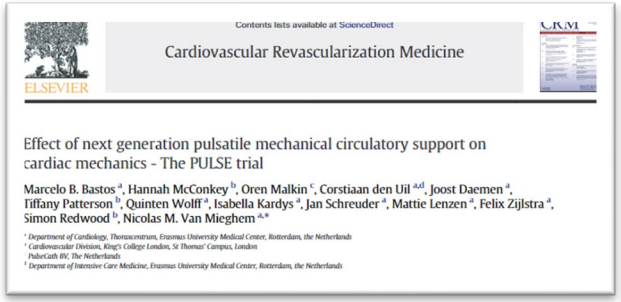
Clinical Studies

- Over 30 articles and trials published
- 15 since 2017
- PULSE Trial* most recently published in the CRM

*Effect of next generation pulsatile mechanical circulatory support on cardiac mechanics - The PULSE trial. Cardiovascular Revascularization Medicine, March 2022
Marcelo B. Bastos , Hannah McConkey, Oren Malkin, Corstiaan den Uil, Joost Daemen, Tiffany Patterson, Quinten Wolff, Isabella Kardys, Jan Schreuder, Mattie Lenzen, Felix Zijlstra, Simon Redwood, Nicolas M. Van Mieghem

Effect of next generation pulsatile mechanical circulatory support on cardiac mechanics – The PULSE trial



Contents lists available at ScienceDirect

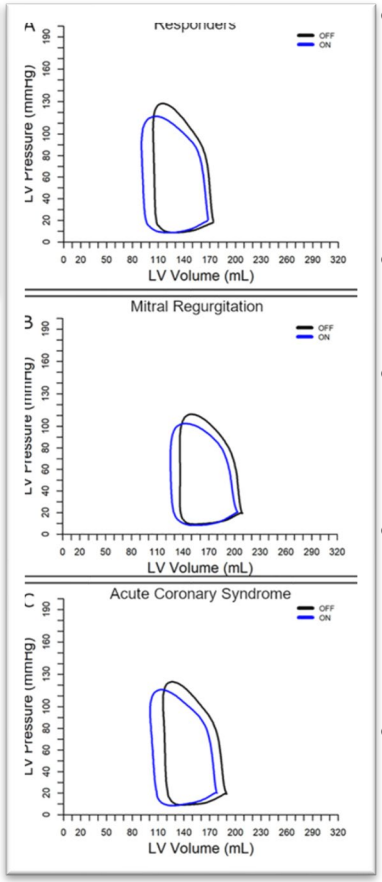
Cardiovascular Revascularization Medicine

ELSEVIER

Effect of next generation pulsatile mechanical circulatory support on cardiac mechanics - The PULSE trial

Marcelo B. Bastos [a], Hannah McConkey [b], Oren Malkin [c], Corstiaan den Uil [a,d], Joost Daemen [a], Tiffany Patterson [b], Quinten Wolff [a], Isabella Kardys [a], Jan Schreuder [a], Mattie Lenzen [a], Felix Zijlstra [a], Simon Redwood [b], Nicolas M. Van Mieghem [a,*]

[a] Department of Cardiology, Thoraxcentrum, Erasmus University Medical Center, Rotterdam, the Netherlands
[b] Cardiovascular Division, King's College London, St Thomas' Campus, London
[c] PulseCath BV, The Netherlands
[d] Department of Intensive Care Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands

