English lecture slide

Optimal Impella management based on the cardiovascular framework

～Basic of Impella physiology～

Keita Saku, MD, PhD
Kyushu University

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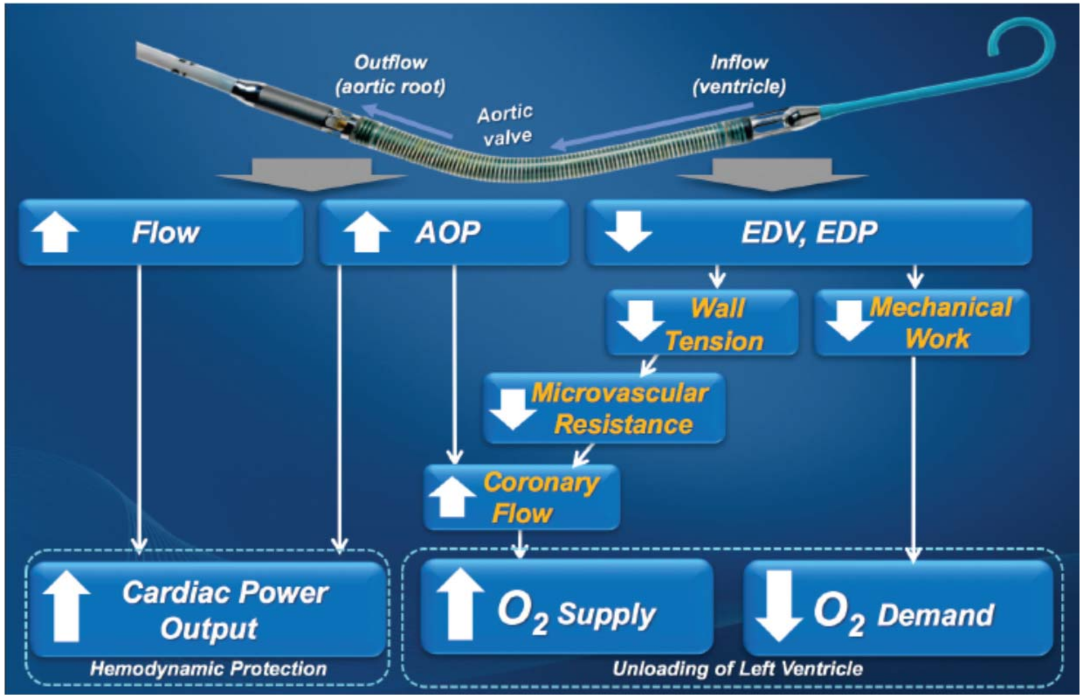
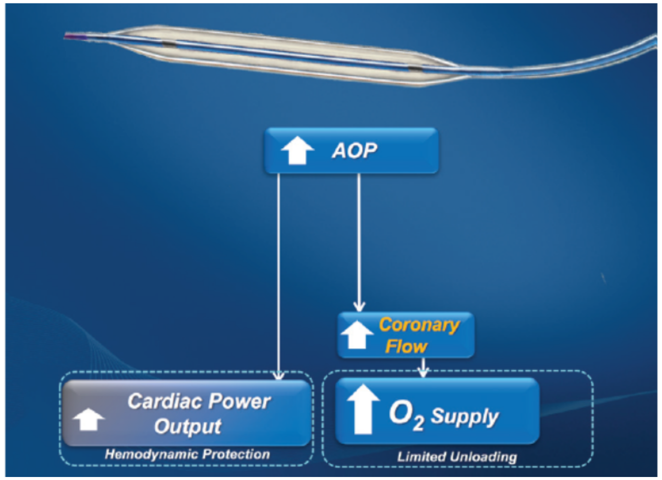
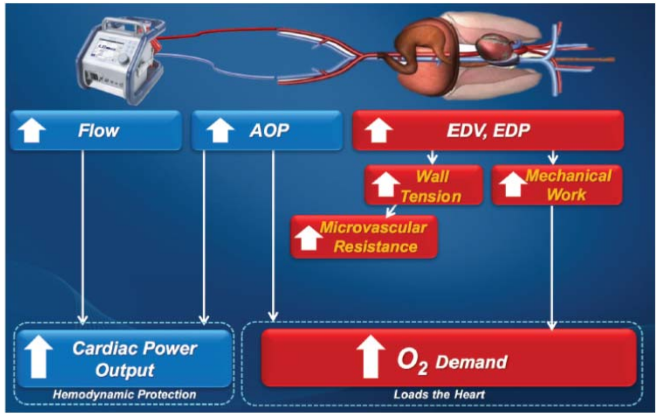
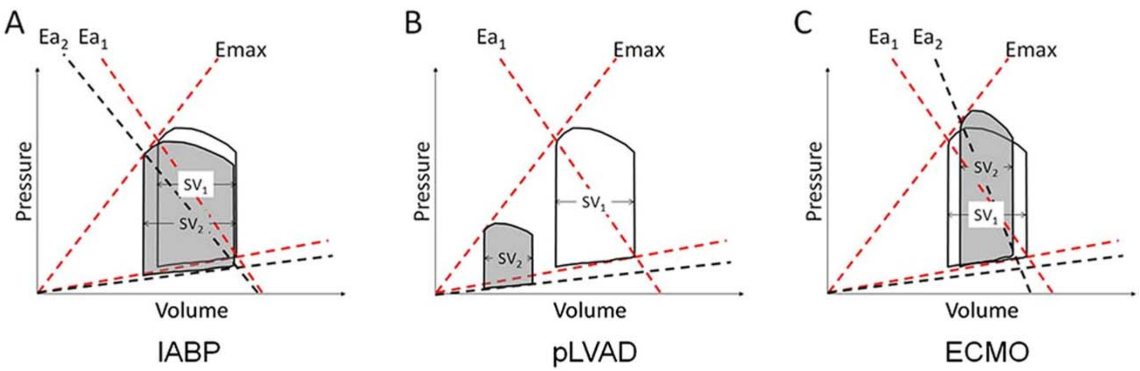
- If you would like to see the movie contents, please contact the office of circulatory dynamics academy (info@circ-dynamics.jp).

Impella effects overview









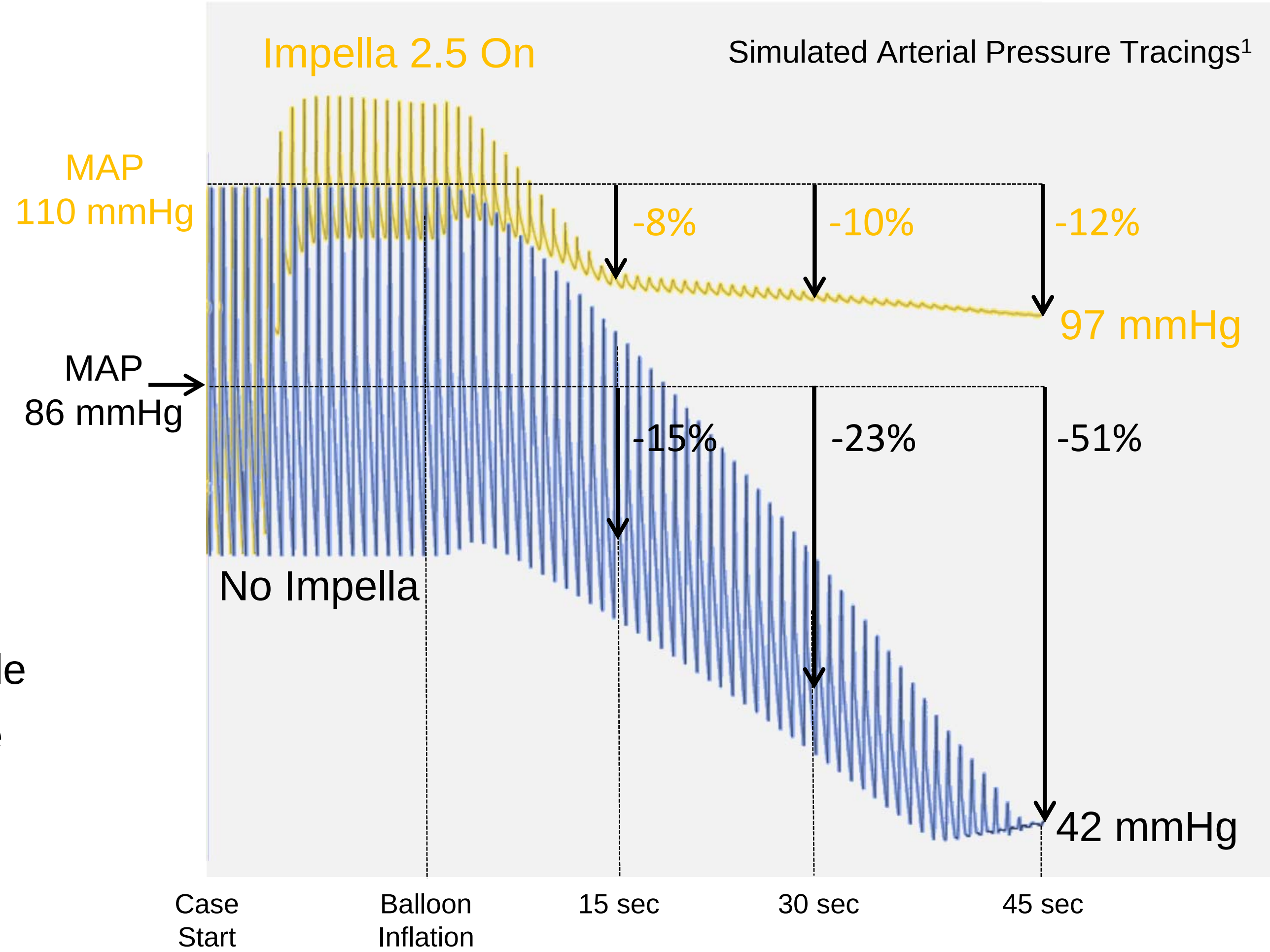
2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care

Endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention*

Impella hemodynamic effect -Simulation-

Case Example*

- 66 yo male
- 85% SVG
- Last patent conduit
- EF = 30%
- NYHA Class IV
- Prior CABG
- Prior PCI
- Hemodynamically stable
- Not Surgical Candidate



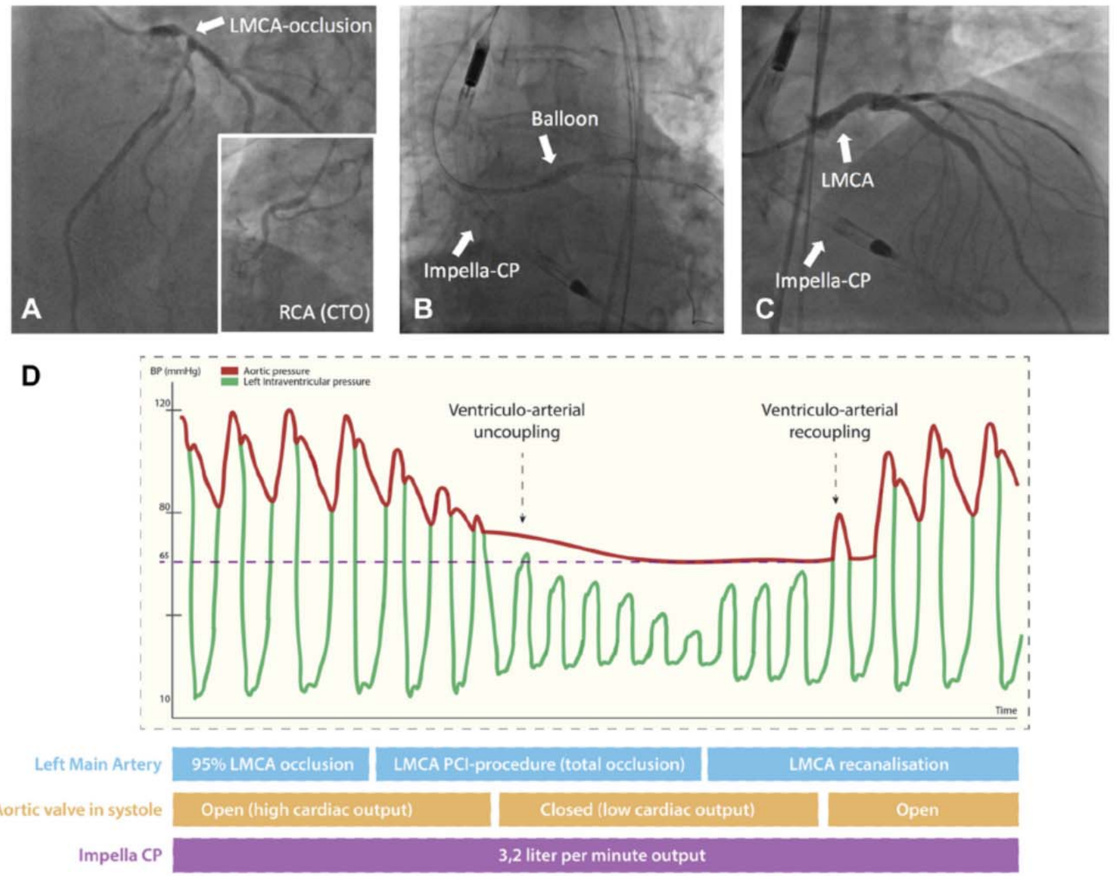
Physiologic computational modeling, *Am J Physiol.* 1991;260 : H146-H157

Impella hemodynamic effect -Case-

Impella Protected PCI

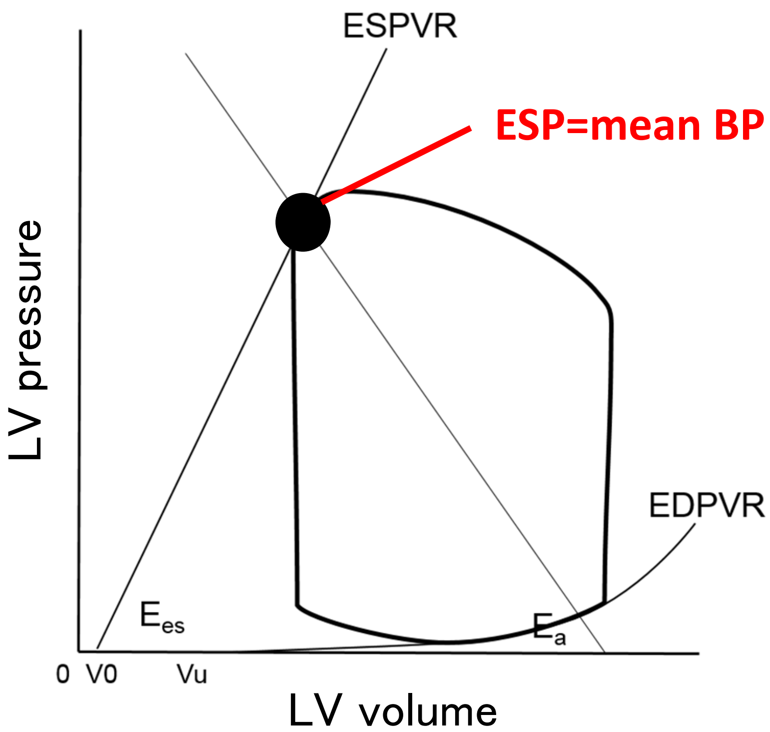
Exploring the Mechanism of Ventriculoarterial Uncoupling

Christophe Vandenbriele, MD, PhD,[a,b] Tim Balthazar, MD,[a] Stefan Janssens, MD, PhD,[a]
Tom Adriaenssens, MD, PhD,[a] Johan Bennett, MD, PhD[a]

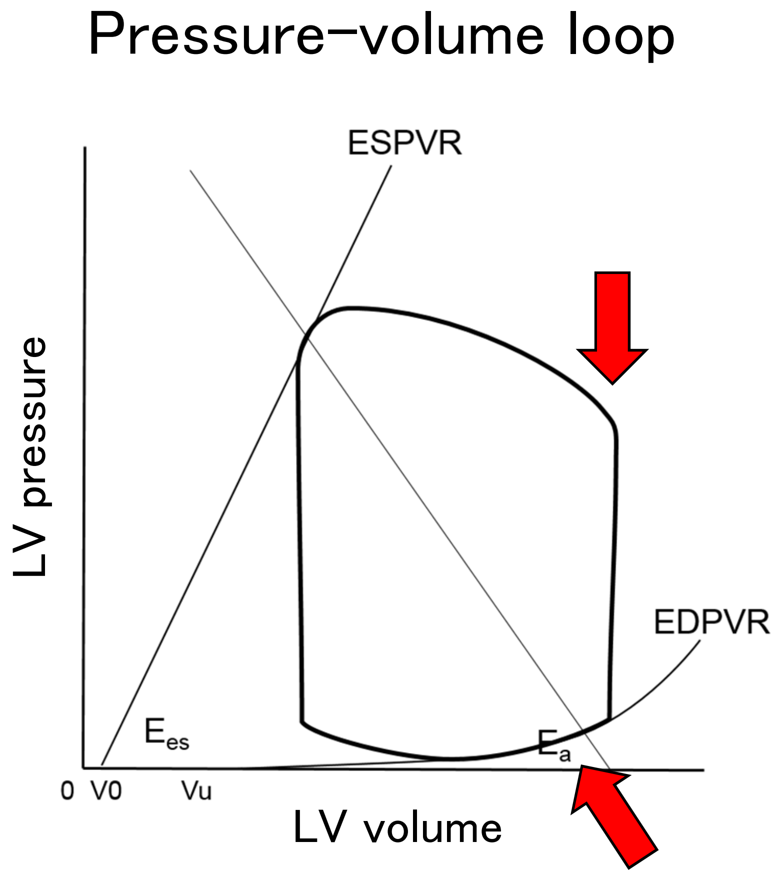


Why we learn PV loop?