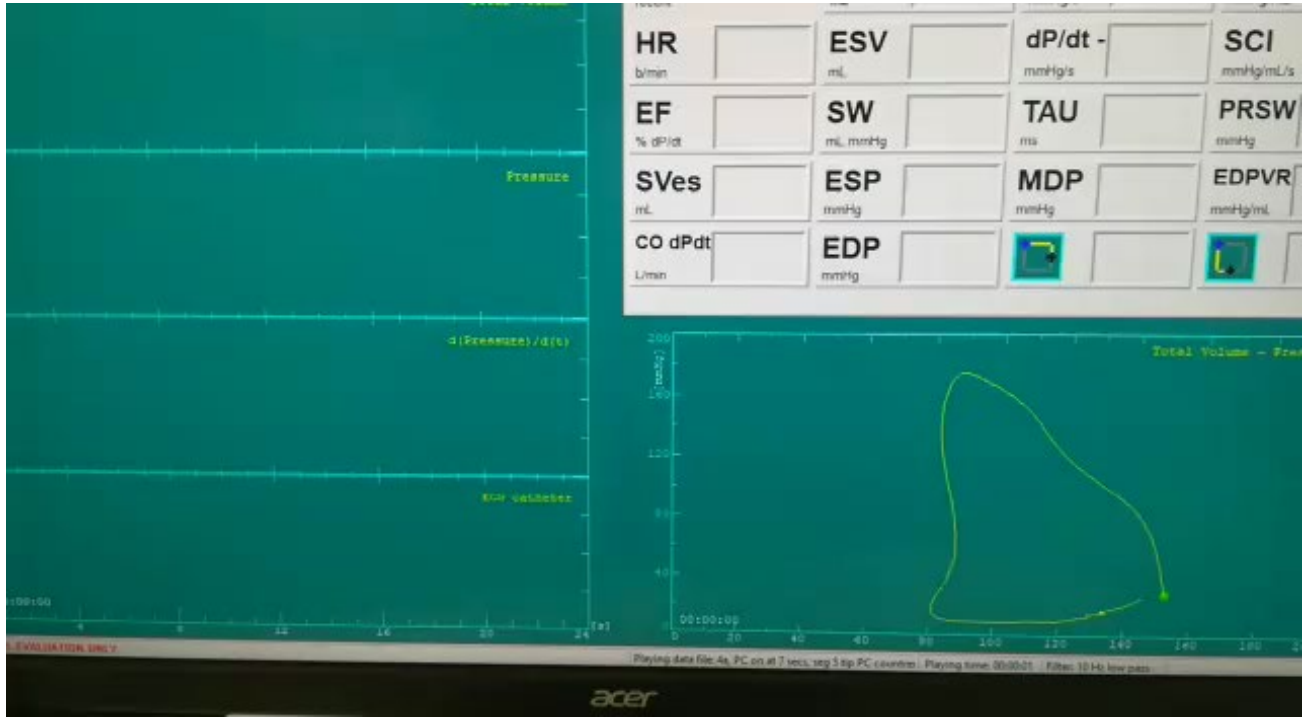


- Mechanical circulatory support with PulseCath iVAC 2L in high-risk percutaneous coronary interventions offers LV unloading and reduces myocardial oxygen consumption particularly in patients with acute coronary syndrome or concomitant mitral regurgitation
- The mean age was 74 (IQR: 70–81) years and the mean SYNTAX score was 31 ± 8.3
- Left ventricular unloading with iVAC 2L MCS was demonstrated in 82% of patients with complete PV studies
- 90% of Patients with moderate or severe mitral regurgitation or presenting with acute coronary syndrome (ACS) were most responsive to iVAC 2L unloading
- In 81% of patients significant reductions in afterload (Ea: −19%) with increases in stroke volume (+11%) and cardiac output (+11%)