Pressure-volume loop



PV loop tells us…



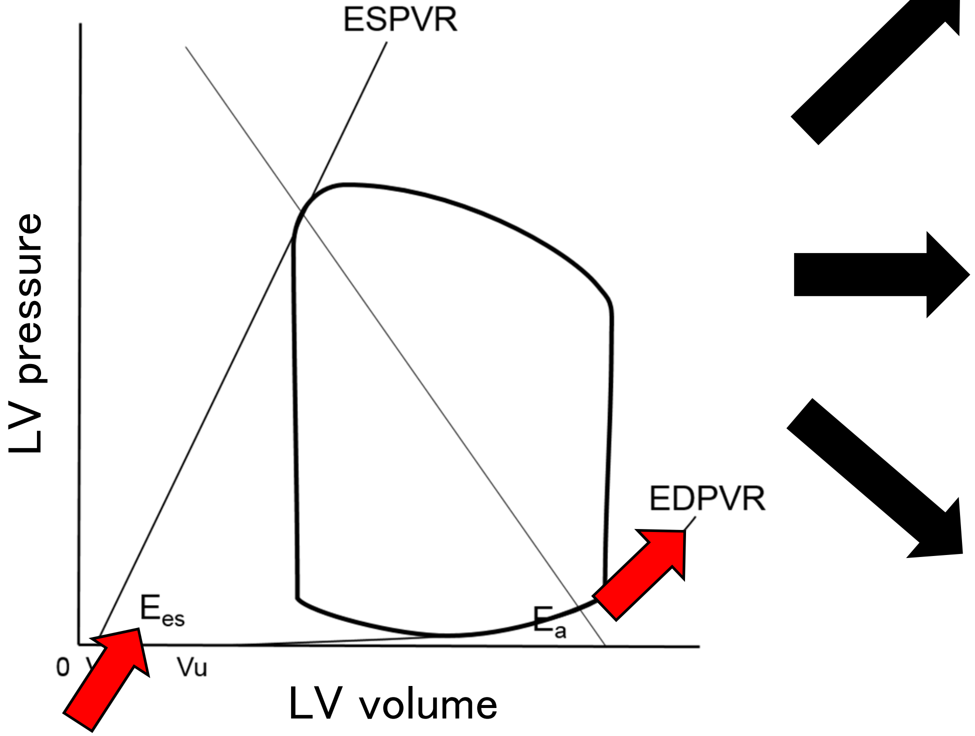
Cardiac preload
Cardiac afterload

Systolic function
Diastolic function

MVO_2

PV loop tells us…

Pressure−volume loop

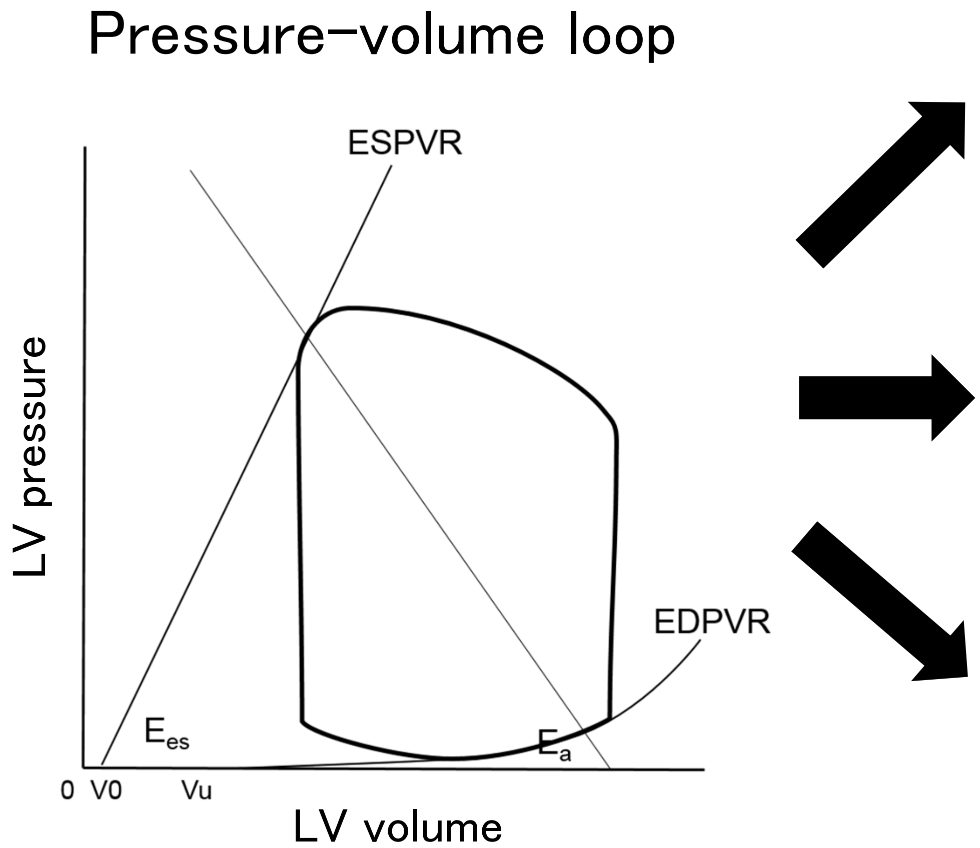


Cardiac preload
Cardiac afterload

Systolic function
Diastolic function

MVO_2

PV loop tells us…

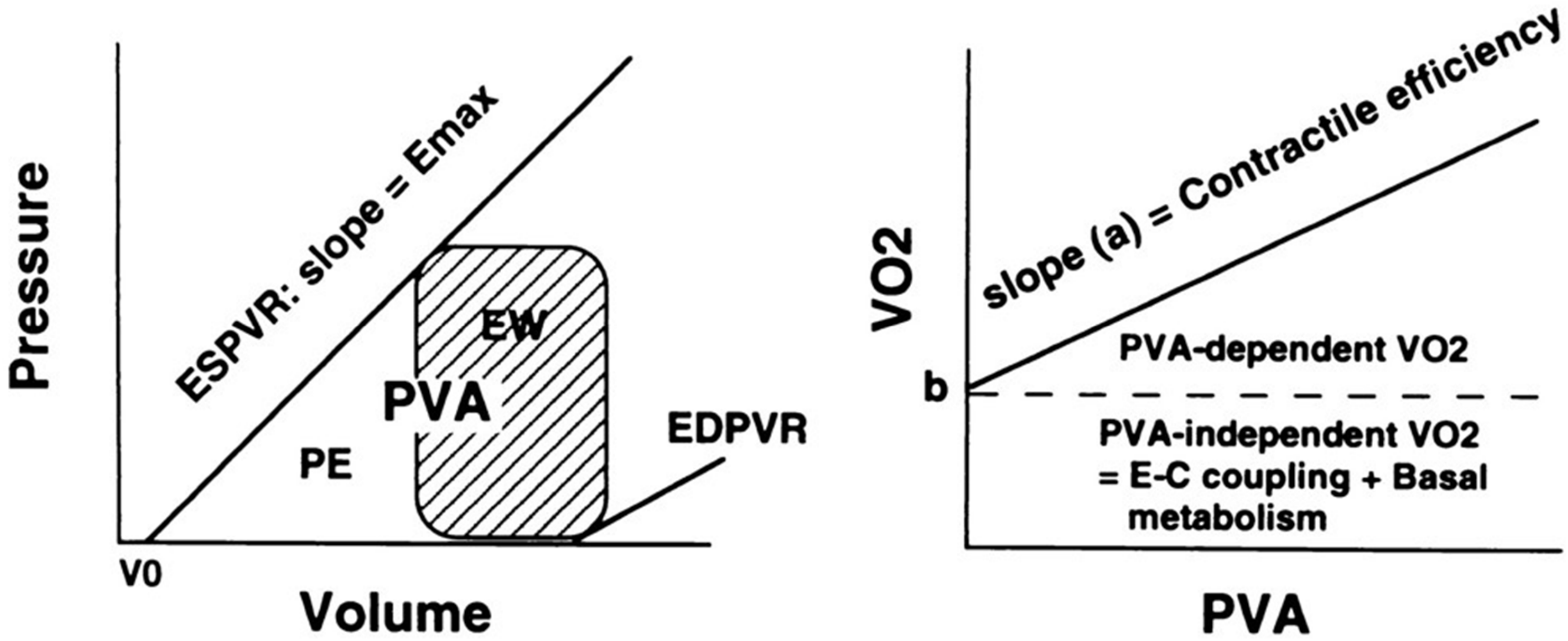


Cardiac preload
Cardiac afterload

Systolic function
Diastolic function

MVO_2

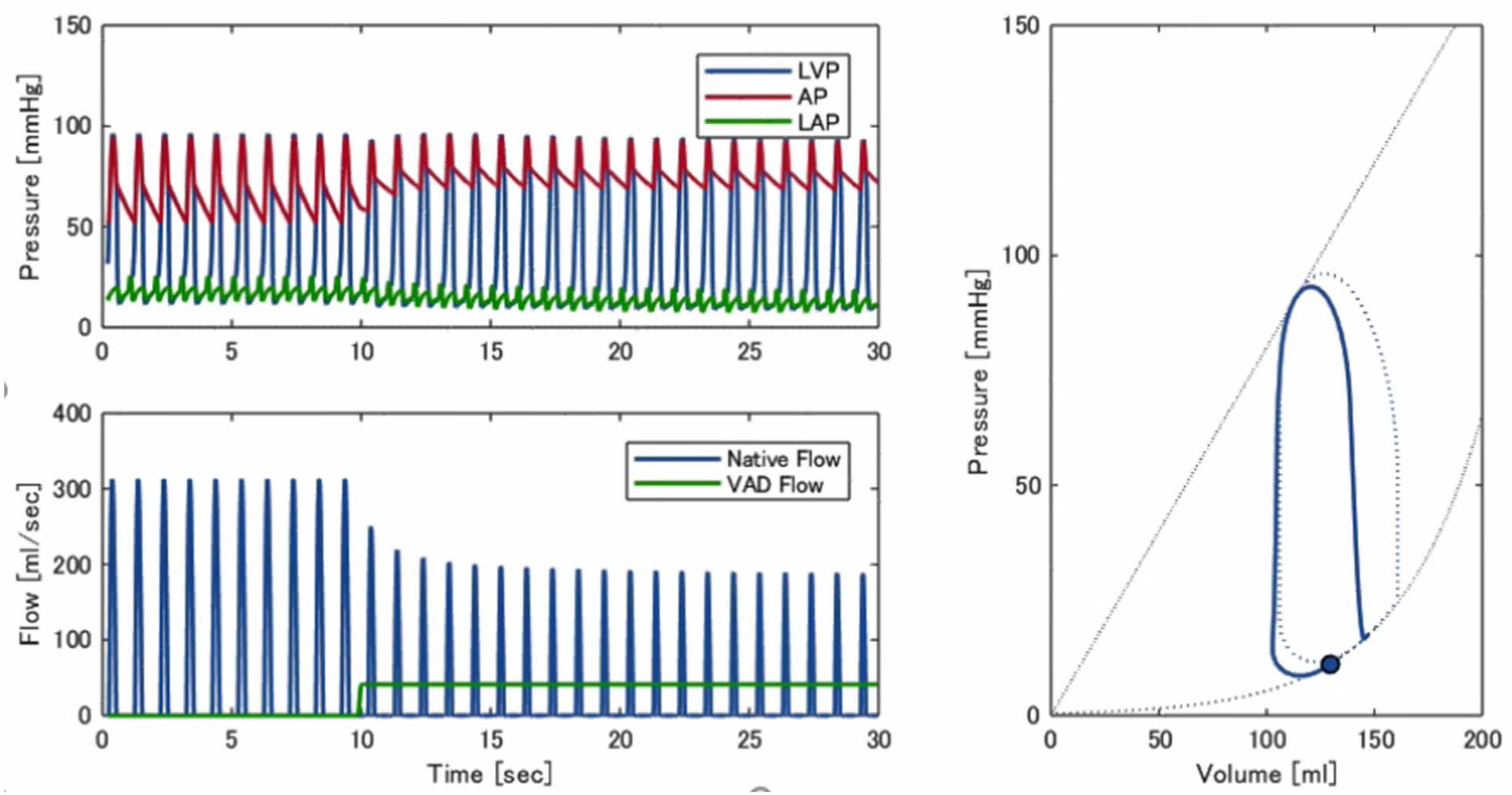
PVA = Myocardial oxygen consumption



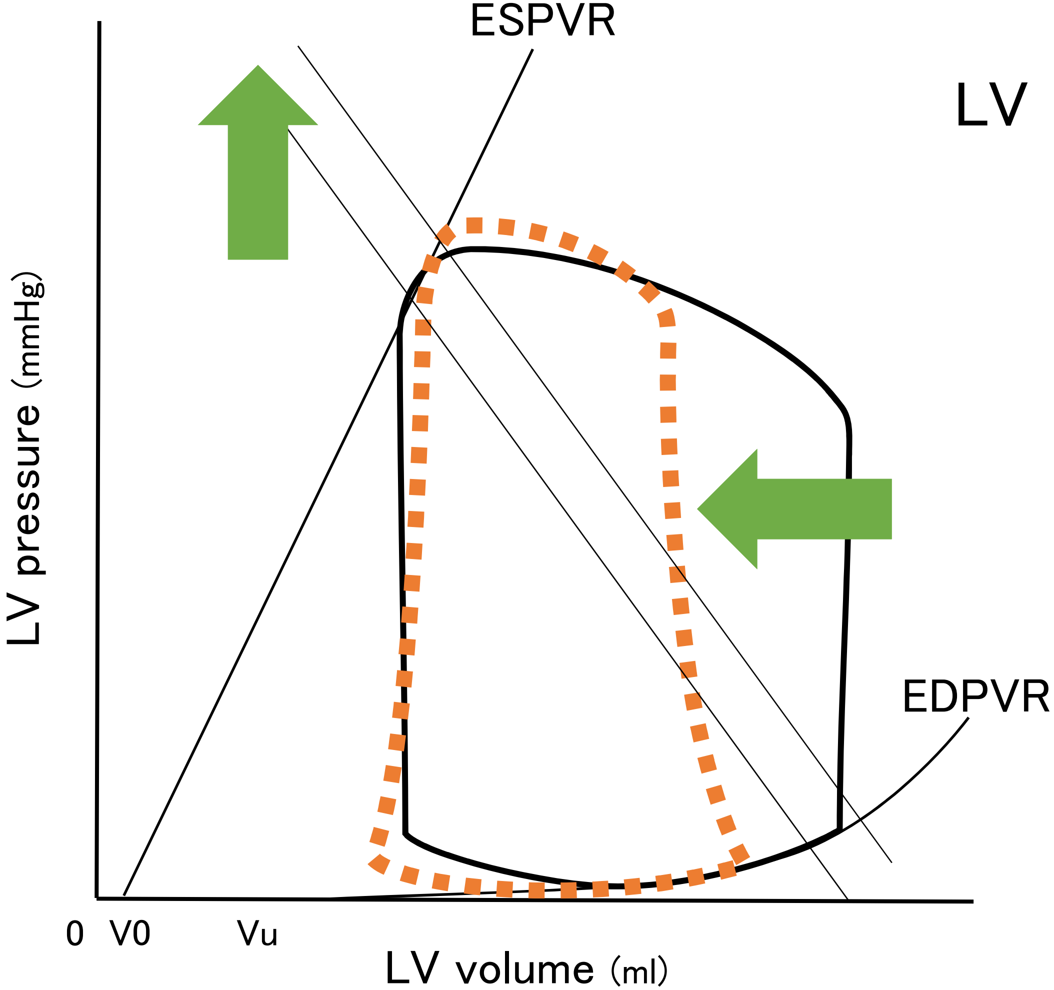
Suga et al. AJP 1981.