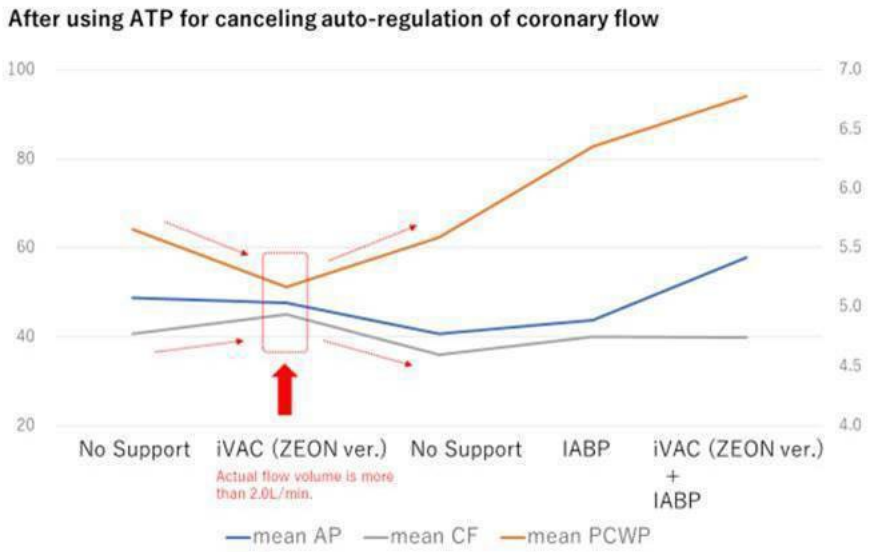
Clinical outcome PULSE trial

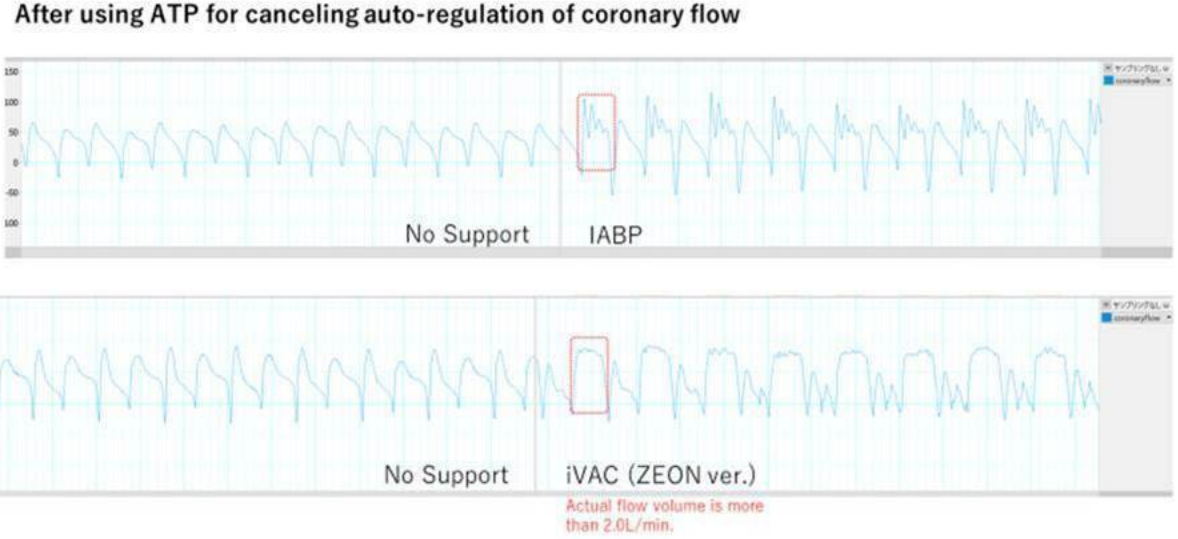
PCI was feasible with iVAC 2L MCS in patients with advanced coronary artery disease and very high to prohibitive operative risks

- Procedural success in 91% of cases
- Reduction in Syntax score from 37± 19 to 4.0 (IQR: 0 to 15.12)
- 30-day mortality 6.9%; comparable to PROTECT II outcomes: IABP 6.2% and Impella 6.9%
- PULSE patients were at higher risk than in PROTECT II study yet procedures were more extensive and support times were shorter



September 2021 Tokyo University – Dr. Saku





Comparison coronary flow iVAC 2L vs IABP

- Total 2L 16 Vol >2L/m (Zeon IABP Console)
- iVAC 2L increased coronary flow with reducing Pressure of left ventricular
- iVAC 2L decrease PCWP (Pulmonary capillary wedge pressure)
- iVAC 2L Waveform of coronary flow is different from its of IABP

Registry PMS - 174 patients – 24 Countries - 67 centers

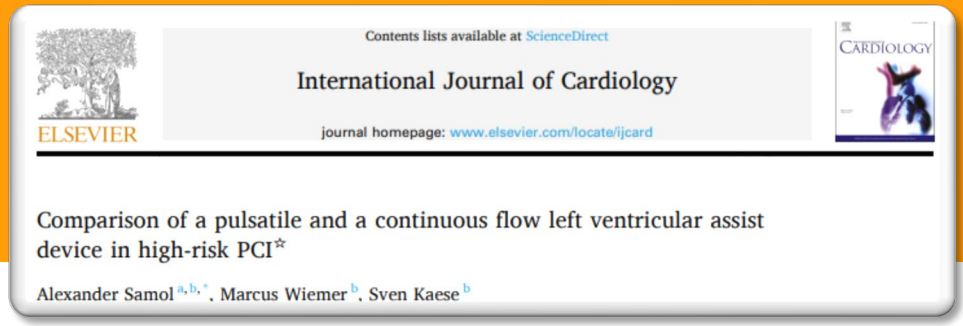
April 2022

- Mean age was 69±11 years. (SYNTAX 37)
- Patients tended to have multivessel disease and low ejection fraction (EF< 35%).
- The median support time (IQR) of 71 (51-114) minutes.
- An average flow of 1.5±0.2L/min.
- Significant LM obstruction and three-vessel disease were present in 59% and 54% respectively.
- **Intraprocedural complications** that resulted in the removal of the device in only two cases (1.1%).
- **Repeat Revascularization 0%** Vs 3.2% Impella and 6.2% IABP*.
- **Major Bleeding 3%.** Vs 5.1% Impella and 3.3% IABP*.
- **Hemodynamic Instability 7.7%** Vs 10.2% Impella and 12.3% IABP*
- **MACCE** 30 Days – 12.1%** Vs 14% Impella and 20% IABP*
- **Hemolysis (Clinical relevant) 0%** Vs 11.8% Impella and 0% IABP*
- **Acute Kidney Injury – 6.1%** Vs 13% Impella and 4.2% IABP*

*Comparison to Protect II and IMP-IT studies

** MACCE: composite endpoint of death, myocardial infarction, stroke and repeat revascularization after 30 days. TIA: Transient Ischemic Attack. AMI

iVAC 2L vs Impella 2.5



- 40 patients iVAC 2L vs Impella 2.5 during protected high-risk PCI(LVEF 33%)
- PCI Success in 98% of cases
- Both devices led to a significant increase in aortic pressure
- Both devices ensured stable hemodynamic conditions for performing successful high-risk PCI
- Complication rates by use of both devices seem acceptable
- Signs of potential hemolysis were only present under Impella 2.5
- High-risk PCI's under mechanical circulatory support by the pulsatile iVAC 2L or the continuous flow Impella 2.5 device are feasible and safe

Alexander Samol, Marcus Wiemer, Sven Kaese. Comparison of a pulsatile and a continuous flow left ventricular assist device in high-risk PCI. International Journal of Cardiology May 2022

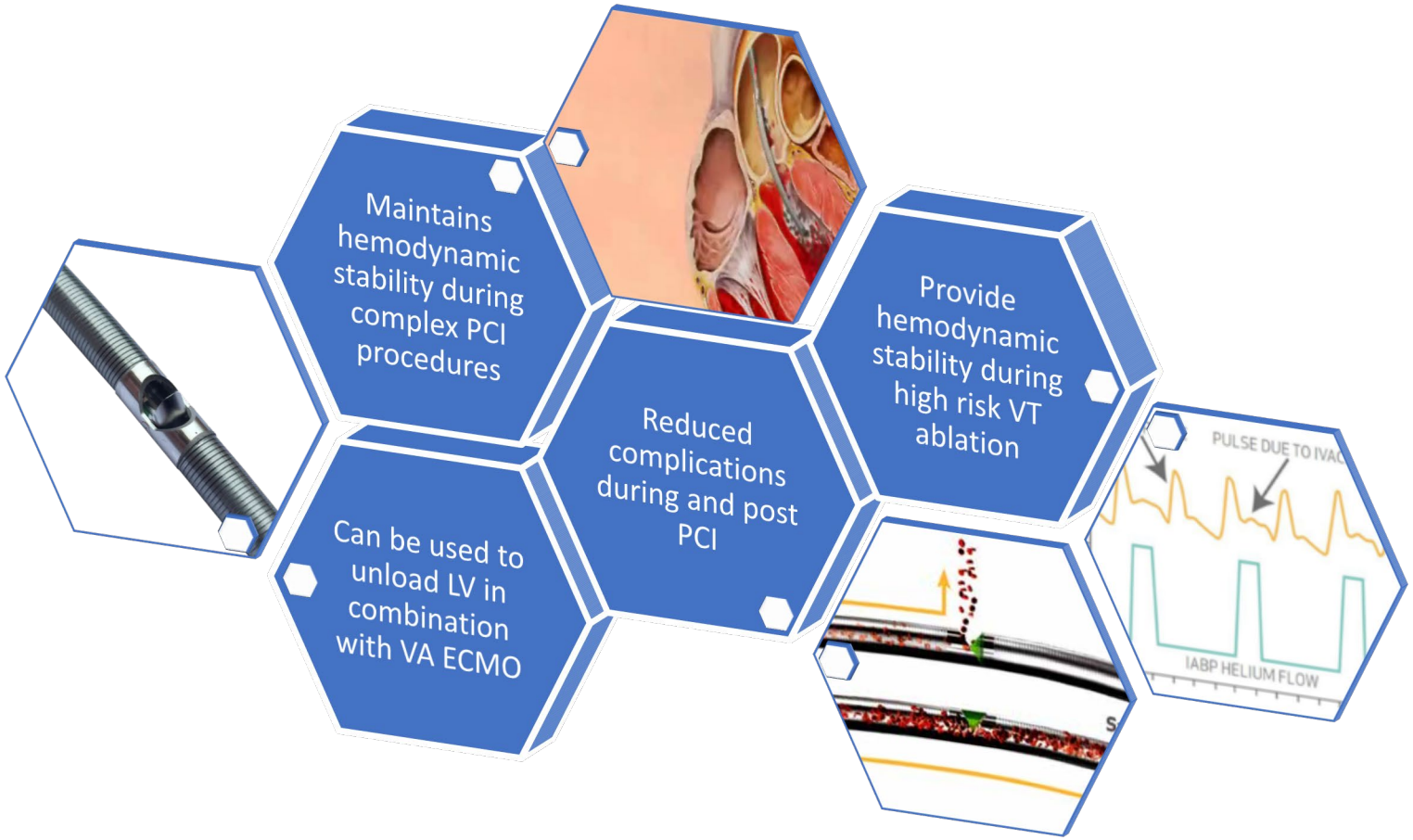
Why use a Short Term Mechanical Circulatory Device during high-risk PCI?