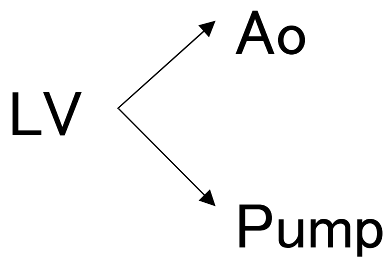
PVA reduction= MVO_2 reduction

Impella→PV loop



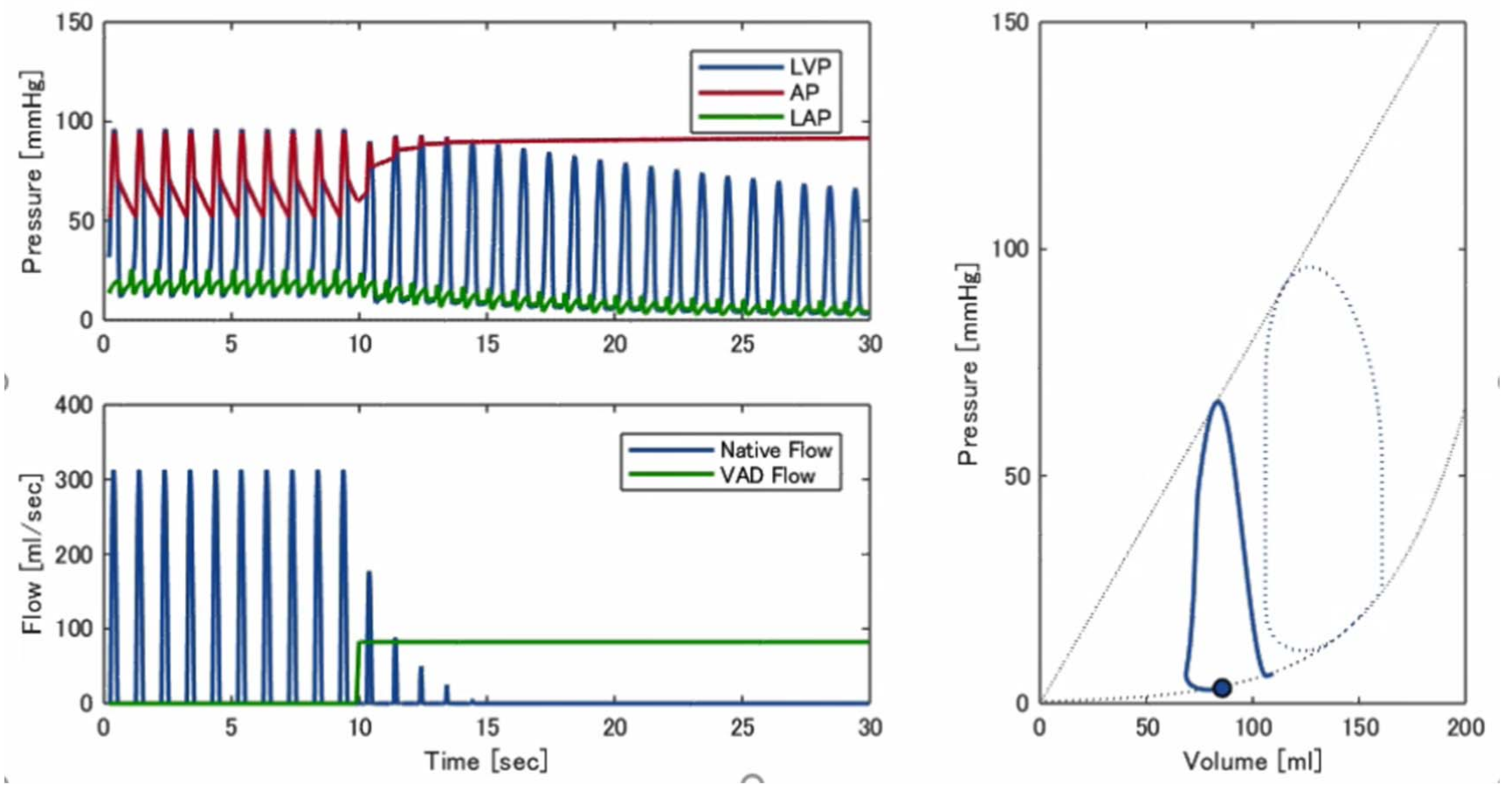
Impella→PV loop -AV open-



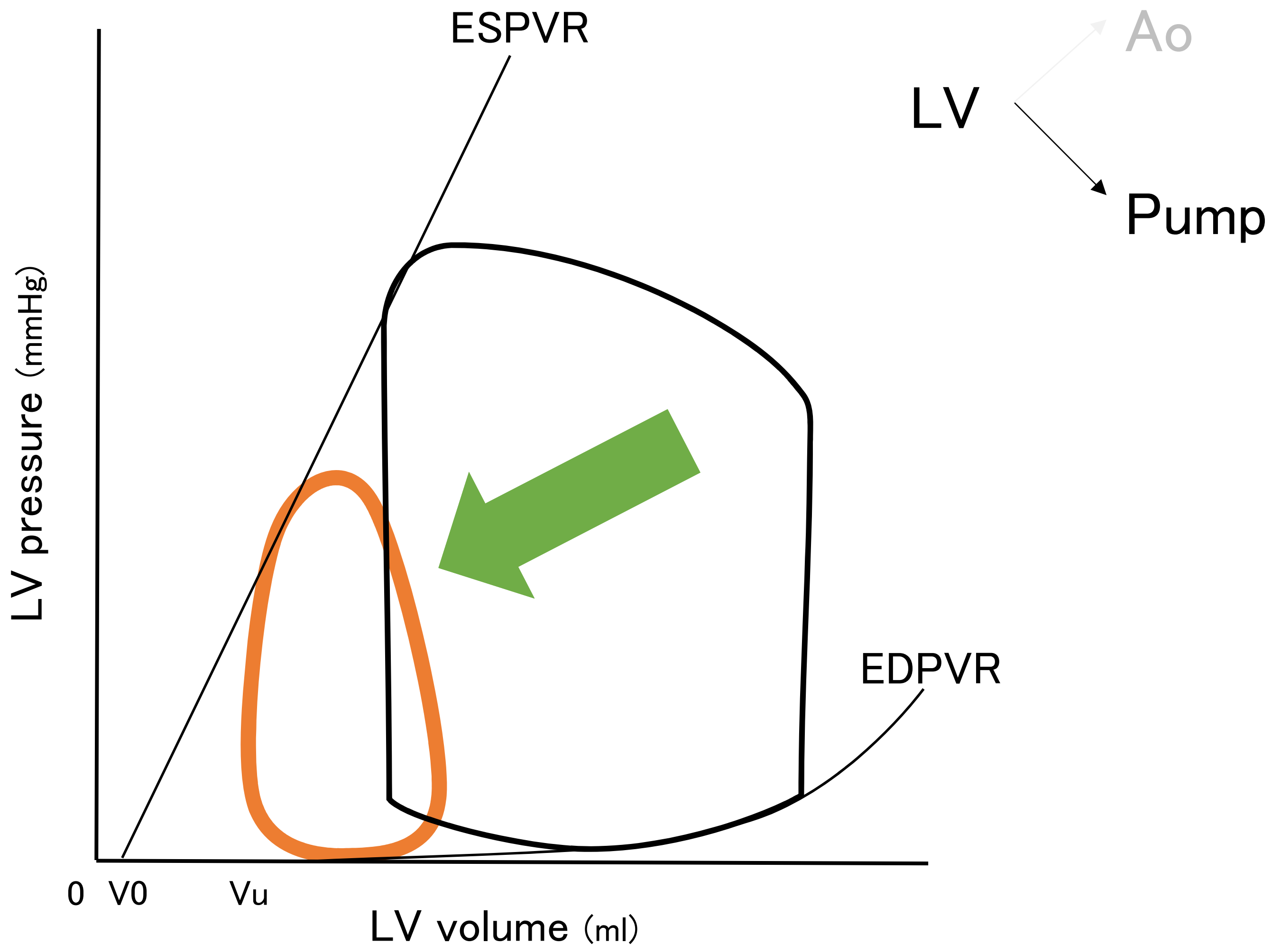


→Partial support

Impella→PV loop

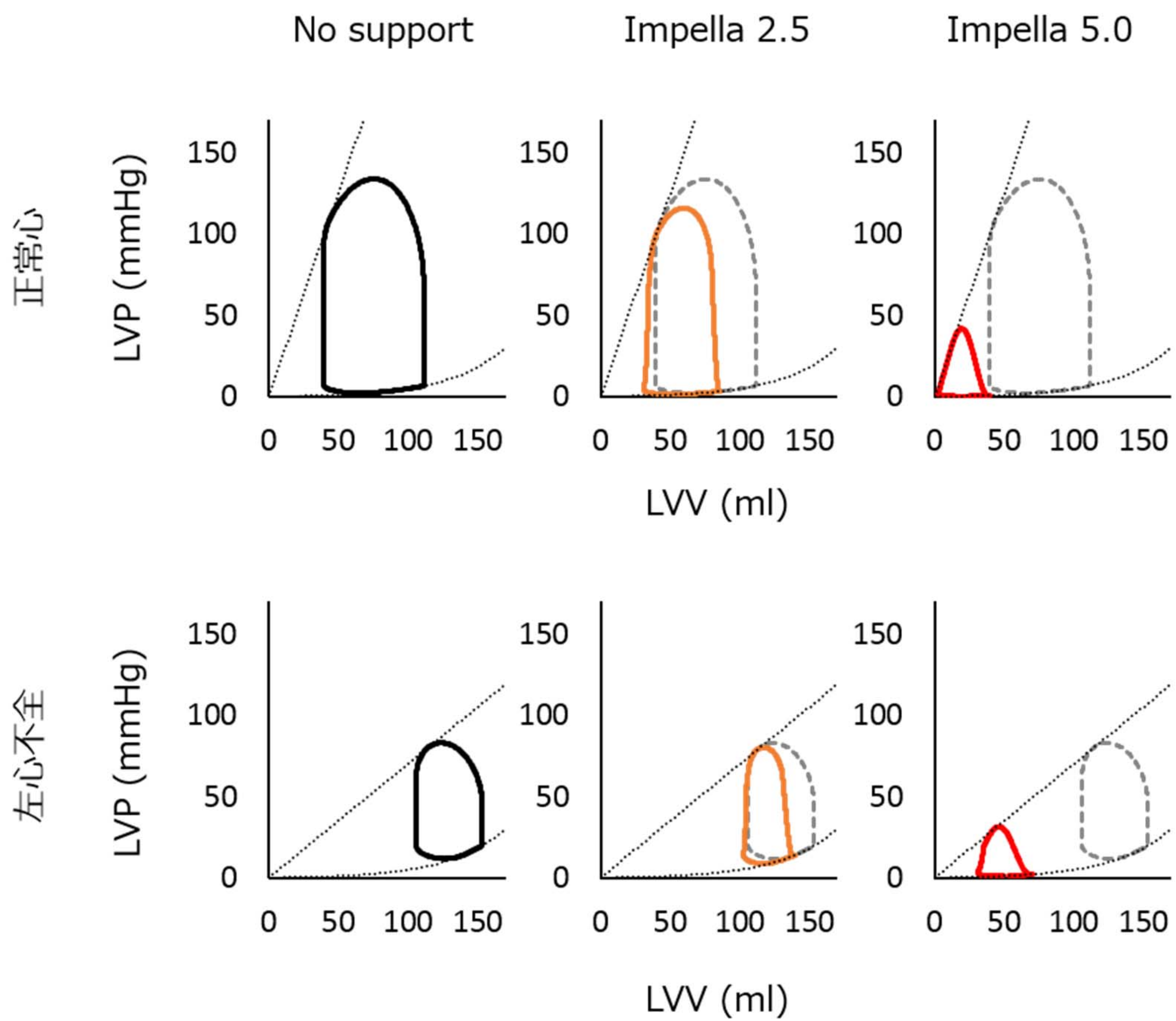


Impella→PV loop -AV close-

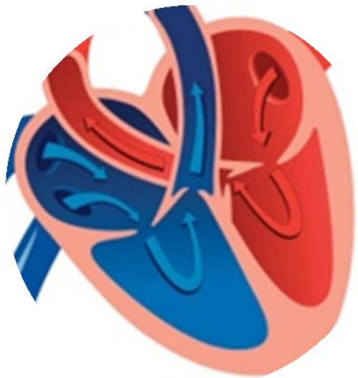


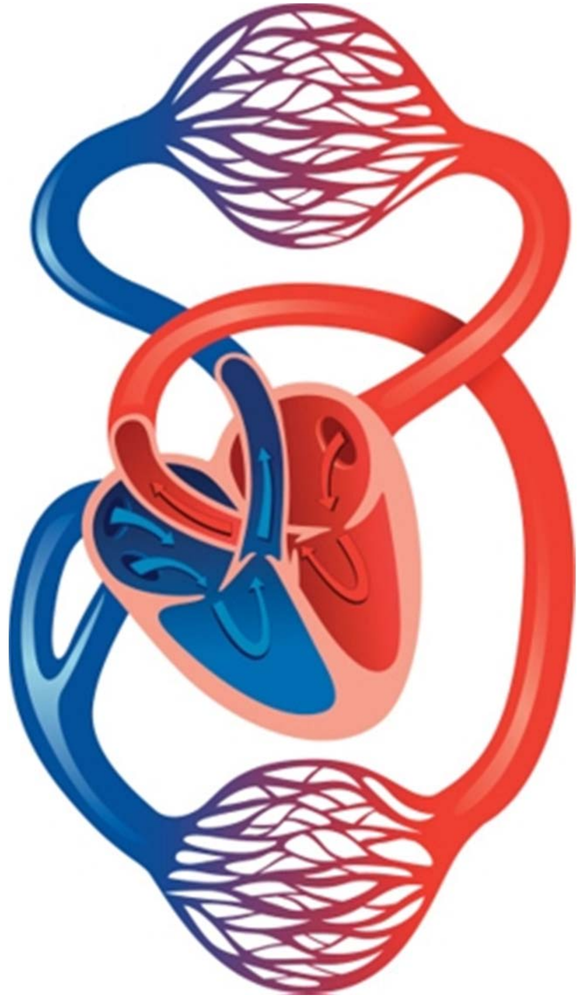
→Total support

Patterns of PV loop under Impella



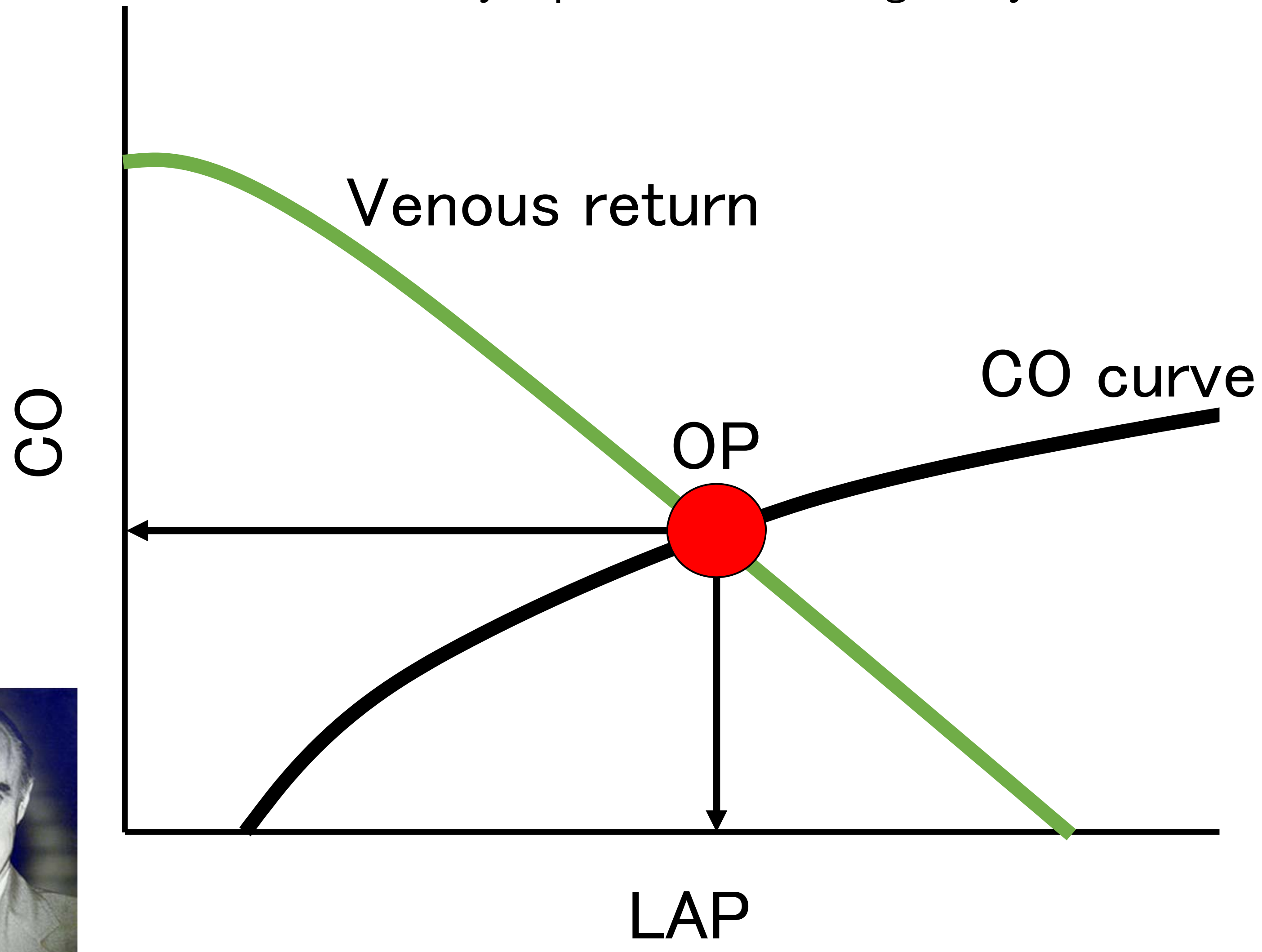
Hemodynamics cannot be described just by cardiac function

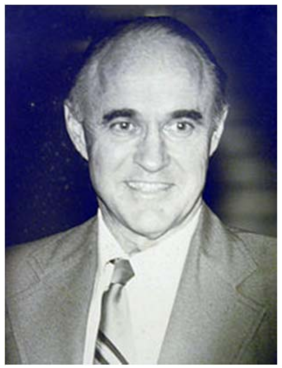




Circulatory equilibrium

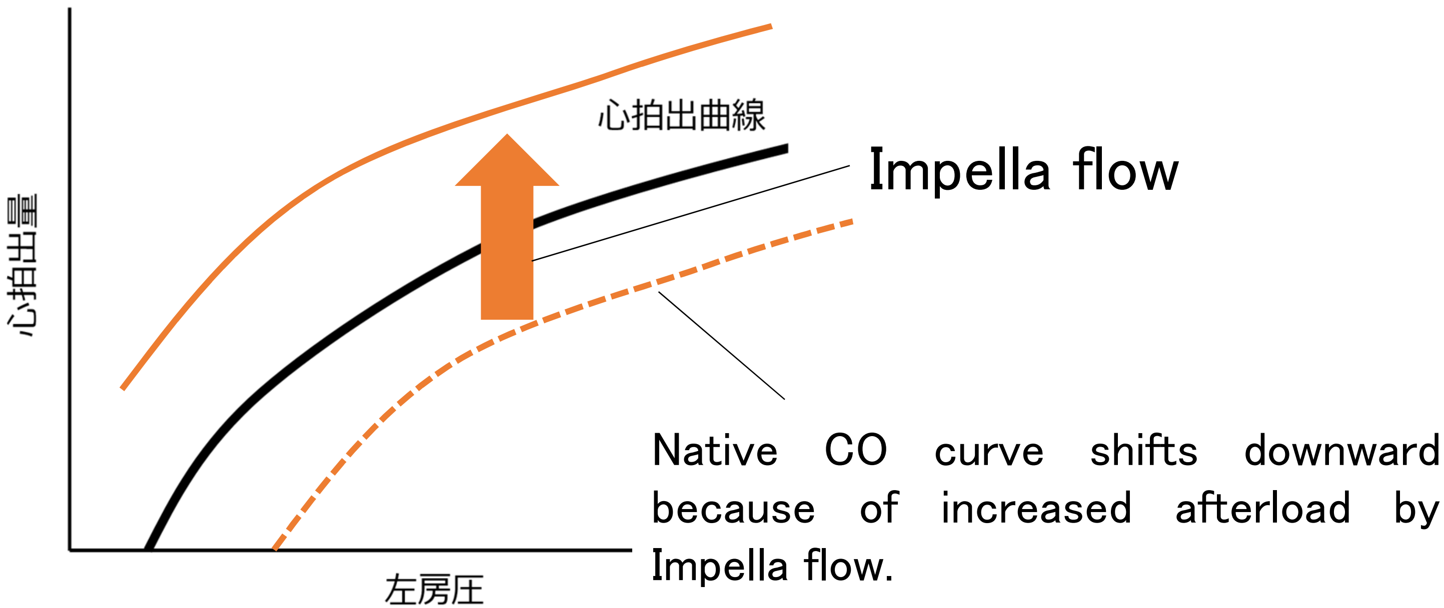
※ Circulatory equilibrium focusing on systemic circulation



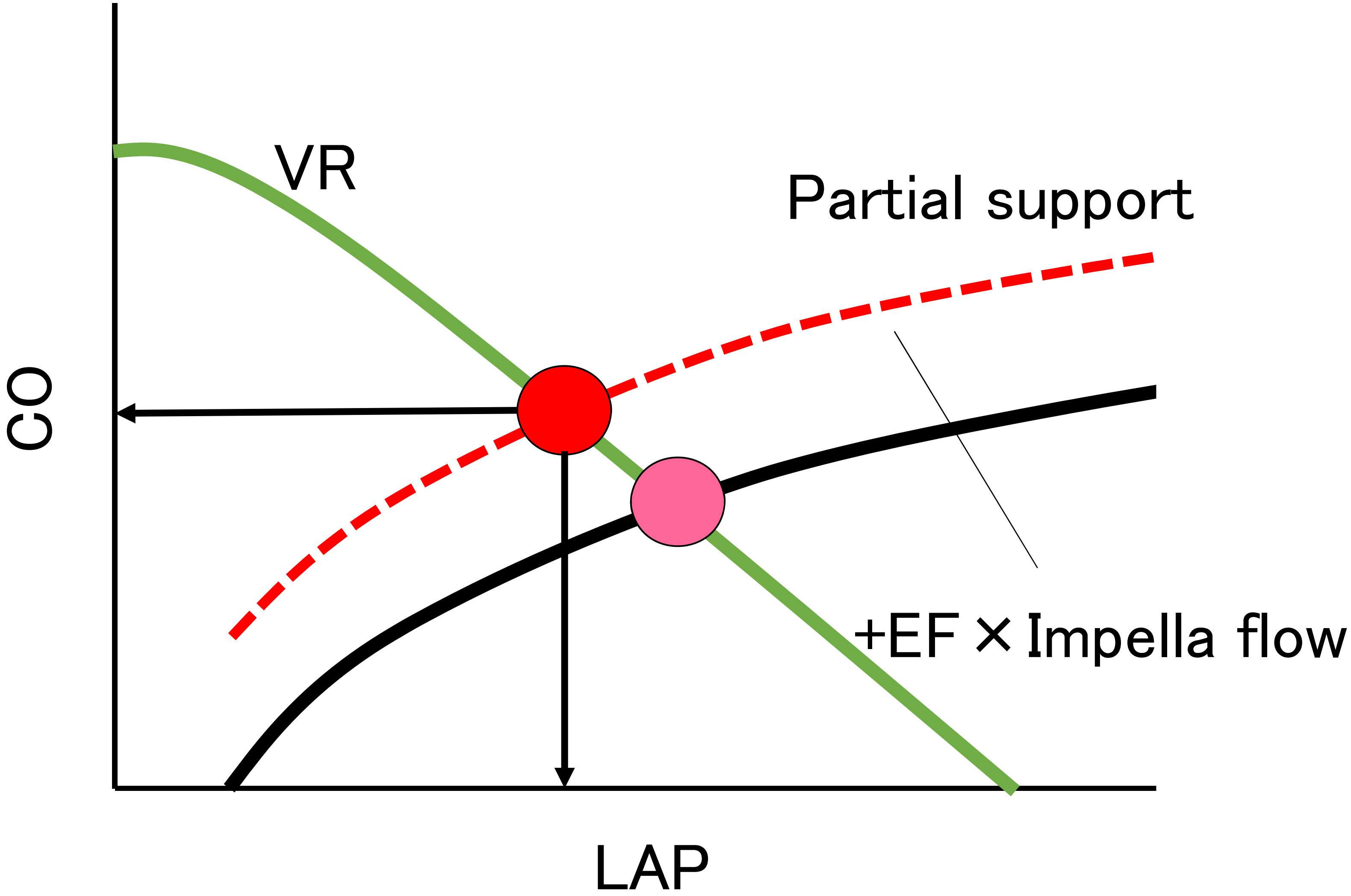


CE curve in Impella partial support

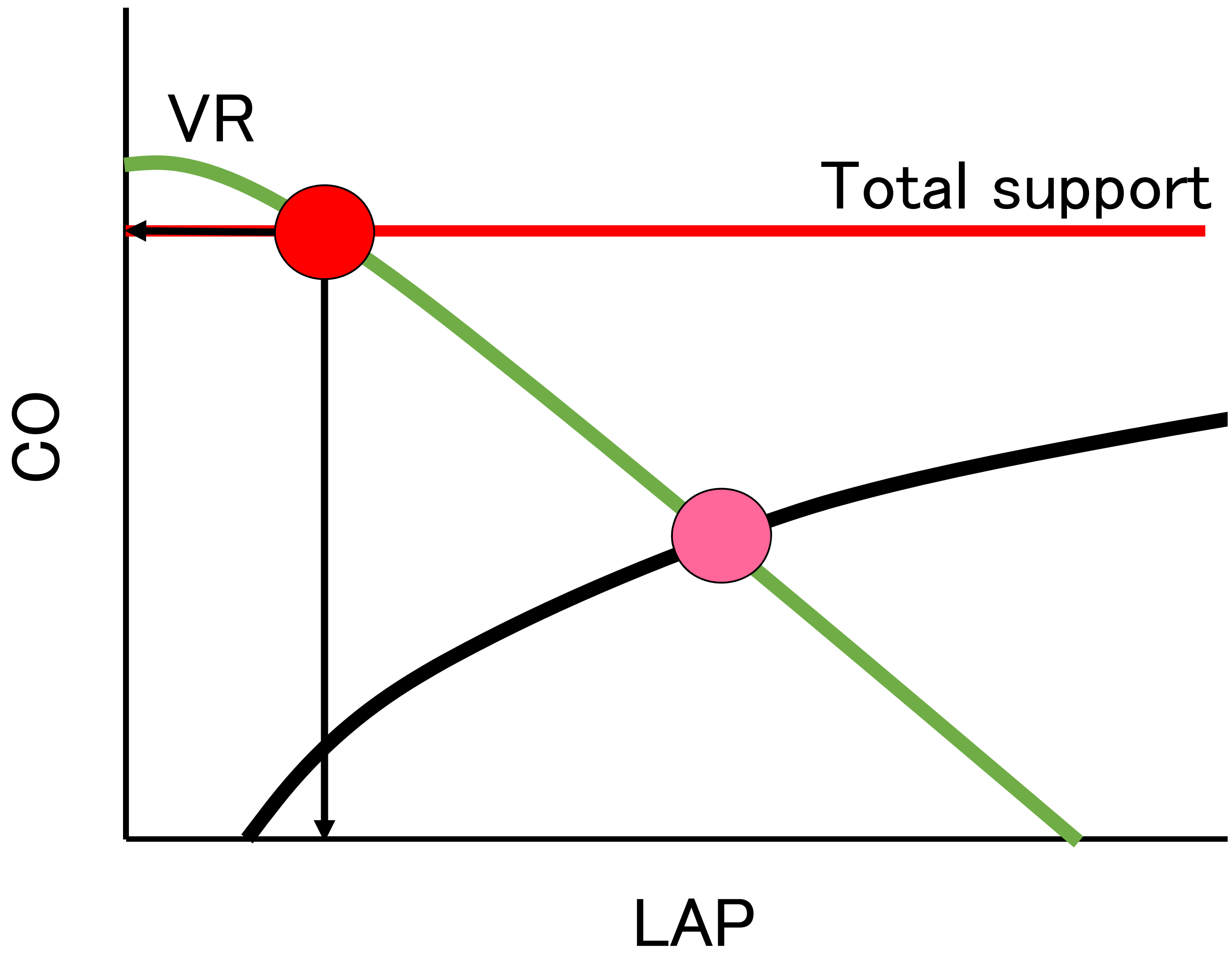
$$CO = S \times (\log(LAP - F) + H)$$
$$- (1 - EF) \times Impella \quad \cdots \quad SV \downarrow$$
$$+ Impella \quad \cdots \quad \text{Impella flow}$$
$$= S \times (\log(LAP - F) + H) + EF \times Impella$$