Performing high-risk PCI's normally create heart deuteration during blocking LM coronary with balloon

In many cases this can force to stop procedure in order to let myocardial to recover

In order to get to maximum outcome from one procedure the iVAC 2L can prevent patient collapsing and give the "safety net" needed to continue for next steps

Not using safety net pump during these cases force you to perform the procedure in high speed only by senior and well experienced doctors



* Ameloot K, B Bastos M, Daemen J, Schreuder J, Boersma E, Zijlstra F, Van Mieghem NM.Top of Form New Generation mechanical circulatory support during high-risk PCI: a cross sectional analysis. EuroIntervention 2019.

Guidelines Europe

IABP is not recommended for use in high-risk PCI procedures

European Guide lines recommendation (July 2021)

- Joint EAPCI/ACVC expert consensus document on percutaneous ventricular assist devices. Eurointervention. 10.4244/EIJY21M05_01
- European CE Mark since 2015 No. 144876 – Valid till April 2024

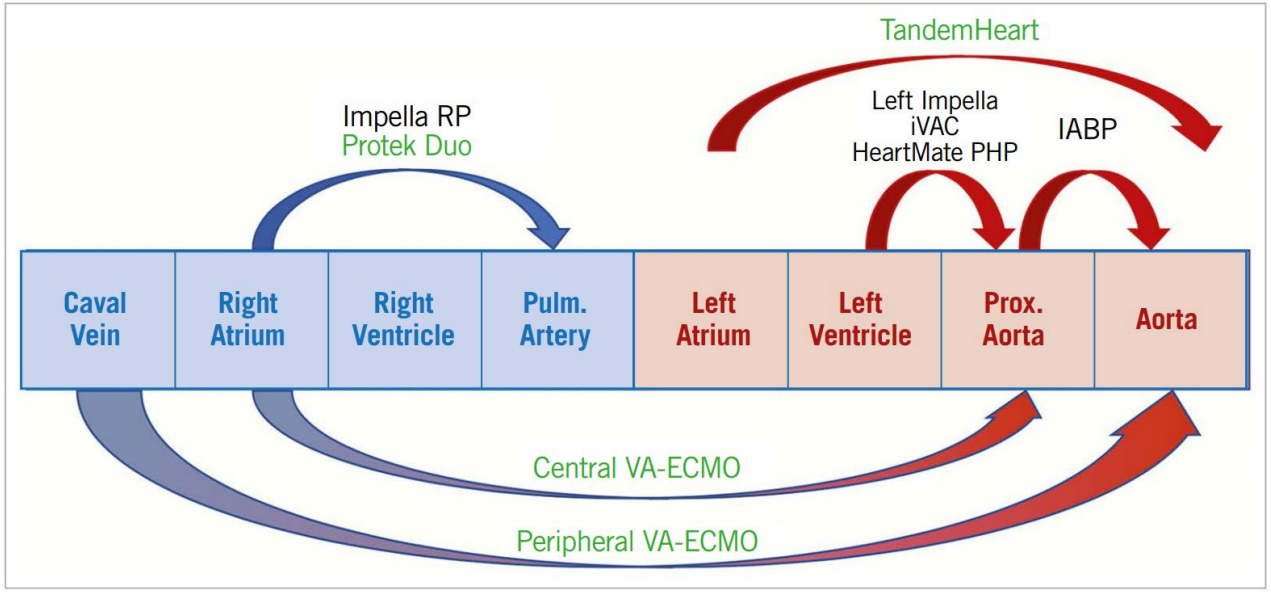


Table 2. Indication for pVAD-support in HR-PCI[a].