The impact of partial Impella on CE

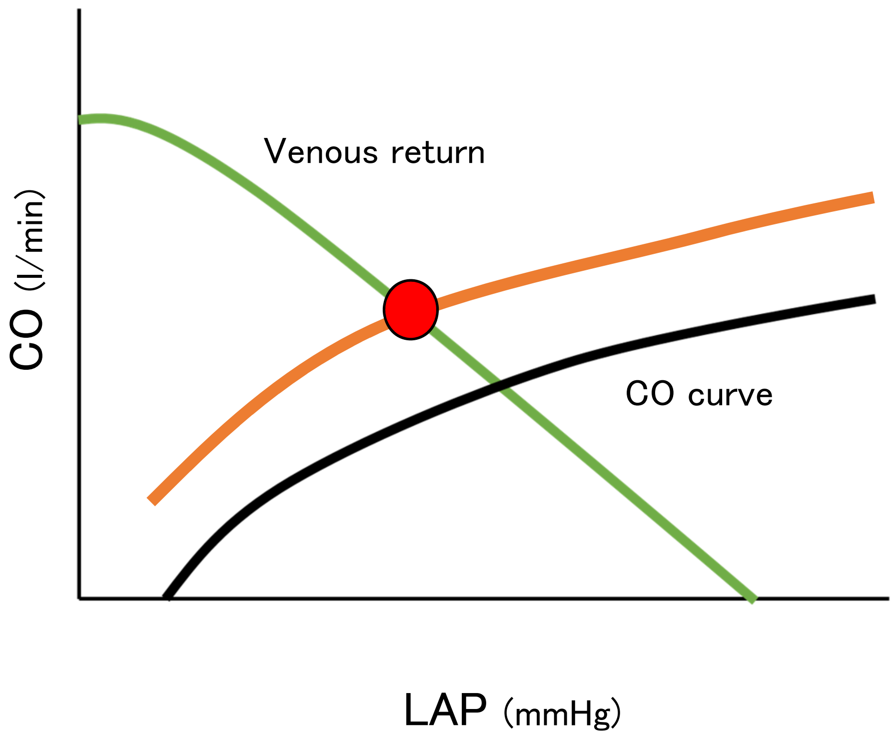


The impact of total Impella on CE

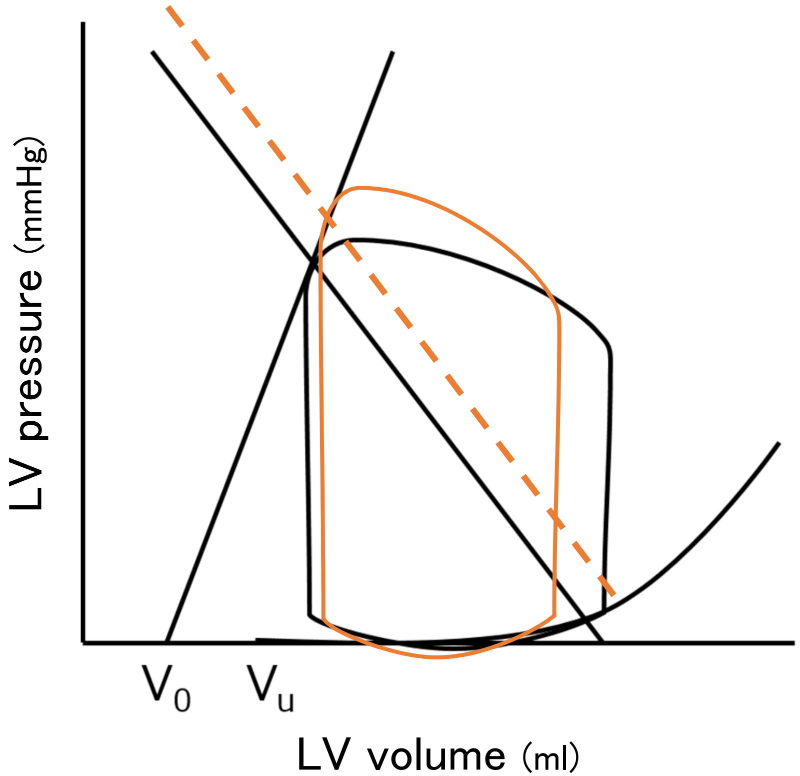


Impella partial support

Circulatory equilibrium

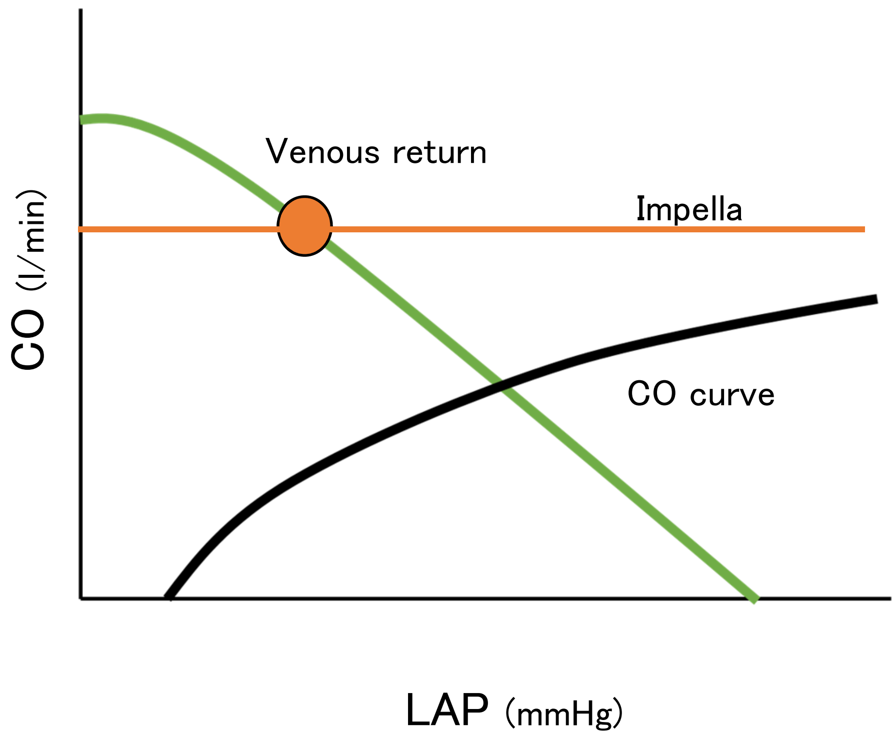


PV loop

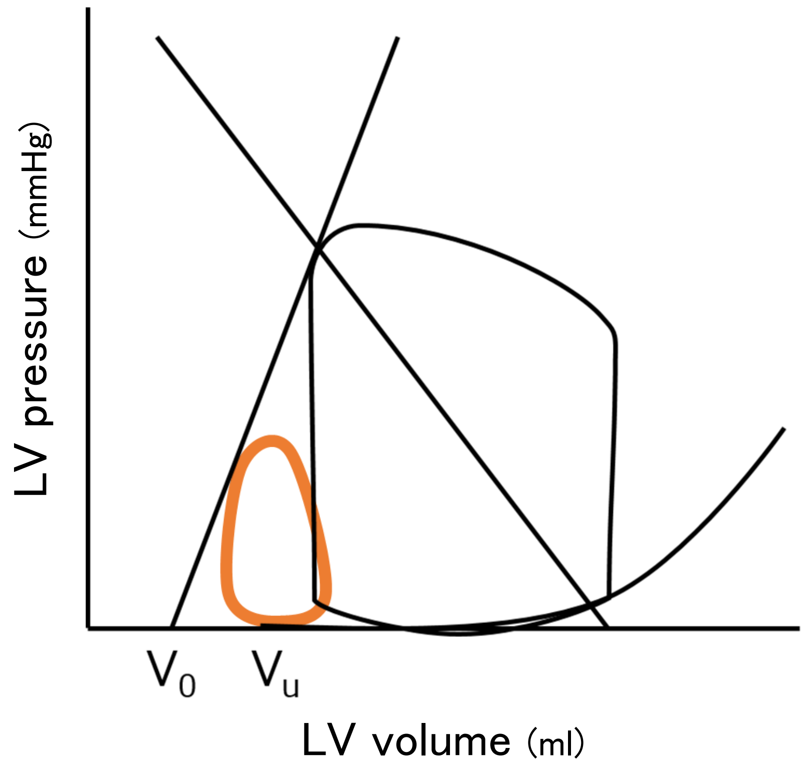


Impella total support

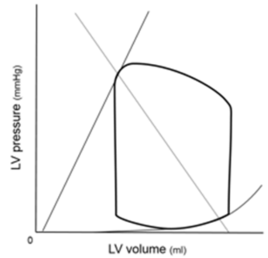
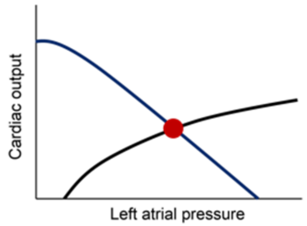
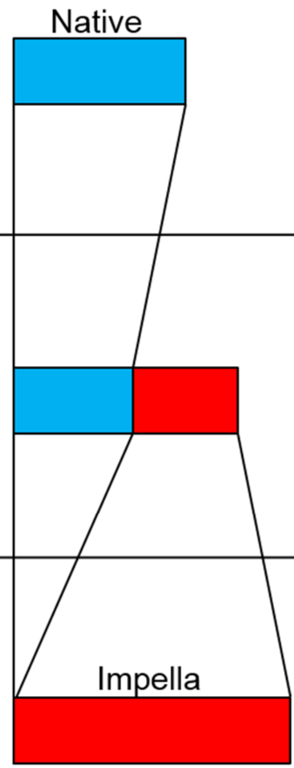
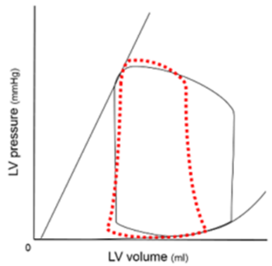
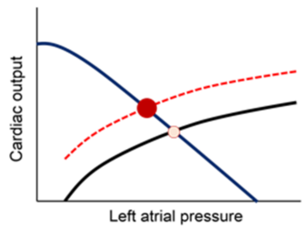
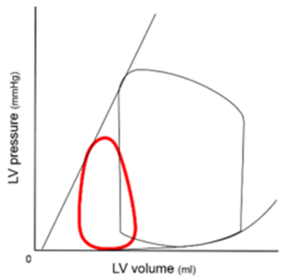
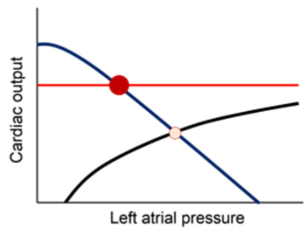
Circulatory equilibrium



PV loop



Hemodynamic support + PVA reduction

Support level	PV loop	Circulatory equilibrium	Total flow	Other parameters
No support				
Partial support				● Pulsatility↓ ● LAP↓ ● Mean AP↑ ● LV wall stress↓
Total support				● Pulsatility ↓↓↓ ● LAP↓↓ ● Mean AP↑↑ ● LV wall stress↓↓

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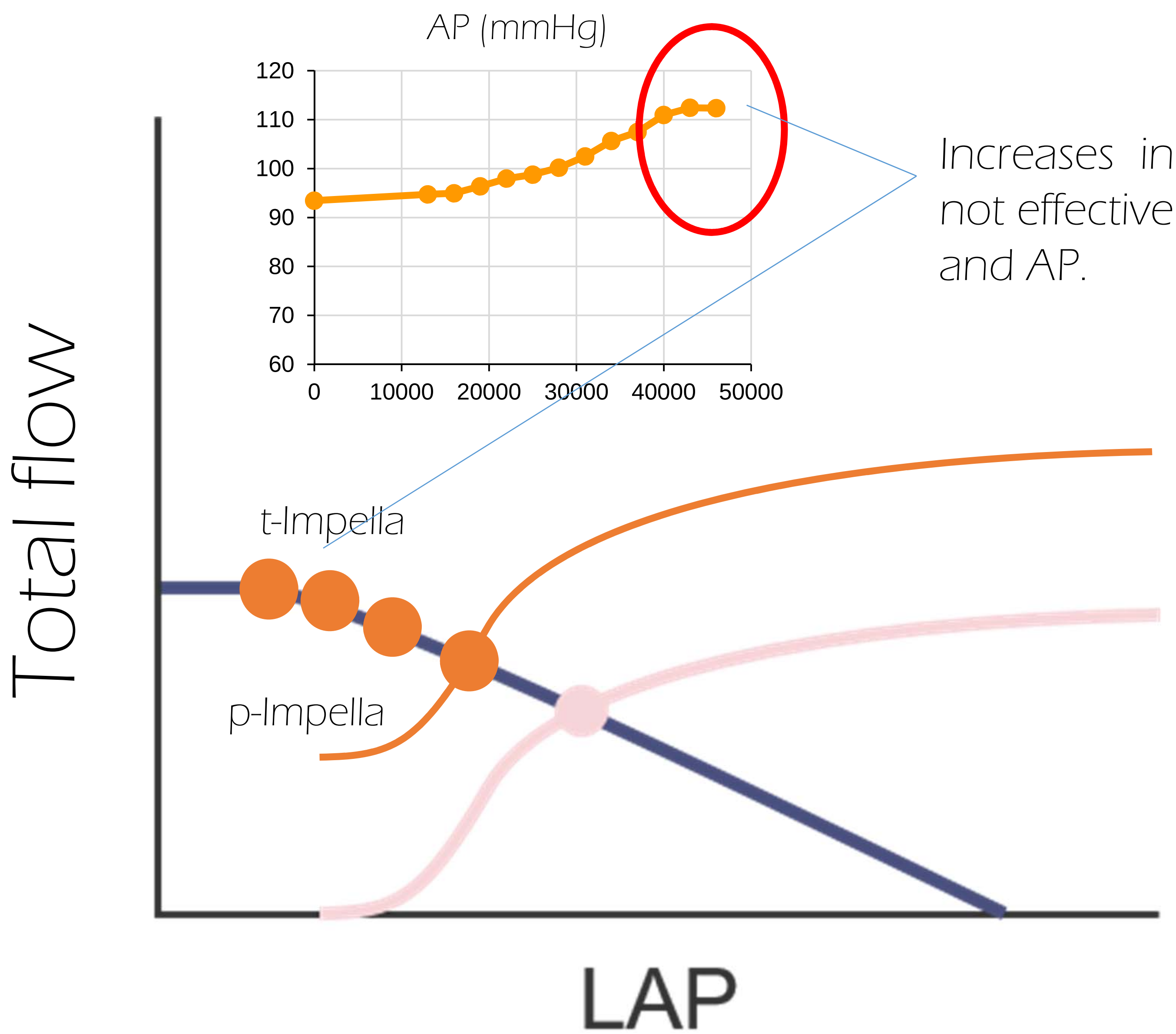
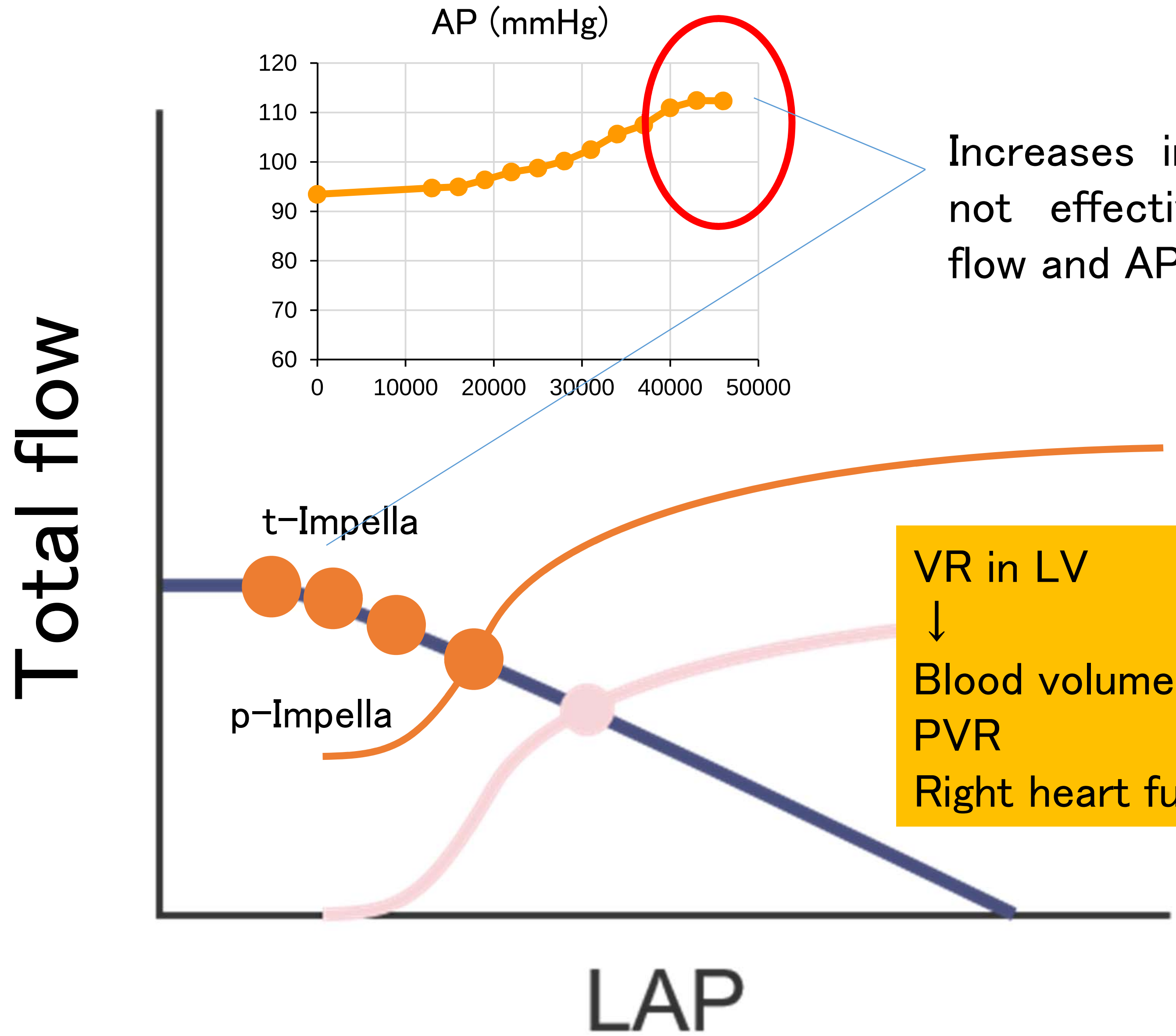
Venous return is important



Increases in Impella flow does not effectively increase total flow and AP.

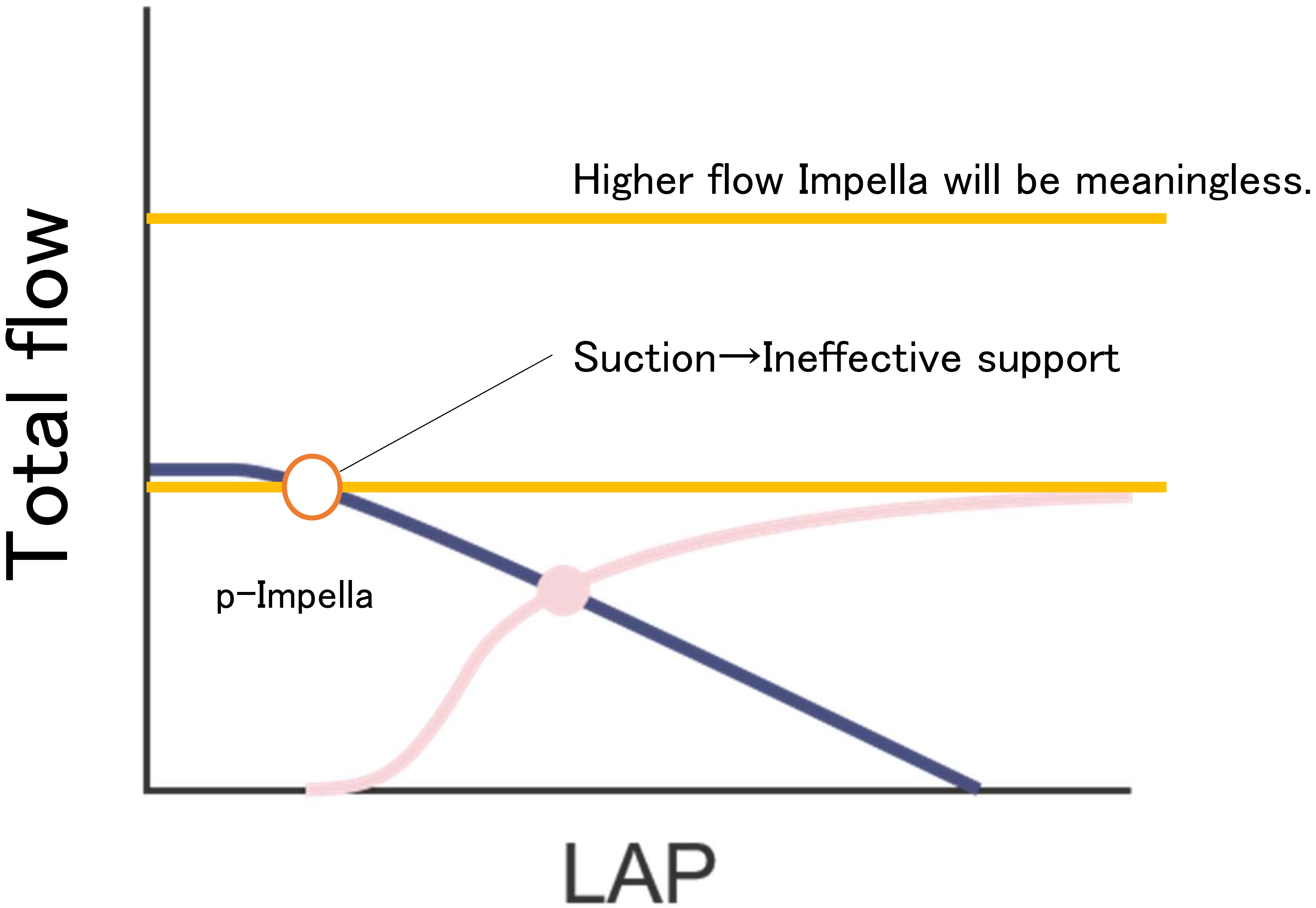
Venous return is important



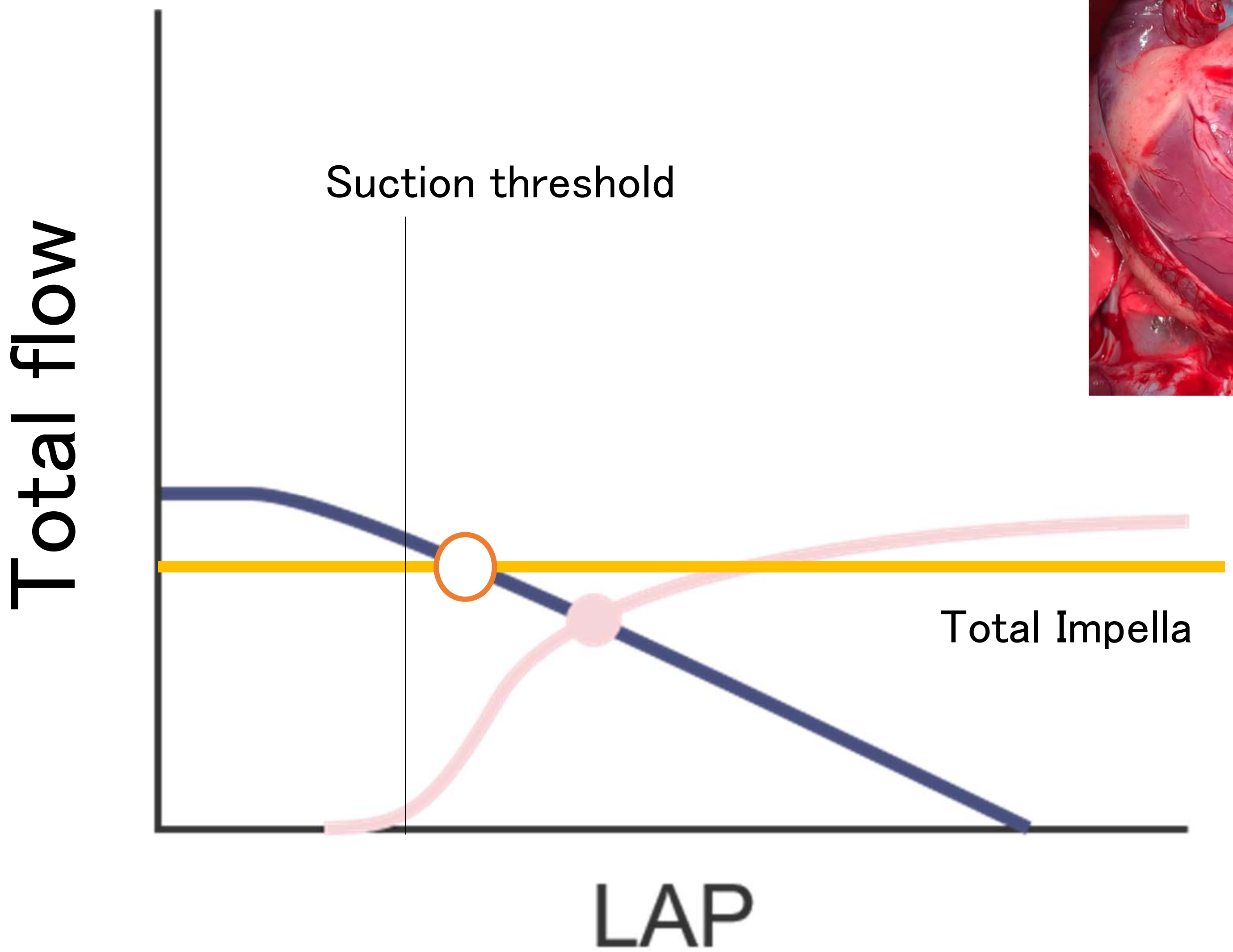
Increases in Impella flow does not effectively increase total flow and AP.

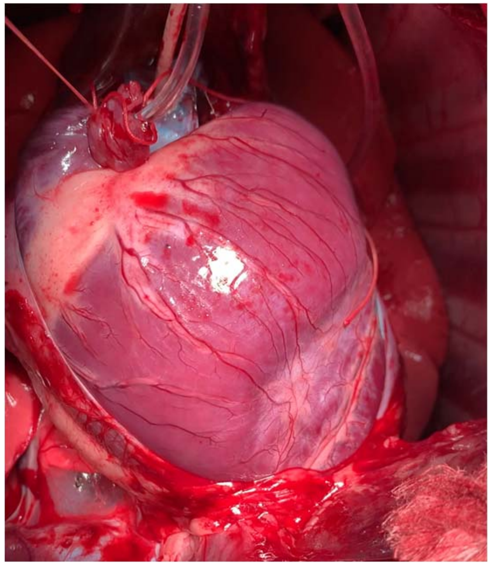
VR in LV
↓
Blood volume
PVR
Right heart function

If venous return is inadequate…

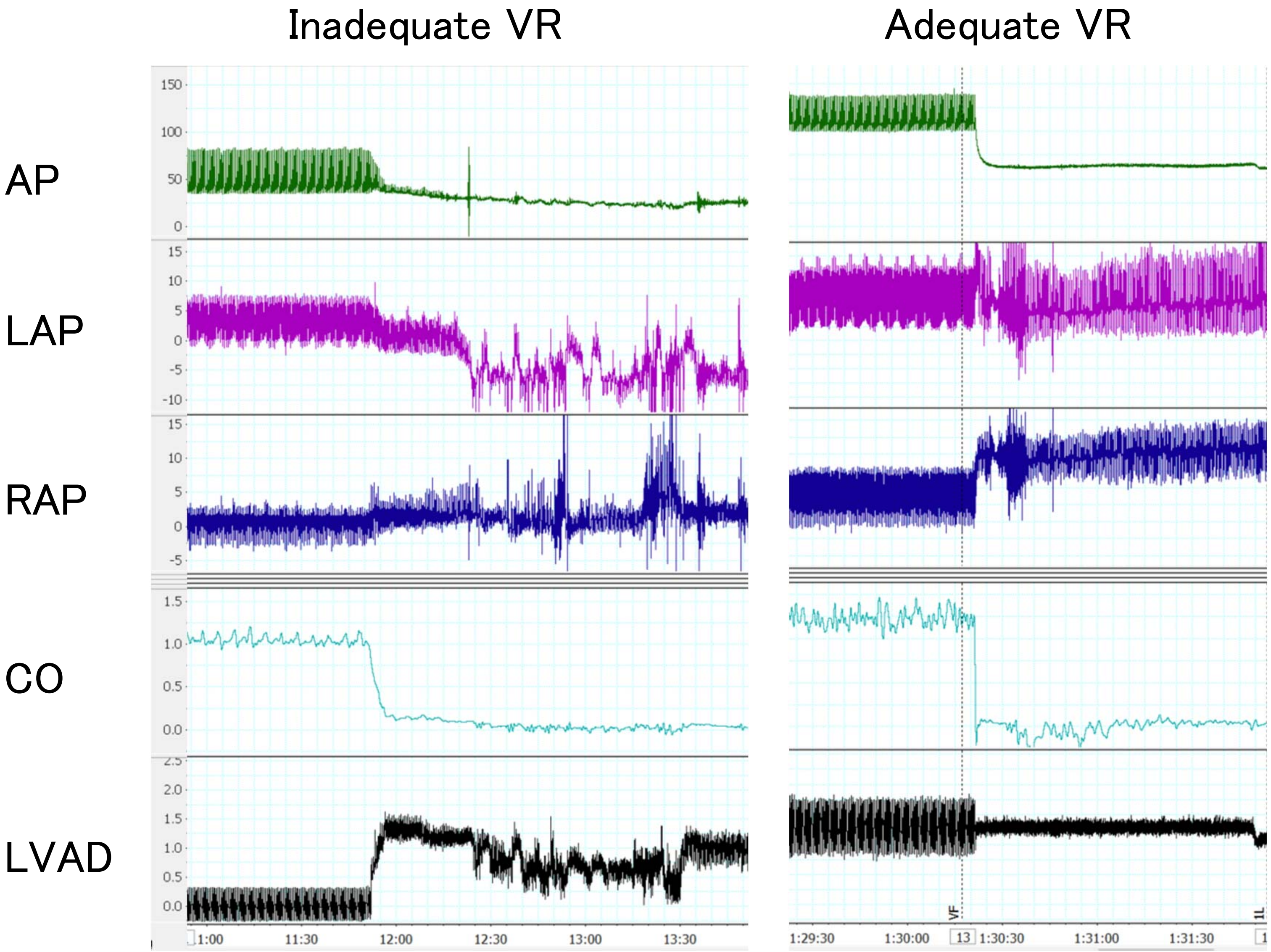


How does Impella work in VF condition?



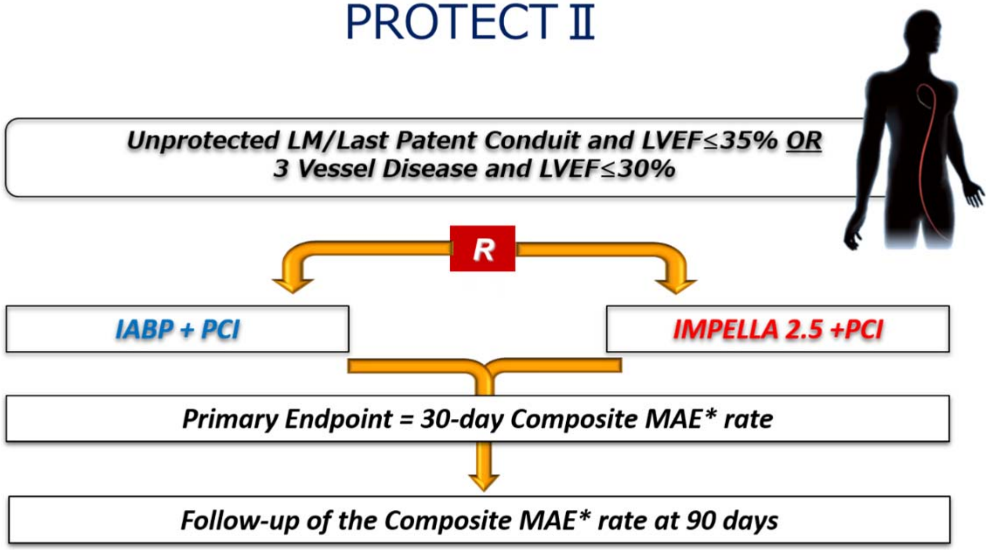


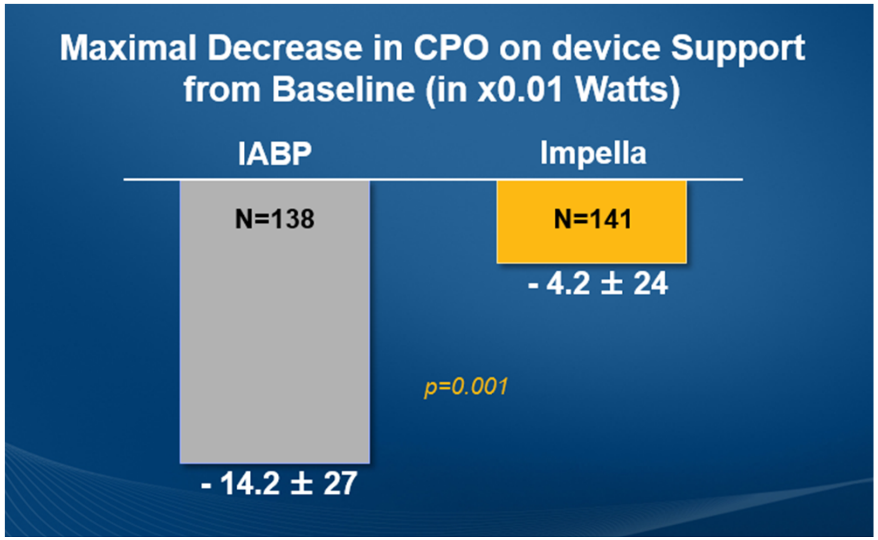
Impella may support VF hemodynamics

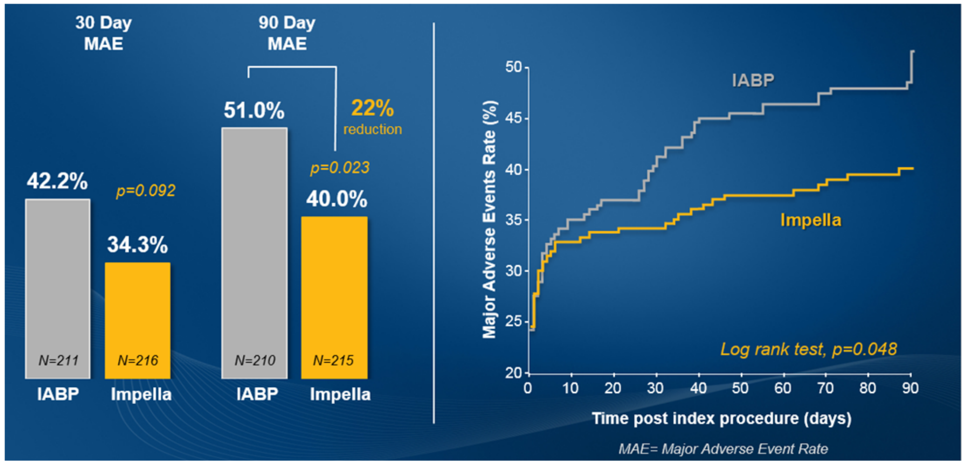


RCT in HRPCI

PROTECT II







O' Neill WW et al. *Circulation*. 2012;54:312-321

RCT in CS

Randomization in Cardiogenic Shock is Challenging

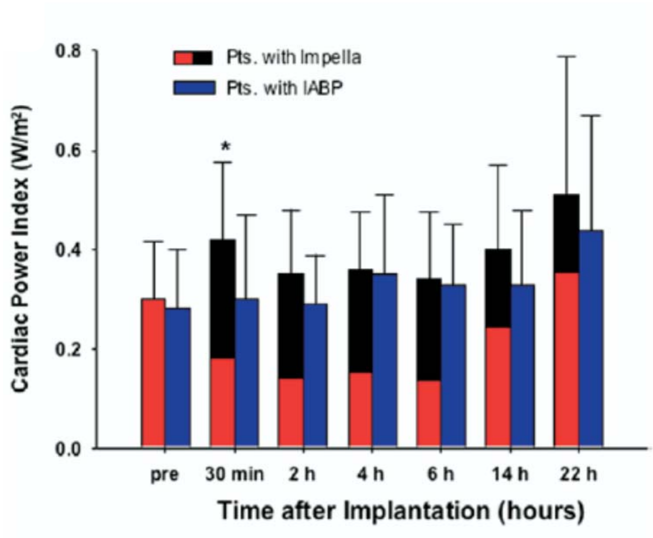
Attempted Randomized Impella® Trials In Emergent Settings

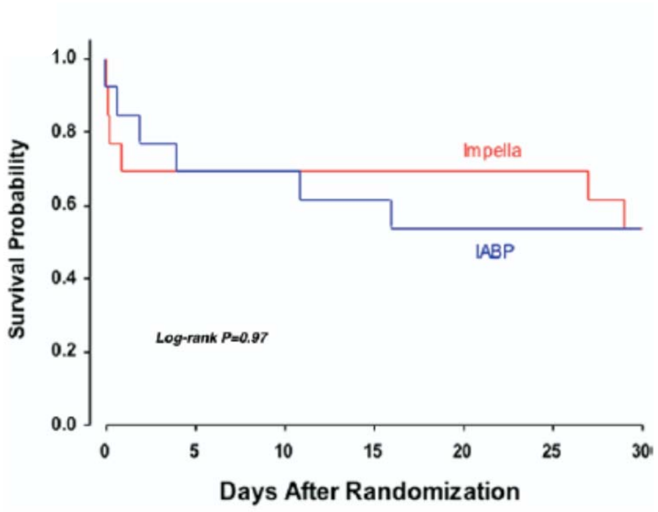
Study	Trial ID	Condition	Pts Required (n)	Pts Enrolled (n)	Duration (months)	Status	Discontinuation Reason/ comment
FRENCH TRIAL (2006)	NCT00314847	AMI CS	200	19	52	Discontinued	Low Enrollment
ISAR-SHOCK (2006)	NCT00417378	AMI CS	26	26	19	Completed	Non-Randomized Execution; Cardiac Output Study
IMPRESS in STEMI (2007)	NTR1079 trialregister.nl	STEMI Pre-CS	130	18	22	Discontinued	Low Enrollment
RECOVER I FDA (2008)	NCT00596726	PCCS	Up to 20	17	28	Completed	Feasibility Study
RECOVER II FDA (2009)	NCT00972270	AMI CS	384	1	18	Discontinued	Low Enrollment; 50 IRBs approved
RELIEF I (2010)	NCT01185691	ADHF	20	1	33	Discontinued	Low Enrollment
IMPRESS in CA (2016)	NTR3450	Cardiac Arrest Mechanical Ventilation	>100	48	52	Discontinued	Low Enrollment; Non-Randomized Execution
DanGer SHOCK (2012)	NCT01633502	AMI CS	360	103	68	Enrolling	ABMD funded, ongoing

RCT in CS -ISAR SHOCK trial-

A Randomized Clinical Trial to Evaluate the Safety and Efficacy of a Percutaneous Left Ventricular Assist Device Versus Intra-Aortic Balloon Pumping for Treatment of Cardiogenic Shock Caused by Myocardial Infarction

Melchior Seyfarth, MD,*† Dirk Sibbing, MD,* Iris Bauer, MS,* Georg Fröhlich, MD,†
Lorenz Bott-Flügel, MD,† Robert Byrne, MB, MRCPI,* Josef Dirschinger, MD,†
Adnan Kastrati, MD,* Albert Schömig, MD*†
Munich, Germany





Impella registry

USpella registry

ACUTE CORONARY SYNDROME

The Current Use of Impella 2.5 in Acute Myocardial Infarction Complicated by Cardiogenic Shock: Results from the USpella Registry

WILLIAM W. O'NEILL, M.D.,[1] THEODORE SCHREIBER, M.D.,[2] DAVID H. W. WOHNS, M.D.,[3] CHARANJIT RIHAL, M.D.,[4] SRIHARI S. NAIDU, M.D.,[5] ANDREW B. CIVITELLO, M.D.,[6] SIMON R. DIXON, M.B., CH.B.,[7] JOSEPH M. MASSARO, PH.D.,[8] BRIJESHWAR MAINI, M.D.,[9] and E. MAGNUS OHMAN, M.D.[10]

VENTRICULAR SUPPORT

The Use of Impella 2.5 in Severe Refractory Cardiogenic Shock Complicating an Acute Myocardial Infarction

FREDERIC CASASSUS, M.D.,[1] JEROME CORRE, M.D.,[1] LIONEL LEROUX, M.D., PH.D.,[1] PIERRE CHEVALEREAU, M.D.,[2] AURELIE FRESSELINAT, PH.D.,[3] BENJAMIN SEGUY, M.D.,[1] JOACHIM CALDERON, M.D.,[4] PIERRE COSTE, M.D., PH.D.,[1] ALEXANDRE OUATTARA, M.D., PH.D.,[4] XAVIER ROQUES, M.D., PH.D,[5] and LAURENT BARANDON, M.D., PH.D[6]

cVAD registry

Effect of Early Initiation of Mechanical Circulatory Support on Survival in Cardiogenic Shock

Mir B. Basir, DO[a], Theodore L. Schreiber, MD[b], Cindy L. Grines, MD[b], Simon F. Dixon, MD[c], Jeffrey W. Moses, MD[d], Brijeshwar S. Maini, MD[e], Akshay K. Khandelwal, MD[a], E. Magnus Ohman, MD[f], and William W. O'Neill, MD[a,*]

EURO-SHOCK registry

Percutaneous Left-Ventricular Support With the Impella-2.5–Assist Device in Acute Cardiogenic Shock
Results of the Impella–EUROSHOCK-Registry

Alexander Lauten, MD; Annemarie E. Engström, MD; Christian Jung, MD; Klaus Empen, MD; Paul Erne, MD; Stéphane Cook, MD; Stephan Windecker, MD; Martin W. Bergmann, MD; Roland Klingenberg, MD; Thomas F. Lüscher, MD; Michael Haude, MD; Dierk Rulands, MD; Christian Butter, MD; Bengt Ullman, MD; Laila Hellgren, MD; Maria Grazia Modena, MD; Giovanni Pedrazzini, MD; Jose P.S. Henriques, MD; Hans R. Figulla, MD; Markus Ferrari, MD

IQ database

Clinical Investigation

Analysis of outcomes for 15,259 US patients with acute myocardial infarction cardiogenic shock (AMICS) supported with the Impella device

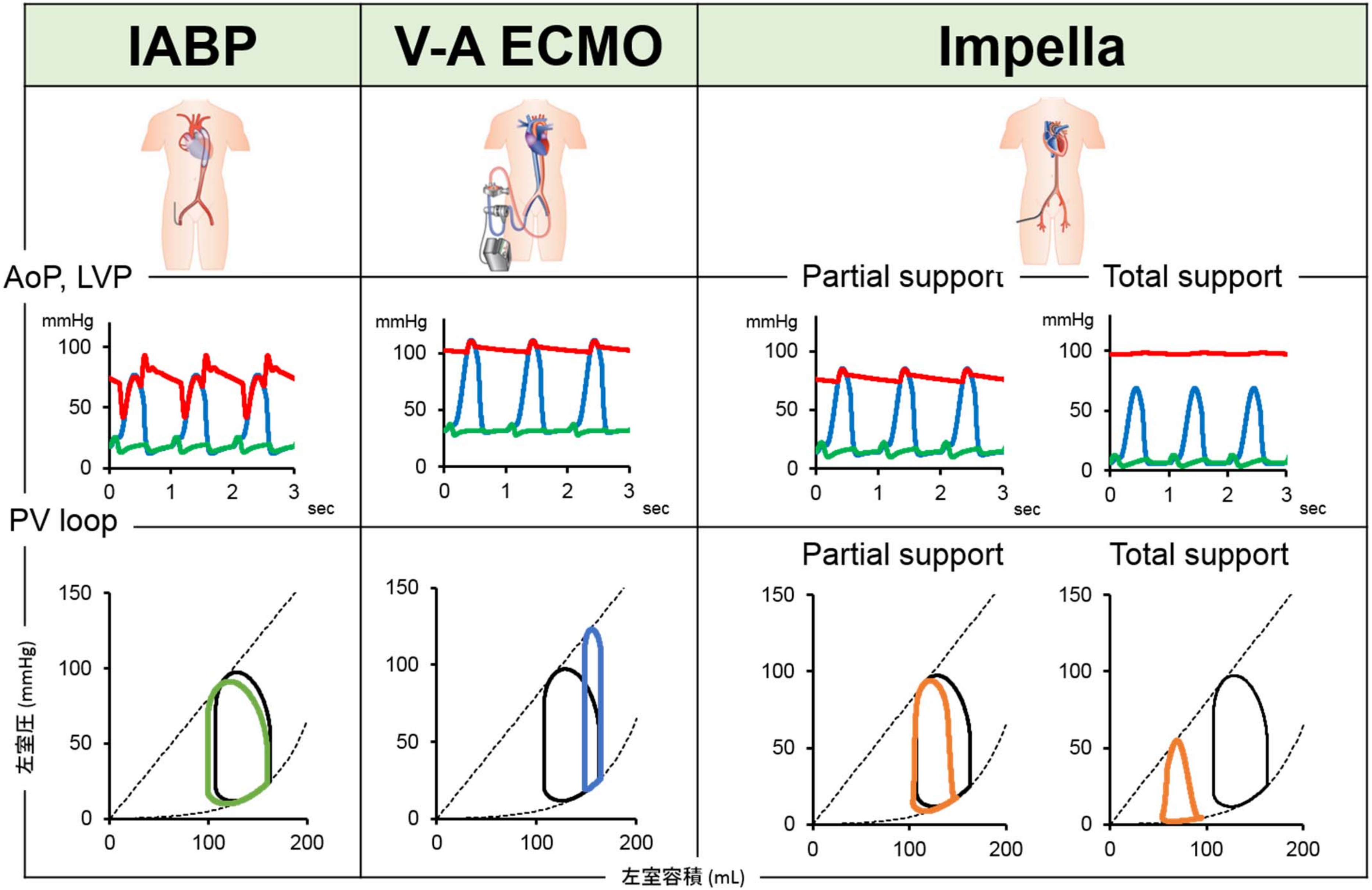
William W. O'Neill, MD, FACC[a], Cindy Grines, MD, FACC[b], Theodore Schreiber, MD, FACC[c], Jeffrey Moses, MD, FACC[d], Brijeshwar Maini, MD, FACC[e], Simon R. Dixon, MBChB, FACC[f], E. Magnus Ohman, MD, FACC[g,*]

- Hemodynamic stable
- Complete revascularization
- LVEF ↑
- Survival ↑, Event risk ↓