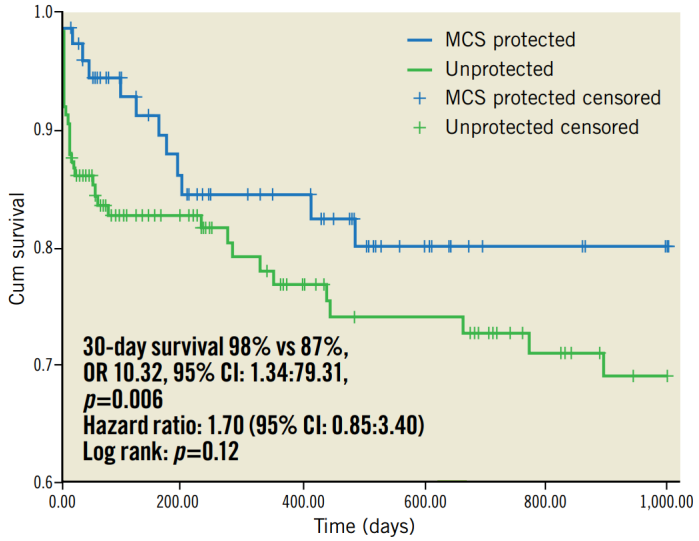
Device	Indication	Evidence
IABP	Should not be used	BCIS-1[10]
AFP	May be considered in highly selected patients undergoing HR-PCI in case of acceptable femoral access (>6 mm diameter common femoral artery, no severe tortuosity)	PROTECT II[11] and cohort studies[12-15]
VA-ECMO	Should not be used	No data available

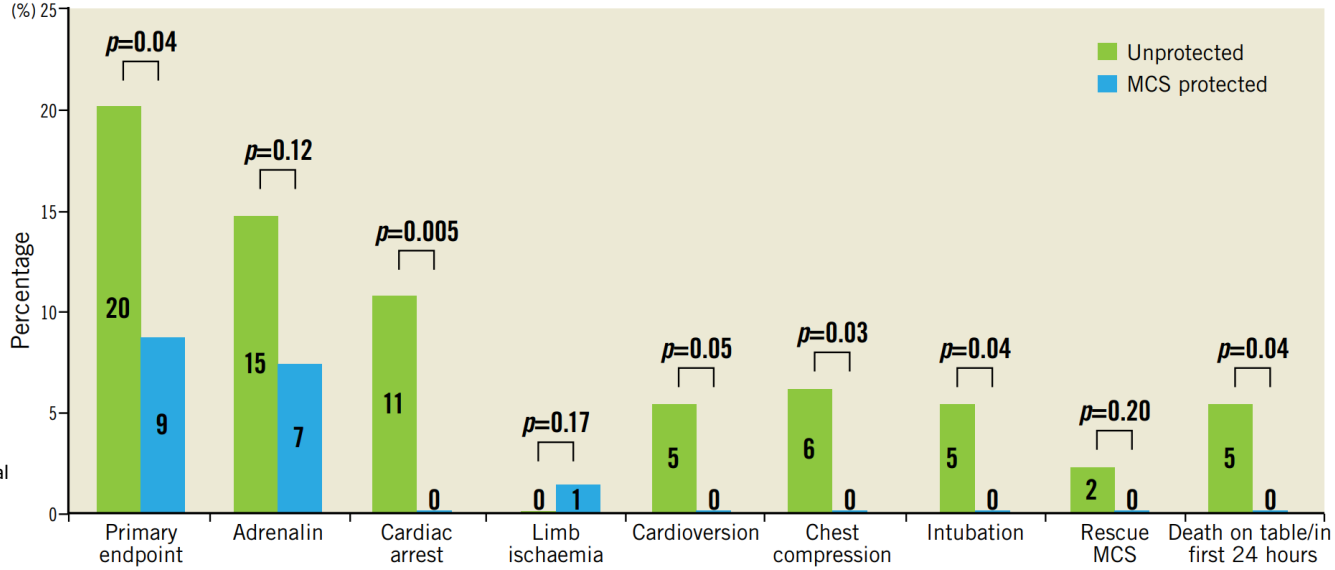
AFP: microaxial flow pump; HR-PCI: high-risk percutaneous coronary intervention; IABP: intra-aortic balloon pump; VA-ECMO: veno-arterial extracorporeal membrane oxygenation. [a]There is no common definition of HR-PCI. PCIs might be considered as high risk in patients satisfying the followings clinical and/or anatomical high-risk criteria: clinical characteristics [stable/decompensated LVEF <35%, haemodynamic instability, diabetes mellitus, acute coronary syndromes (ACS), previous cardiac surgery, chronic kidney disease] angiographic characteristics (diffuse CAD, multivessel disease, unprotected left main coronary disease involving bifurcation, severe coronary total occlusion, severely calcified lesions needing rotational atherectomy, last patent conduit).[2]