➡

- Strategy
- Algorithm
- Pre-PCI

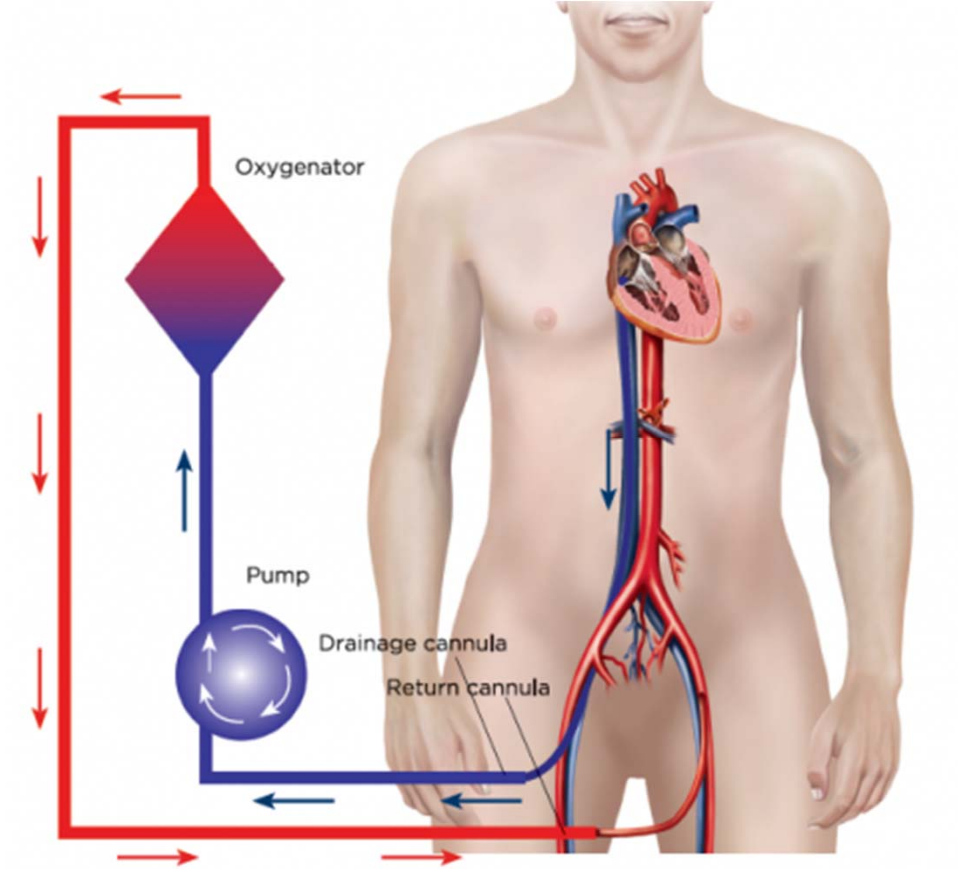
Impella and other MCS devices



ECPELLA

ECMO

Impella



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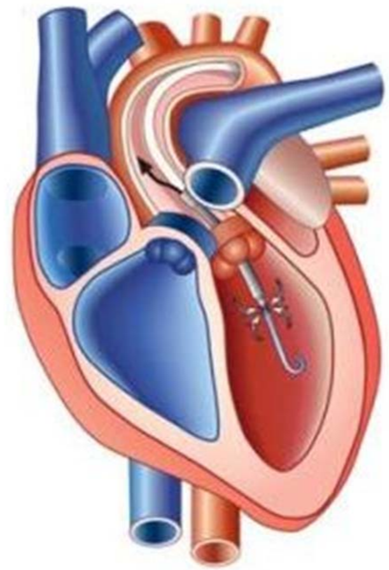
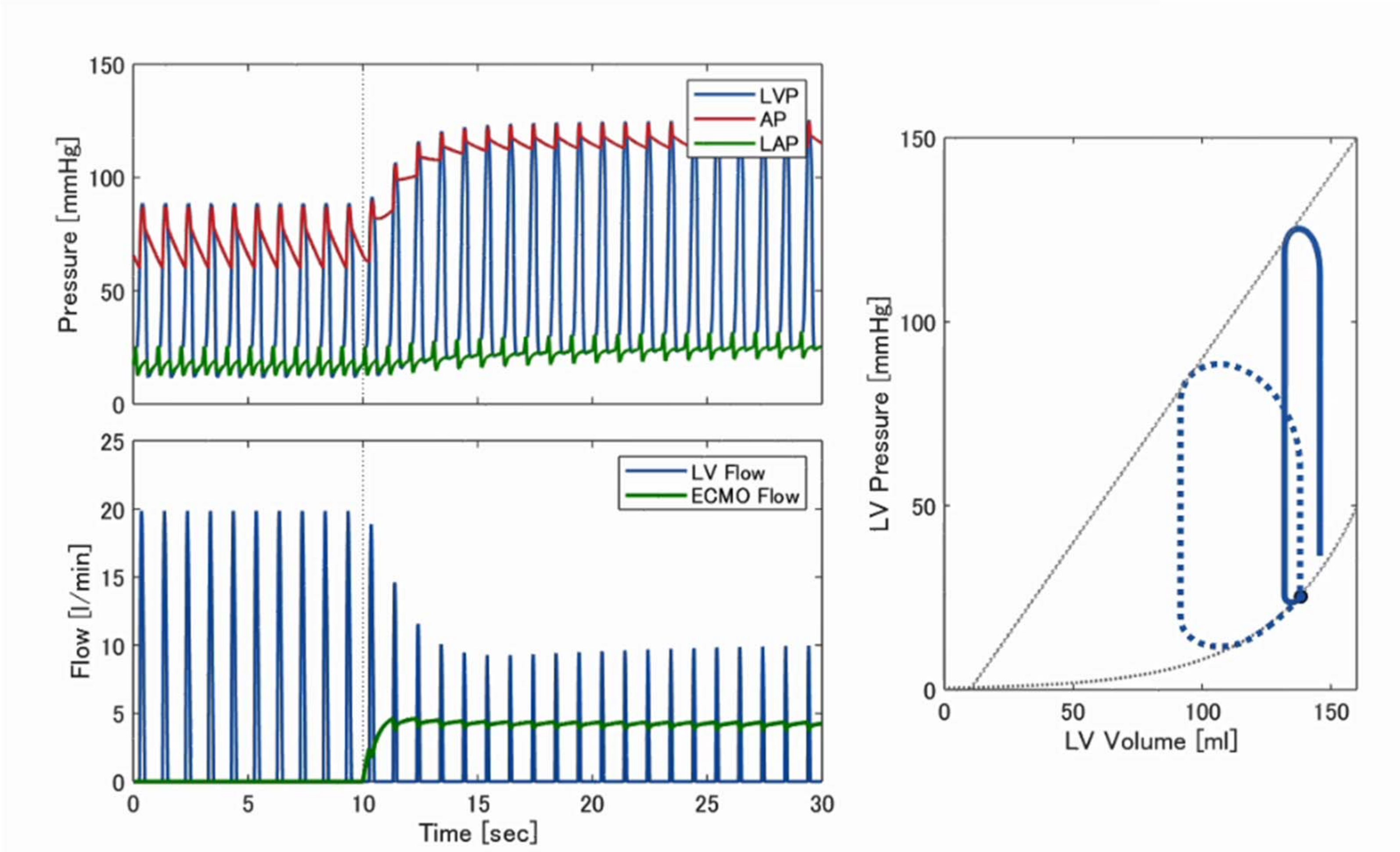
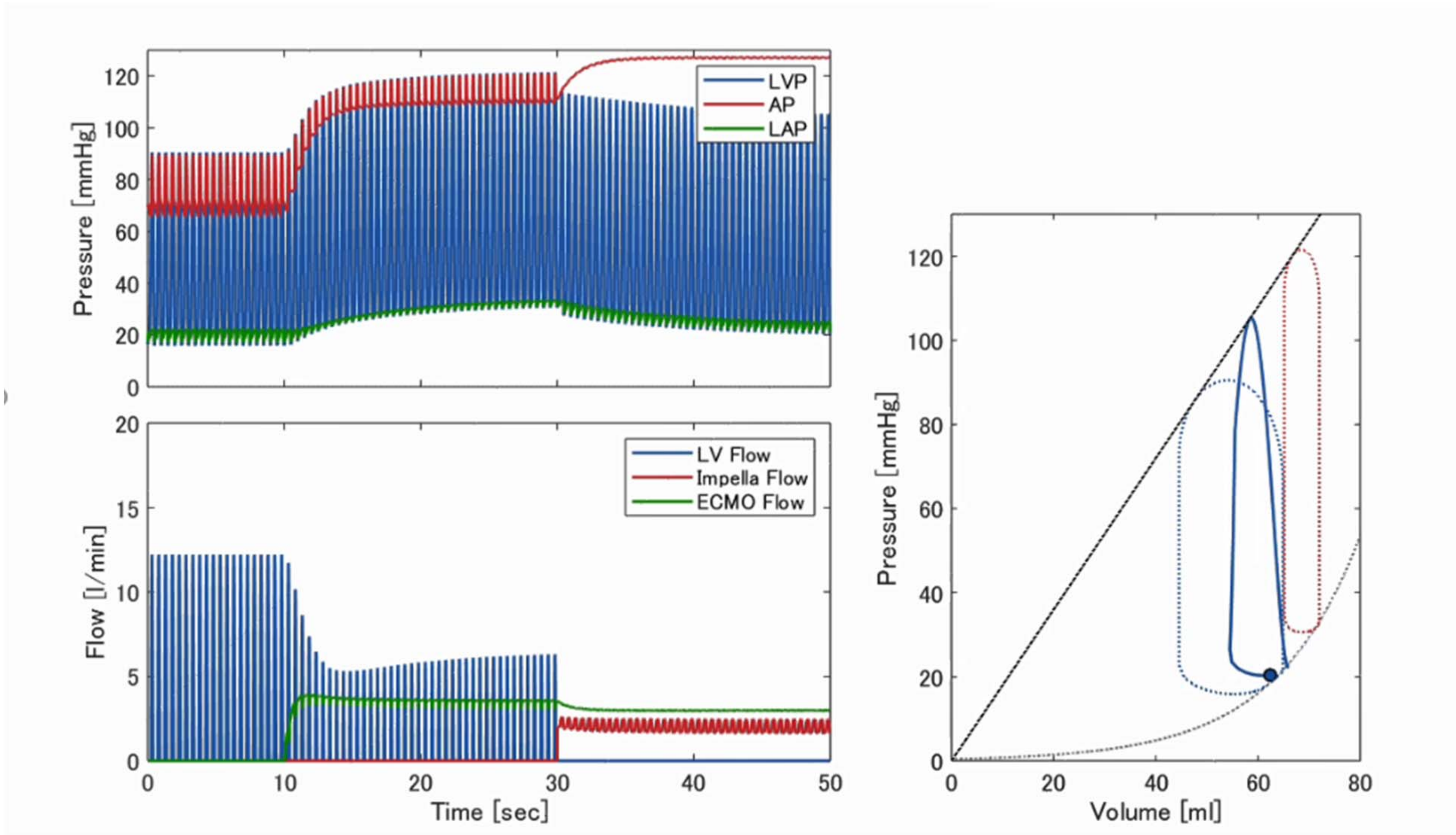


PV loop in ECMO

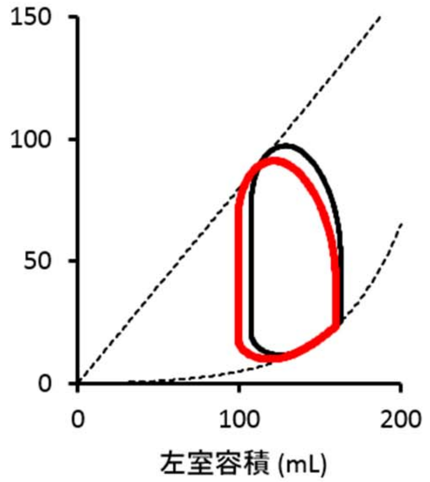


PV loop in ECPELLA

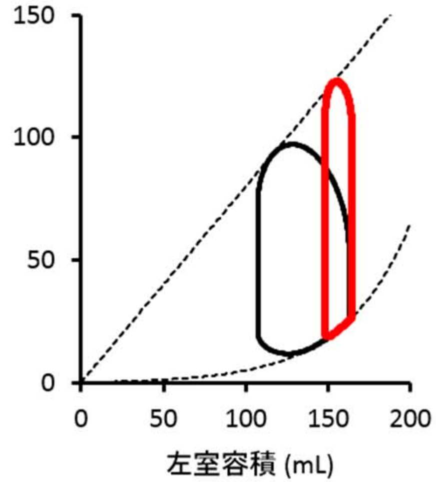


PV loop under MCS

IABP



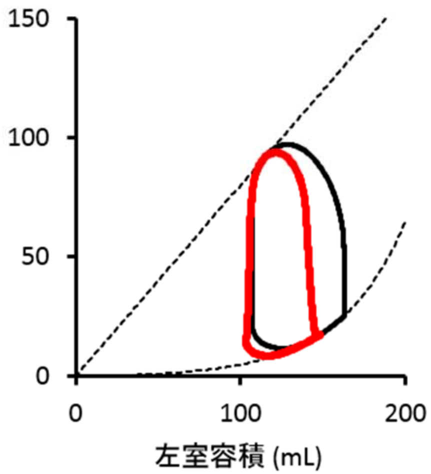
ECMO



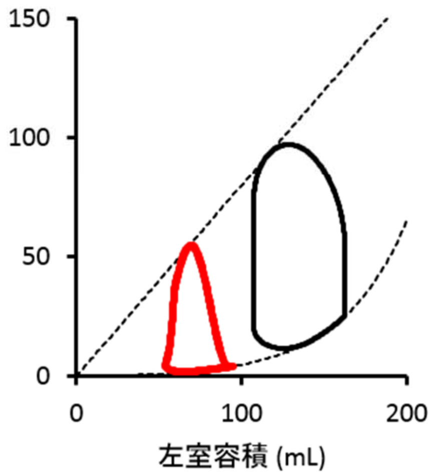
PV loop
知ると聞こえる
「心」の声

Impella

Partial support

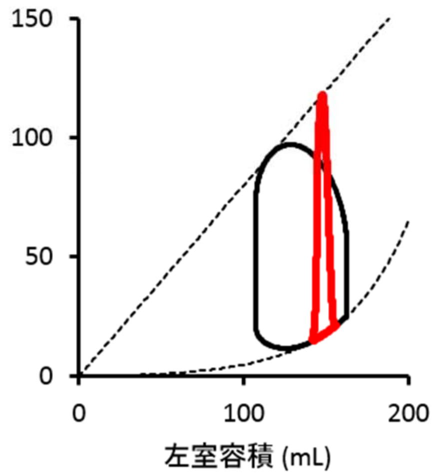


Total support

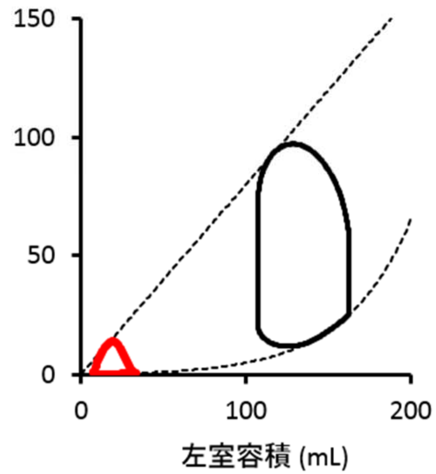


EC-pella

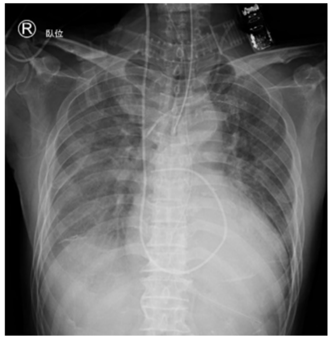
EC-pella (low)

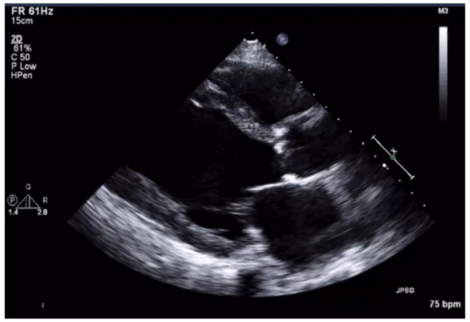


EC-pella (high)



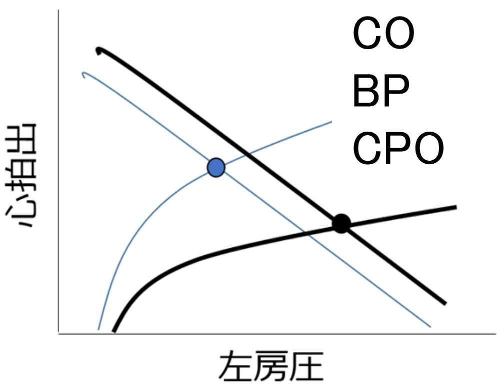
CV framework for clinical setting



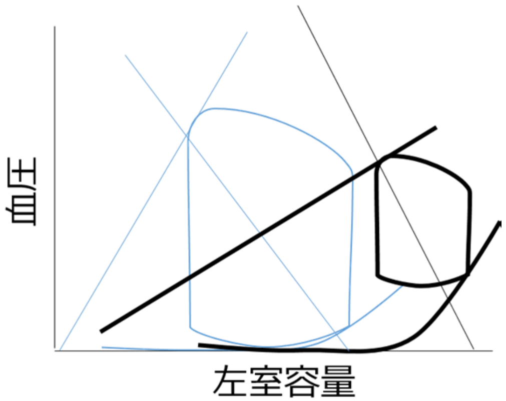


SBP 99 mmHg
DBP 68mmHg
MBP 78 mmHg
CVP 11mmHg
PCWP 24 mmHg

To CV framework



Circulation



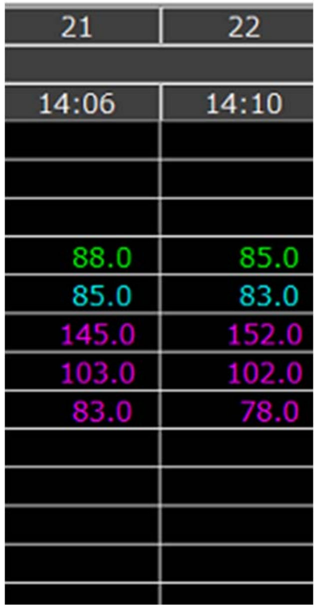
Heart

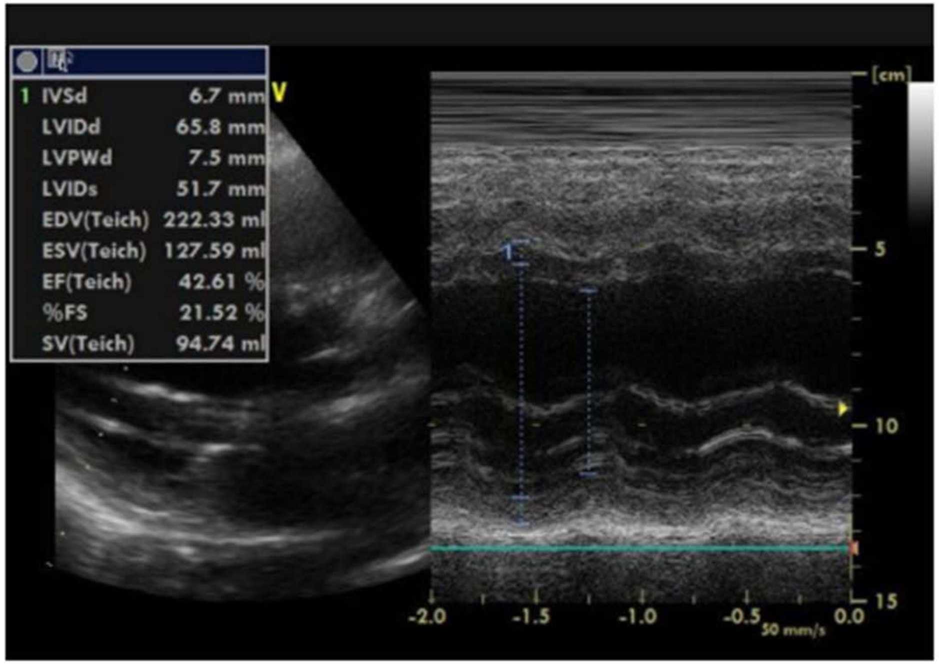
Peripheral

Answer

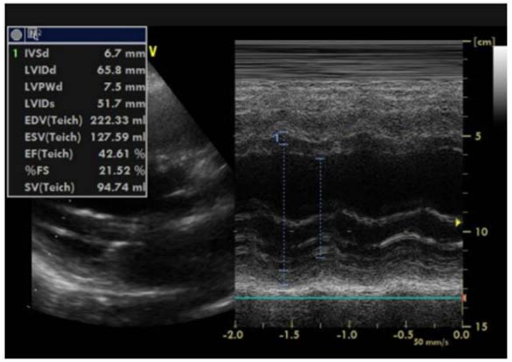
Real data simulation

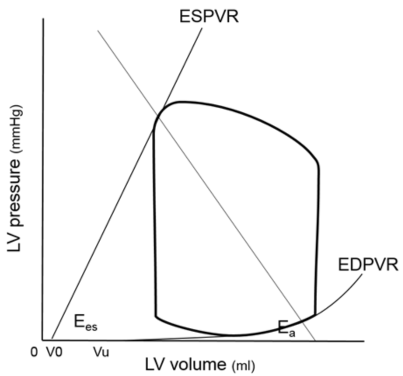
Visualization of hemodynamics

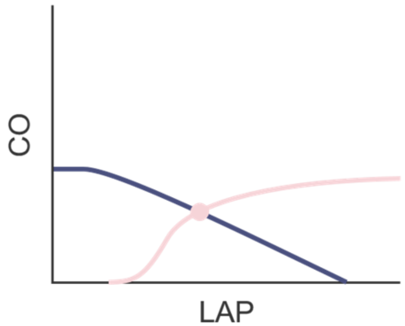




Cardiovascular properties







E_{es} ↓

※Moderate

EDPVR→

LVEDP ↑

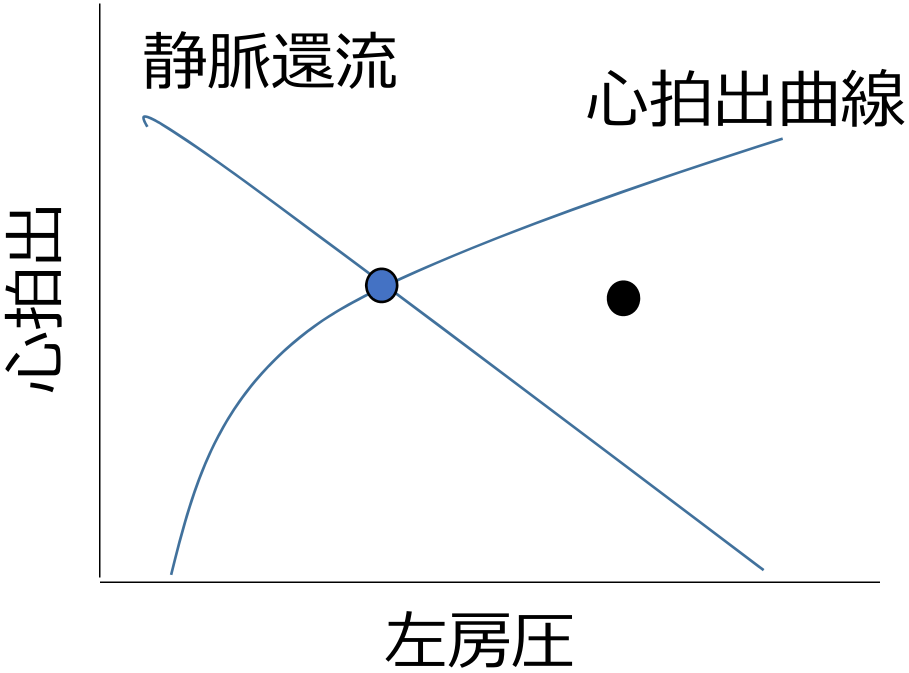
E_a ↑

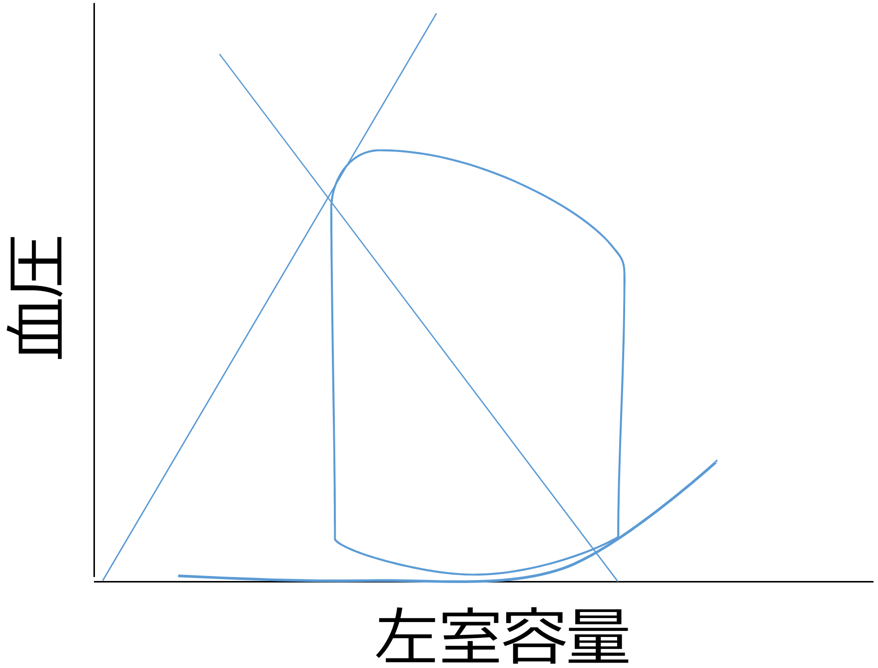
BP ↑

Framework simulation

Hemodynamic visualization by CE and PV loop

Normal/Present case

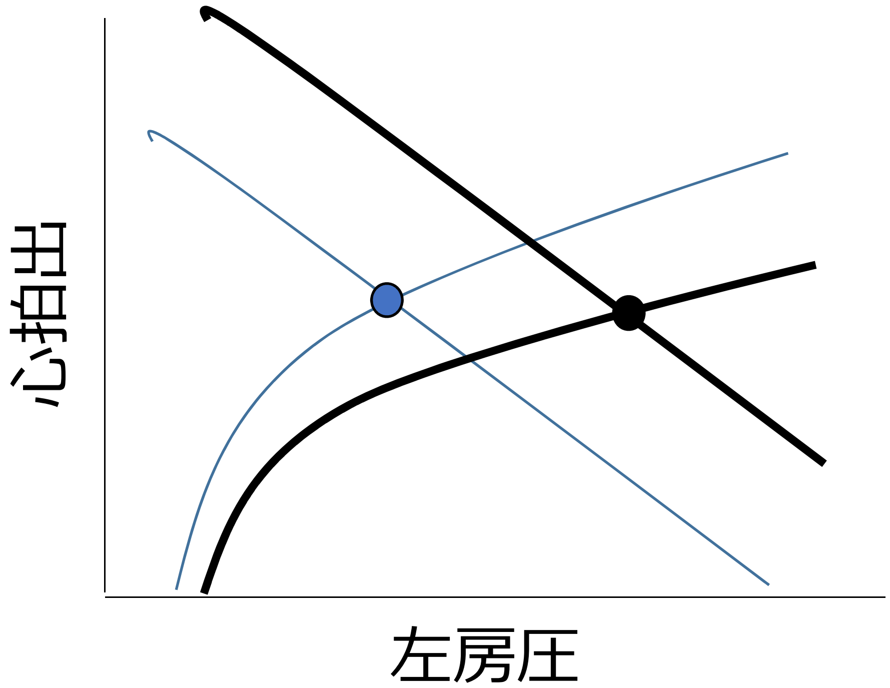


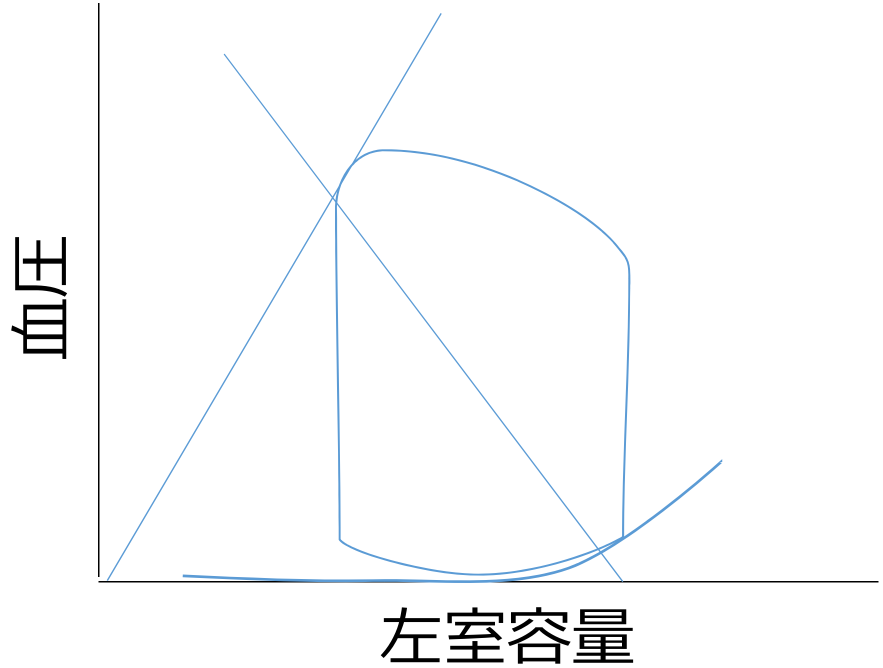


Framework study

Hemodynamic visualization by CE and PV loop

Normal/Present case

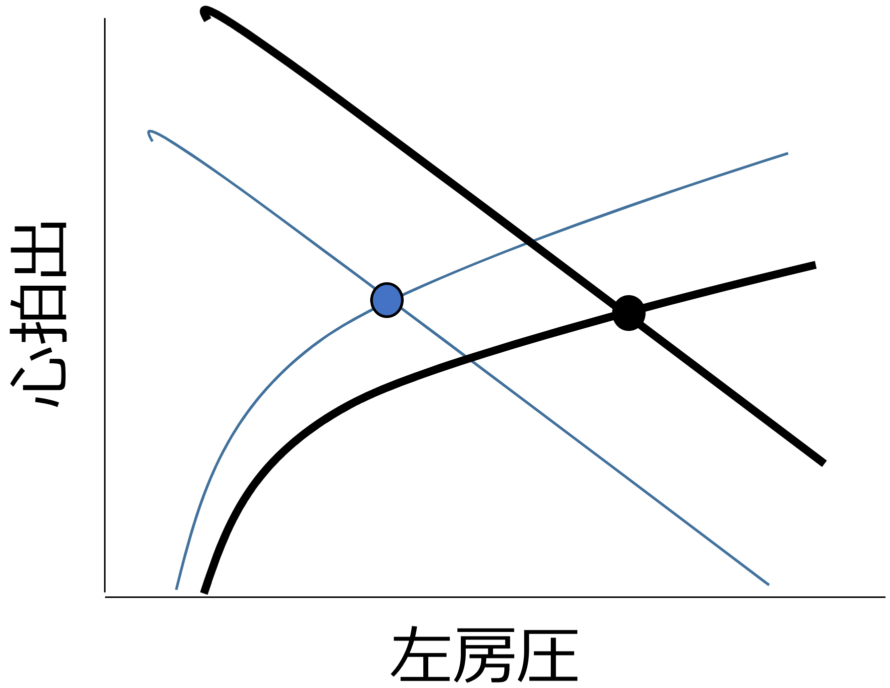


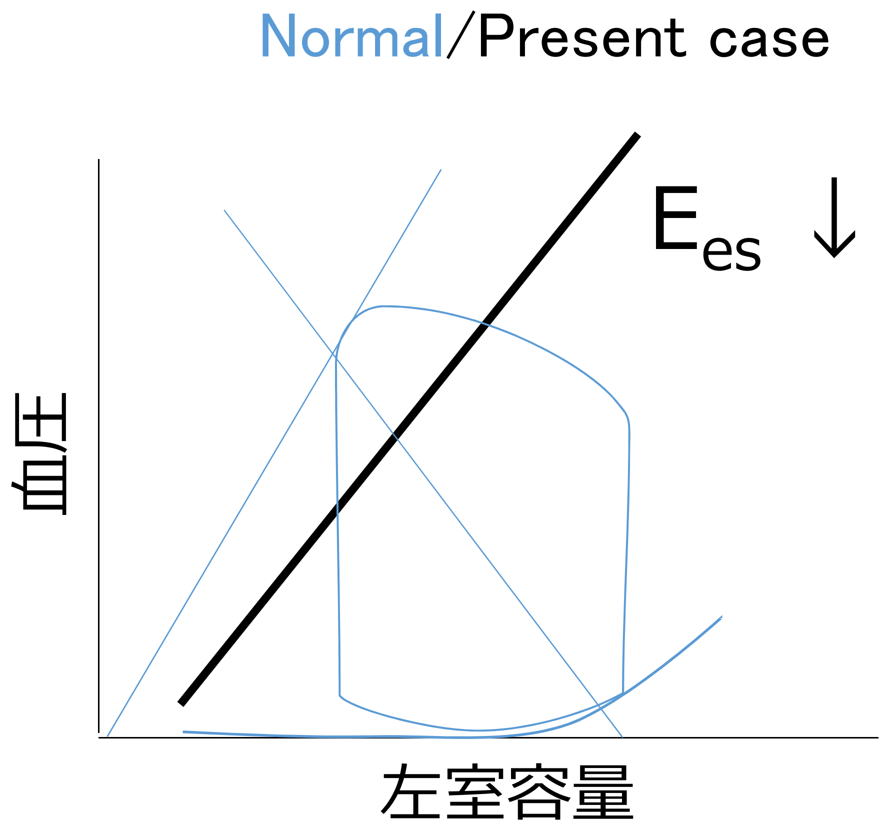


➡ 心拍出曲線は低下し、静脈還流曲線は上昇

Framework study

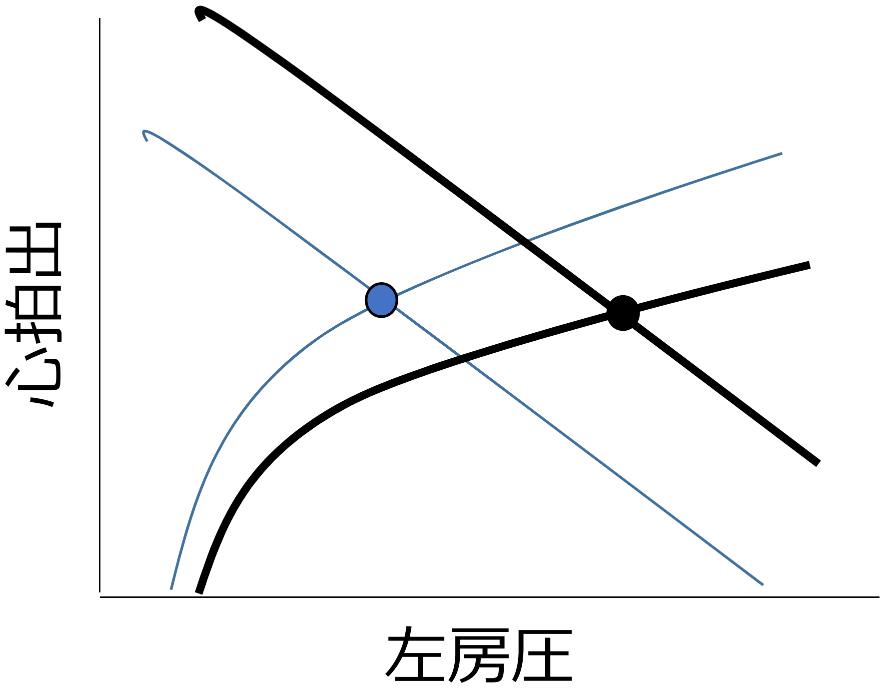
Hemodynamic visualization by CE and PV loop

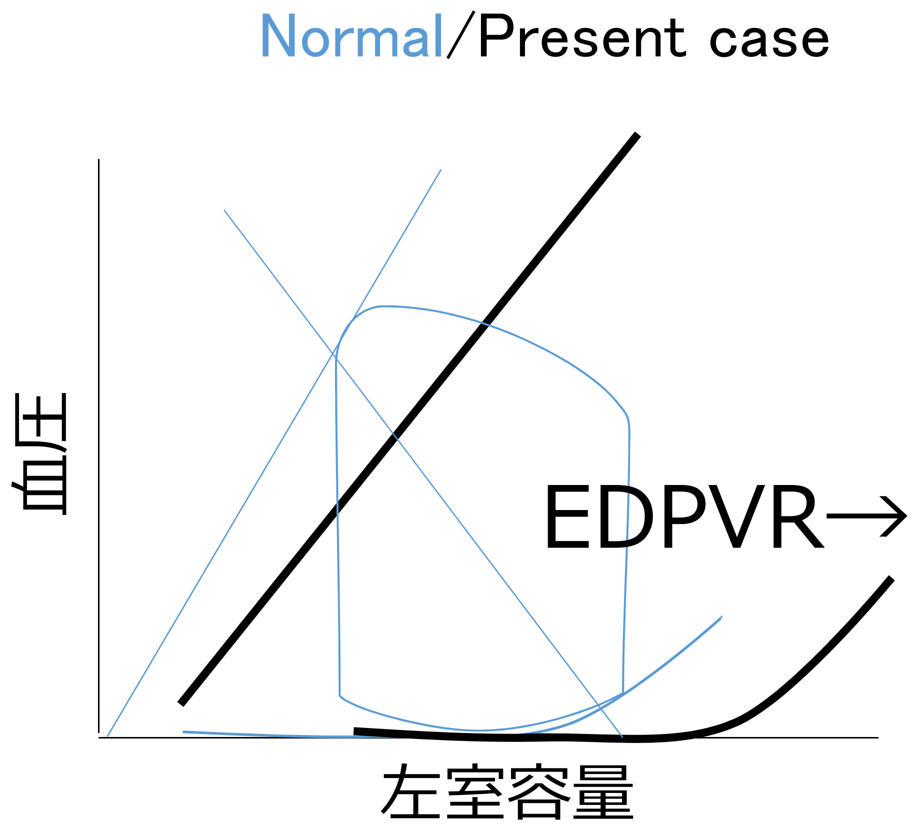




Framework study

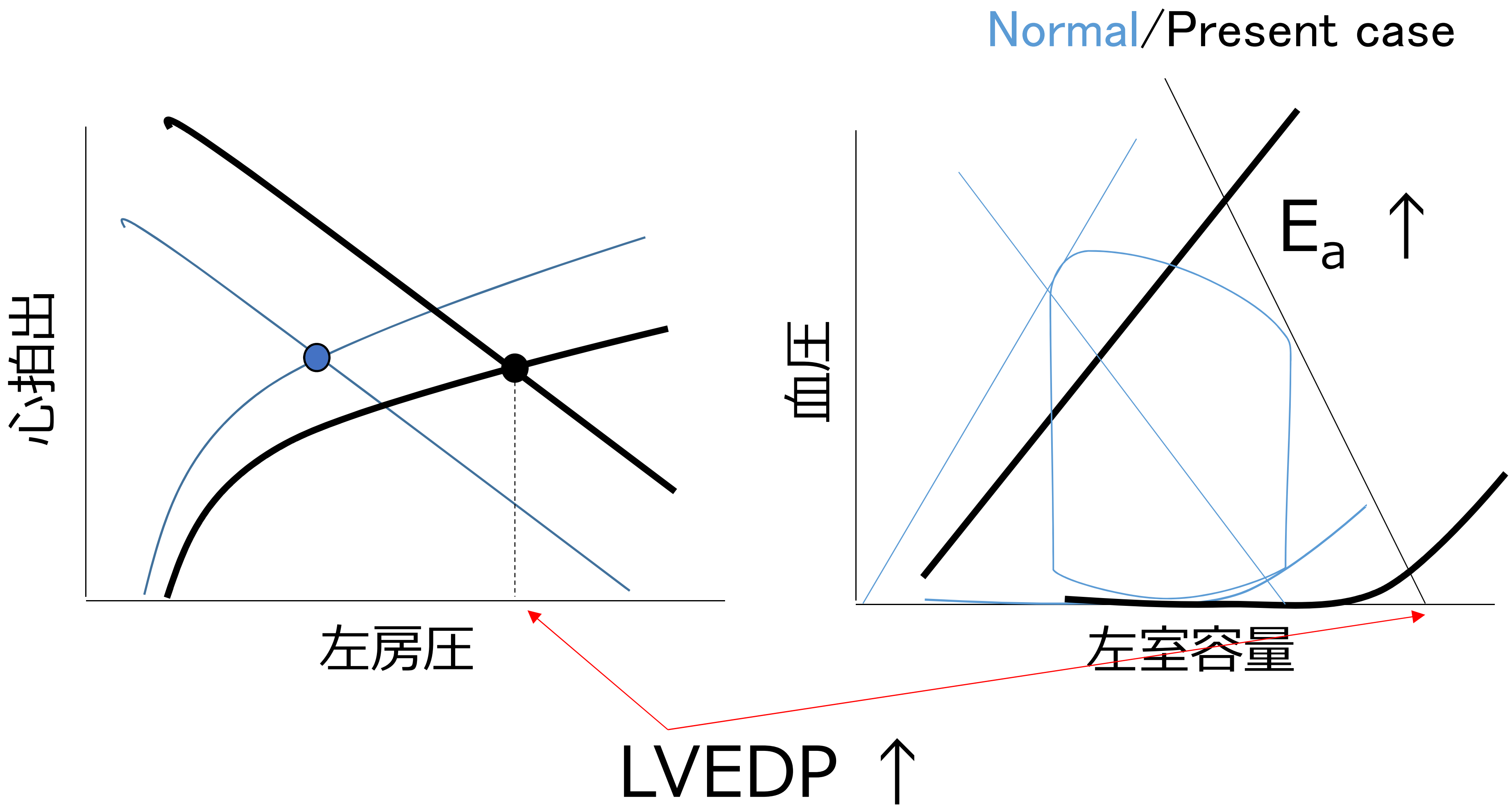
Hemodynamic visualization by CE and PV loop