* Joint EAPCI/ACVC expert consensus document on percutaneous ventricular assist devices. European Heart Journal: Acute Cardiovascular Care (2021) 10, 570–583 doi:10.1093/ehjacc/zuab015

In conclusion

" In a consecutive real-world cohort of high-risk PCI patients, **protection with new-generation MCS resulted in better procedural outcomes** despite worse EF and more complex coronary artery disease at baseline"





Ameloot K, B Bastos M, Daemen J, Schreuder J, Boersma E, Zijlstra F, Van Mieghem NM.Top of Form New Generation mechanical circulatory support during high-risk PCI: a cross sectional analysis. EuroIntervention 2019.

The effect of pulsatile support over continuous flow?

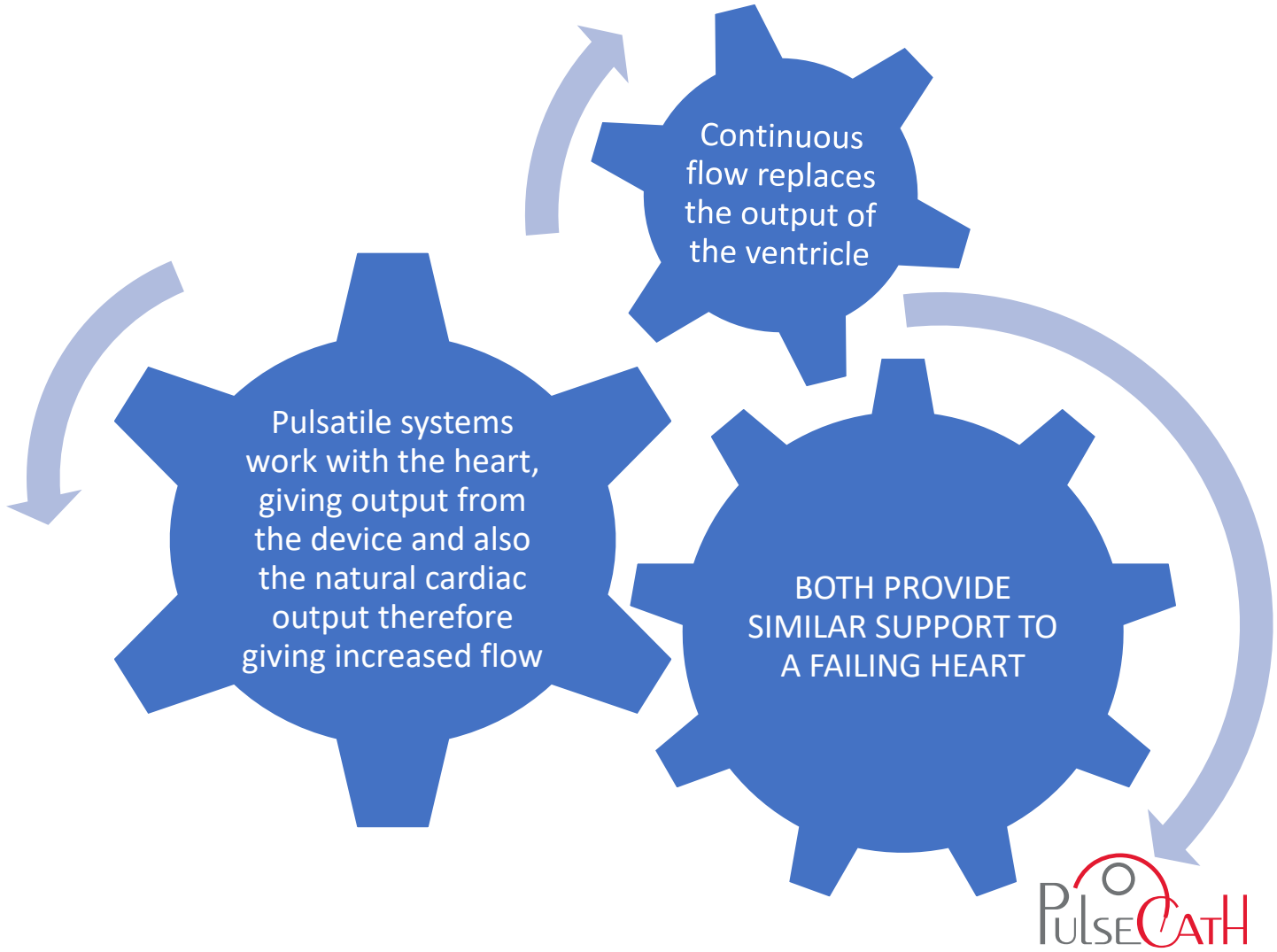
Stroke volume of heart

+

stroke volume of device

≈

pumping greater volume of blood through the body



Bastos, Marcelo B et al. "PulseCath iVAC2L: next-generation pulsatile mechanical circulatory support." Future cardiology vol. 16,2 (2020): 103-112.

What are the risks of hemolysis using iVAC 2L?

- Every pump creates some level of blood destruction
- iVAC 2L almost does not damage the RBCs due to low negative pressure during suction and smooth membrane pump that keep smooth circle blood flow
- Level of FHb is significantly lower than the Impella pump <10mg/DL in comparison to 50-100mg/DL in continuance flow pumps

Concerns about 18Fr sheath and limb ischemia…

- Patient selection is key to success, similar to TAVI femoral Artery size need to be >5.7mm
- Occluding lower extremities during PCI and then taking out the device, up to 3-4H have no significant effect on lower limb - never had a complication with this
- In case using the device for more than 4H it is recommended to assess the lower limb Oxygen level with SPO2, if levels are low then it is recommended to perform bypass as per ECMO
- There is always a possibility of a sheathless approach. This involves a small cutdown and using a purse-string surgical technique to close after the procedure. In this option, the size is dramatically smaller (comparable with that of a 15Fr sheath)

Wound closure and IABP console compatibility

How do I close the big wound?

- You may use the same technique as with a TAVI procedure.
  Double Proglide / Prostar closer device or the new Manta can be also used

What console shall I use with iVAC 2L ?

- The iVAC 2L can be driven by any IABP drive (Arrow or Maquet) the setting is similar to IABP settings so not a huge learning process

Comparison of iVAC 2L to Impella CP

- Different functions – Pulsatile support Vs Continuous flow
- iVAC 2L although a smaller pump generates equivalent results to Impella CP
- Works with the heart
- No significant hemolysis in comparison to Impella CP
- Easy to operate and time efficient
- Cost effective

Clinical Effect	IVAC 2L	Impella CP
Cardiac output and systematic pressure changes*	LV volumes and pressures showed a significant increase.	LV volumes and pressures showed a significant increase.
The Effective Arterial Elastance (Ea)*	Decrease	Increase
Total Systemic Resistance*	Decrease	Increase
Global Cycle Efficiency*	Increase	No change
Aortic Afterload*	Decrease	Increase
PV Loop Changes*	Shifting to left and down	Shifting to right and Up
Hemolysis (fHb)*	<10 mg/dL	>50 mg/dL
Principle of action	Pulsatile	Continuance flow
Indications		
	High risk PCI, Unloading LV during ECMO (CS), High risk Ablation and Mapping	High risk PCI, Unloading LV during ECMO (CS)
Use and complications		
Bleeding complications*	Very low	High
Procedure steps	Easy and intuitive	Complicated and involve high skill user
Learning time	Short	long
Learning new procedure and console	Not needed	needed
Economics		
Cost (Europe)	++	++++
Console	Standard IAB console	Dedicated Impella console

Based on clinical studies and publications

Alexander Samol, Marcus Wiemer, Sven Kaese. Comparison of a pulsatile and a continuous flow left ventricular assist device in high-risk PCI. International Journal of Cardiology May 2022

Bastos, Marcelo B et al. "PulseCath iVAC2L: next-generation pulsatile mechanical circulatory support." Future cardiology vol. 16,2 (2020): 103-112.

Thank you for Listening