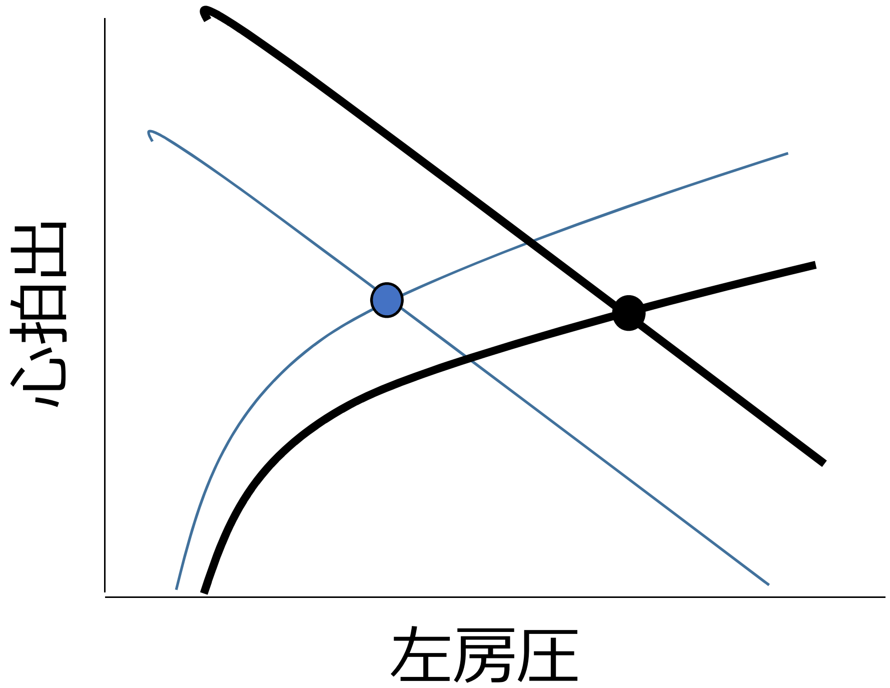
Framework study

Hemodynamic visualization by CE and PV loop

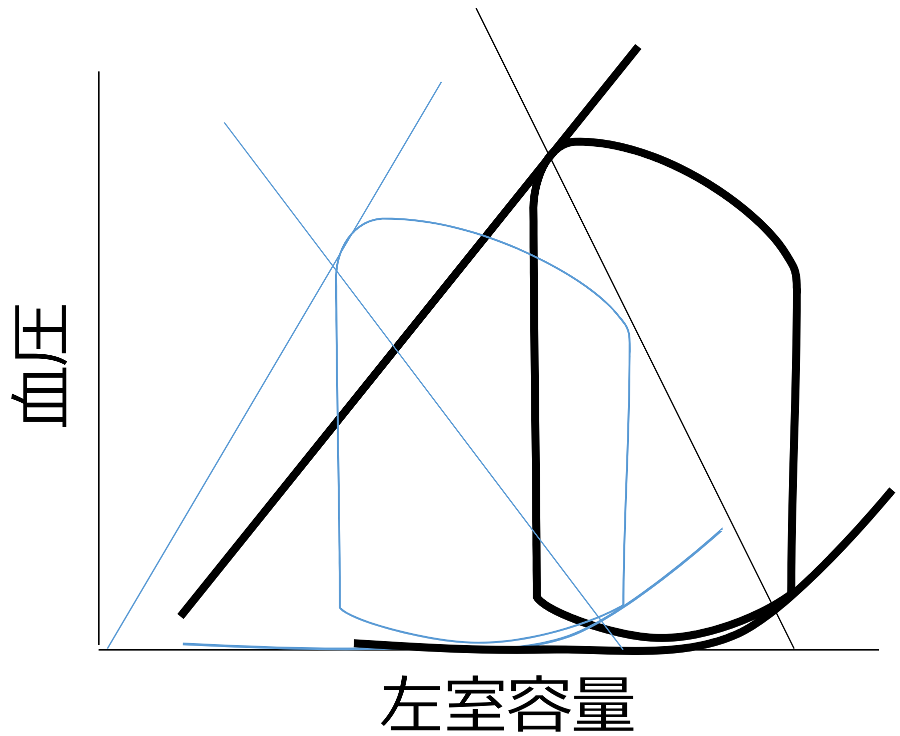


Framework study

Hemodynamic visualization by CE and PV loop

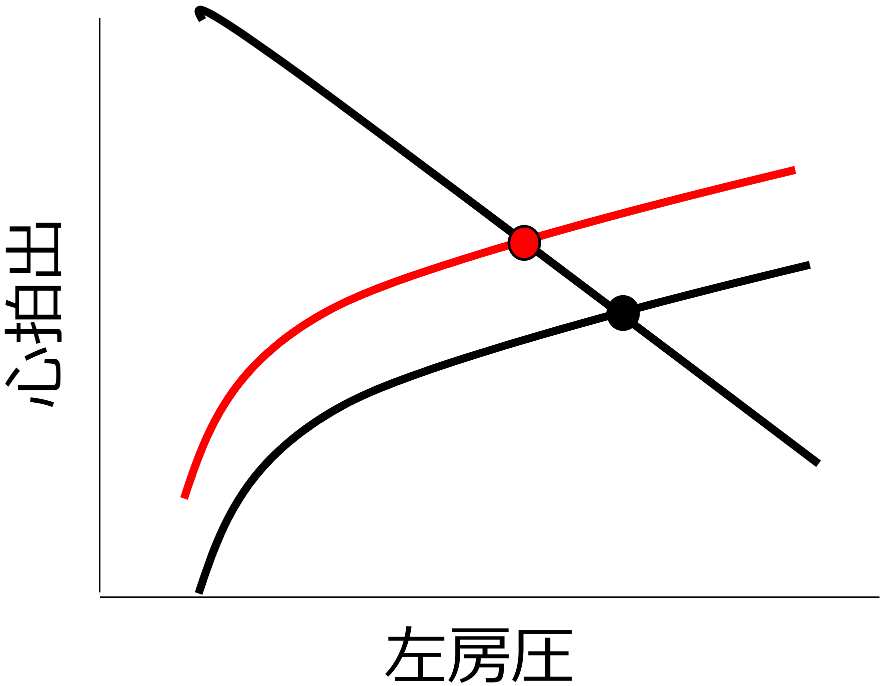


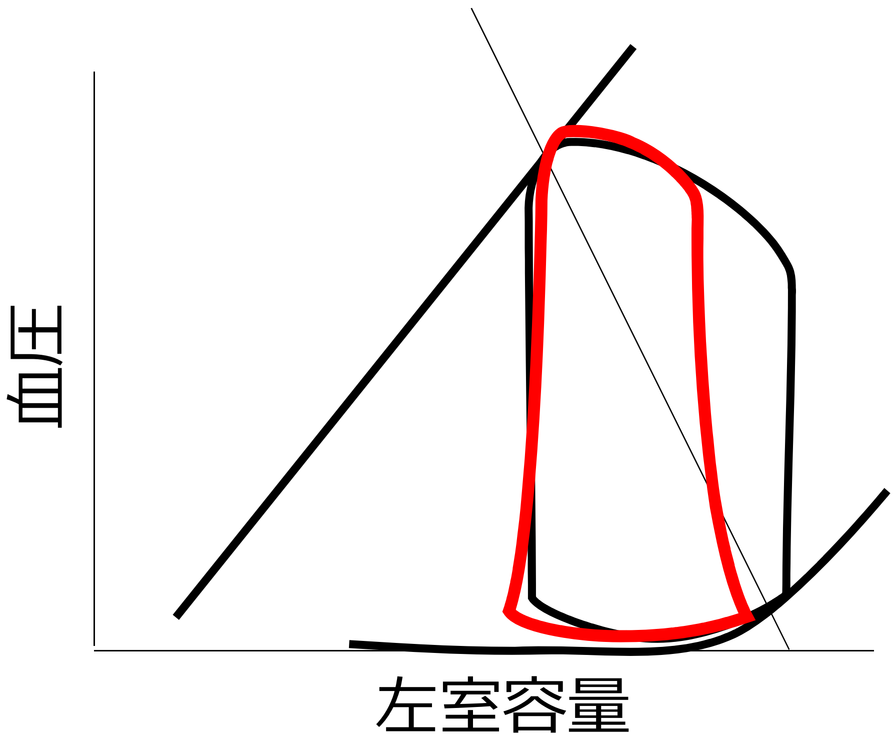
Normal/Present case



Framework study

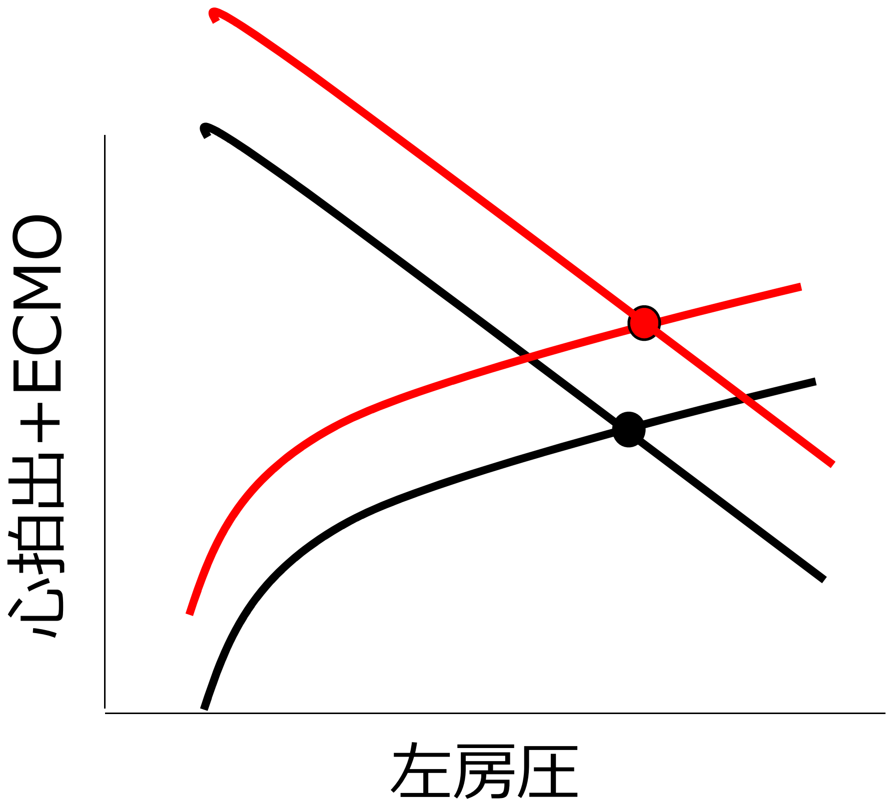
If Impella 2.5

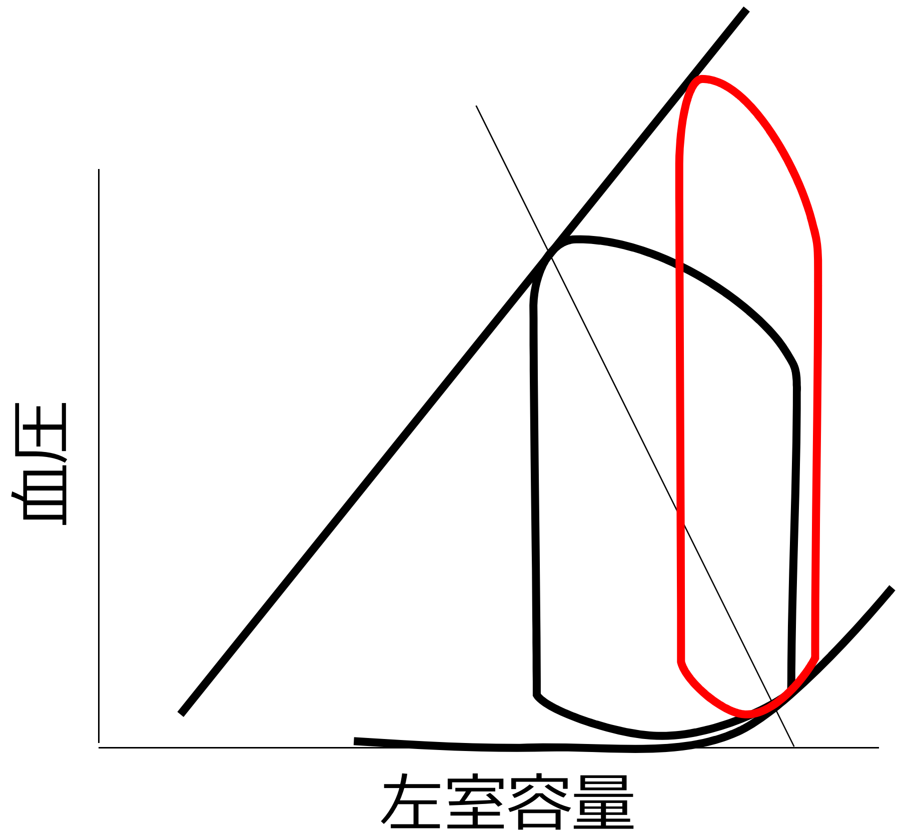




Framework study

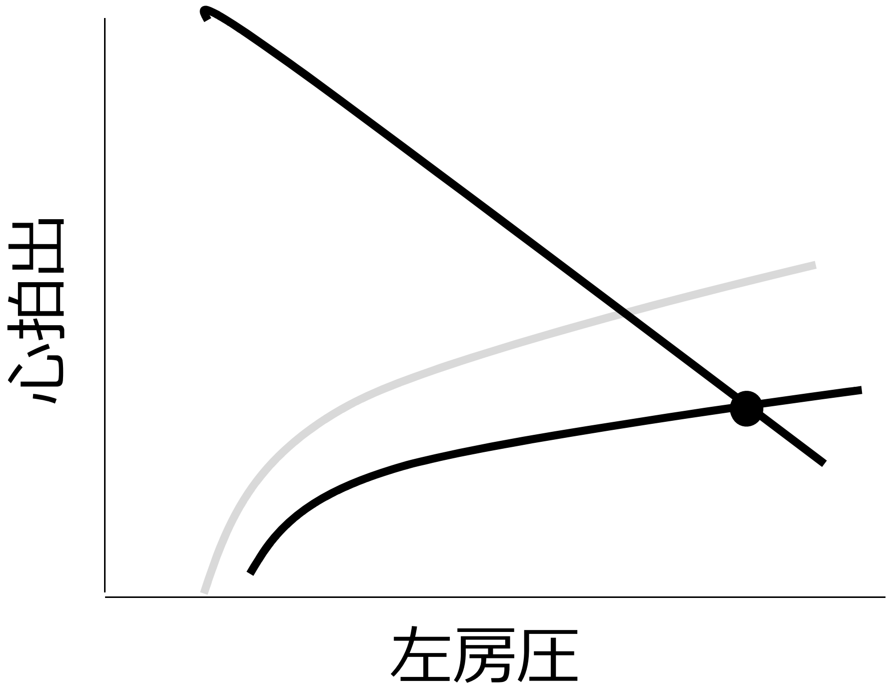
If ECMO

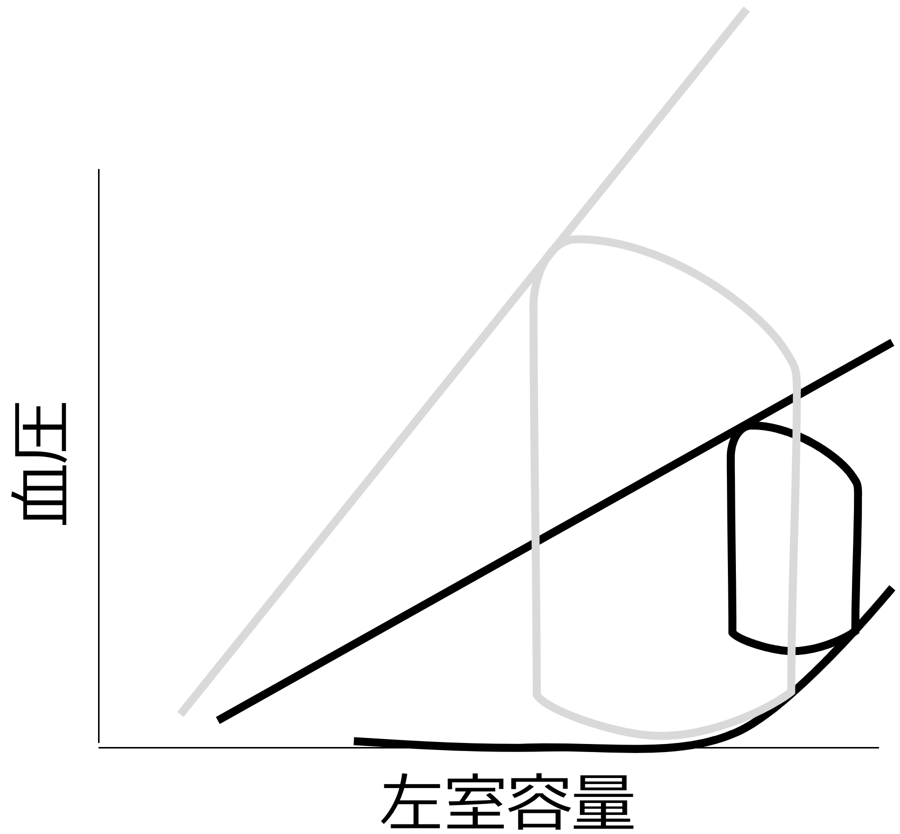




Framework study

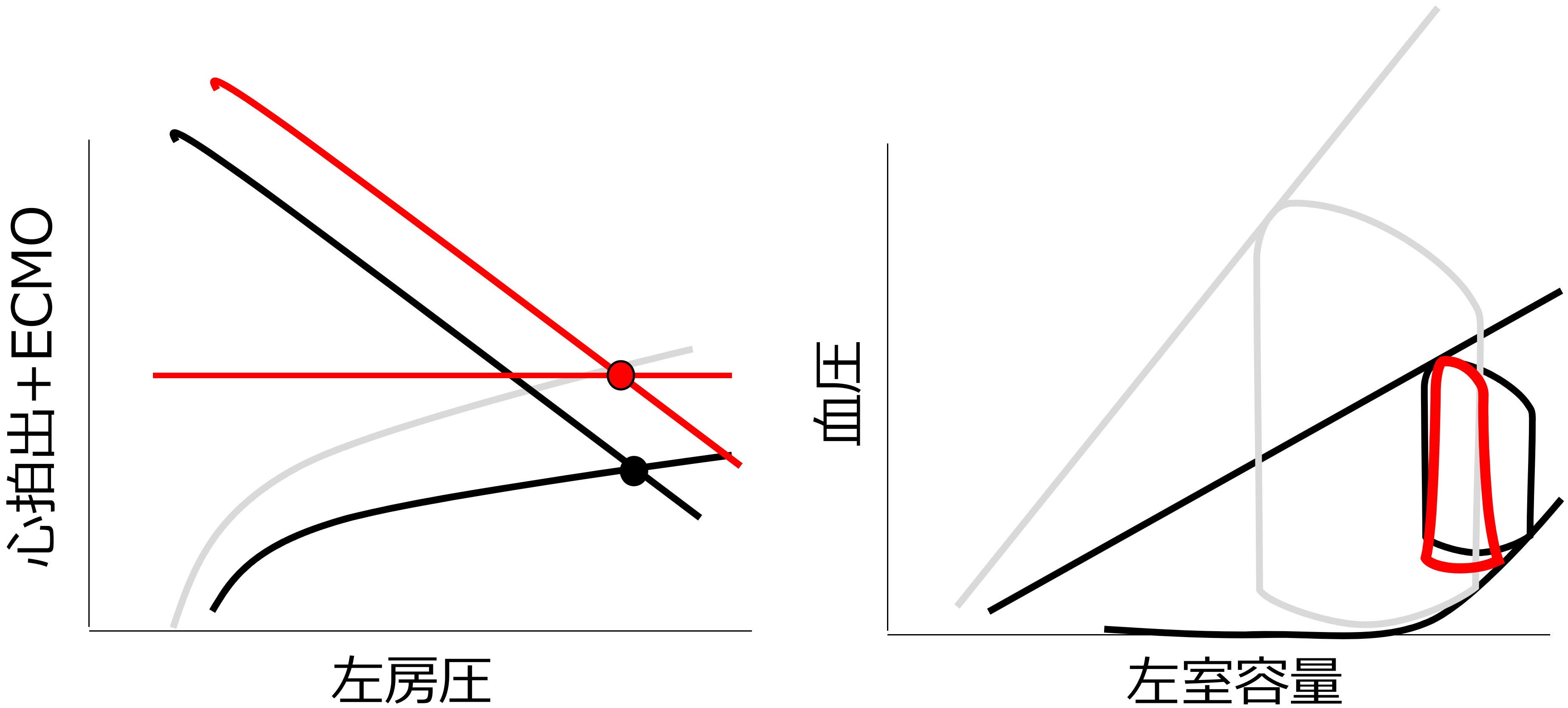
Further LV dysfunction occurred after VF…



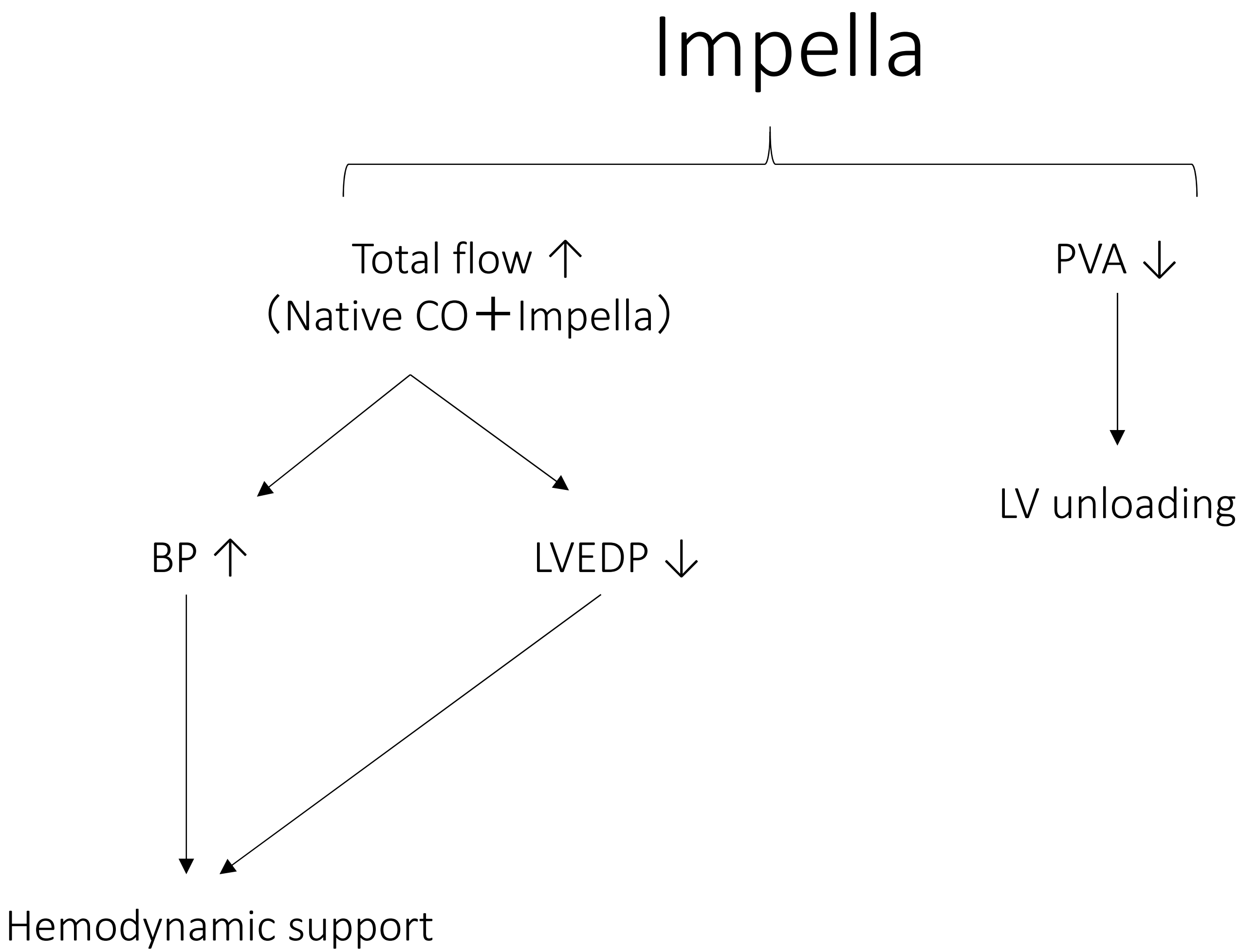


Framework study

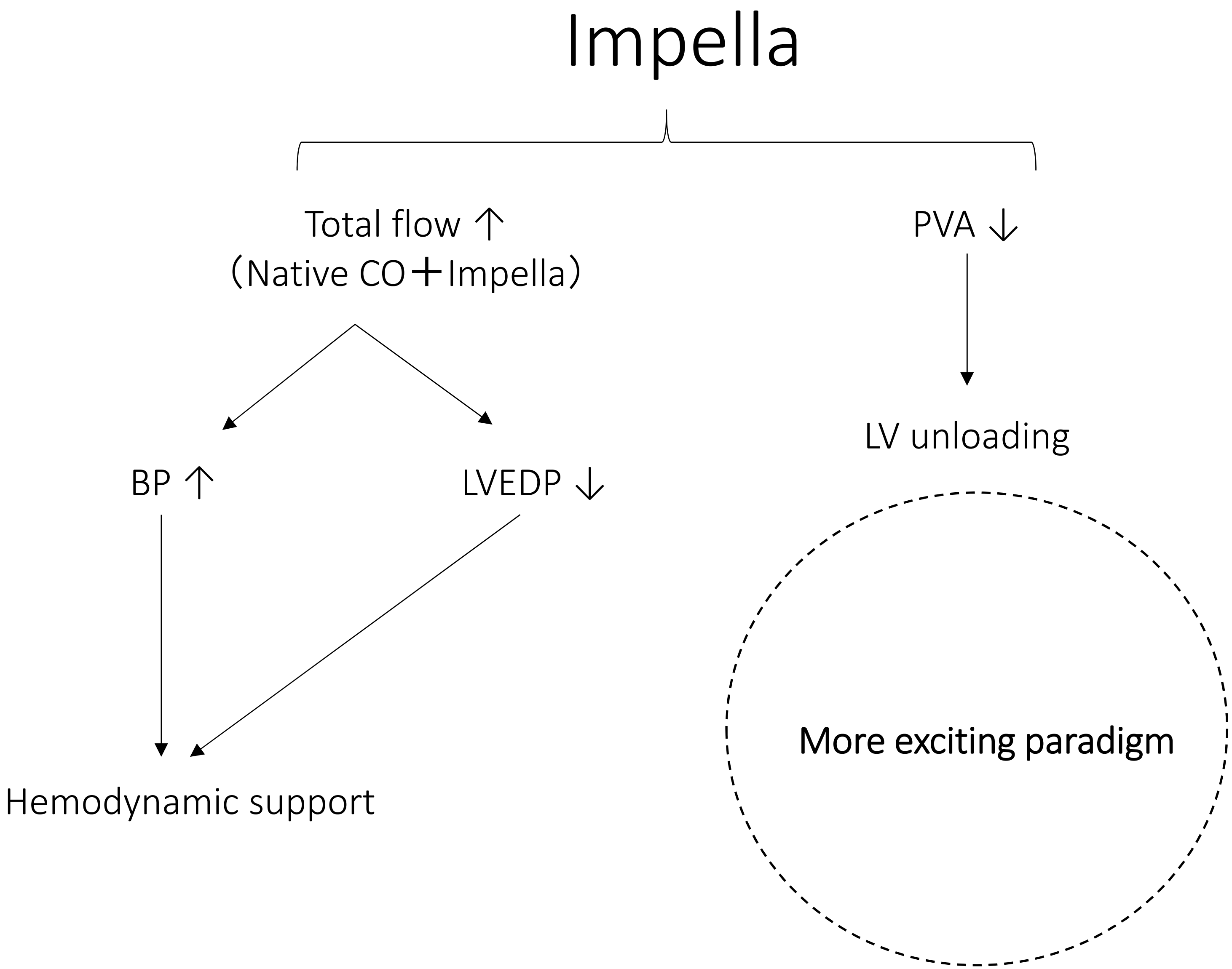
ECPELLA



Impella effects overview



Impella effects overview

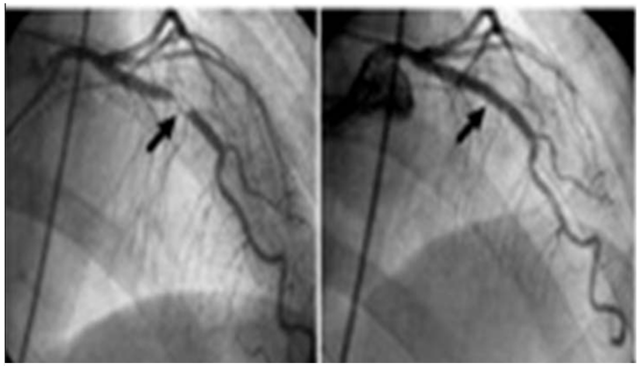


Clinical option of Impella unloading

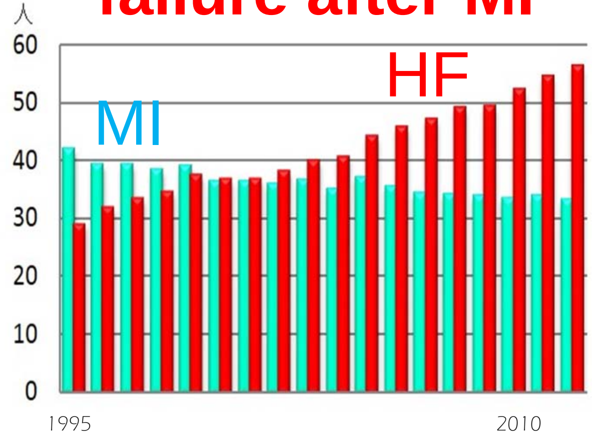
- ✓ Recent progress in the treatment of acute myocardial infarction (AMI) has lowered acute mortality to less than 10%.
- ✓ However, the presence of myocardial damage leads to heart failure in about 30% of patients in the long term.
- ✓ The latest reperfusion therapy is still unsatisfactory for preventing future heart failure.

AMI

Early reperfusion

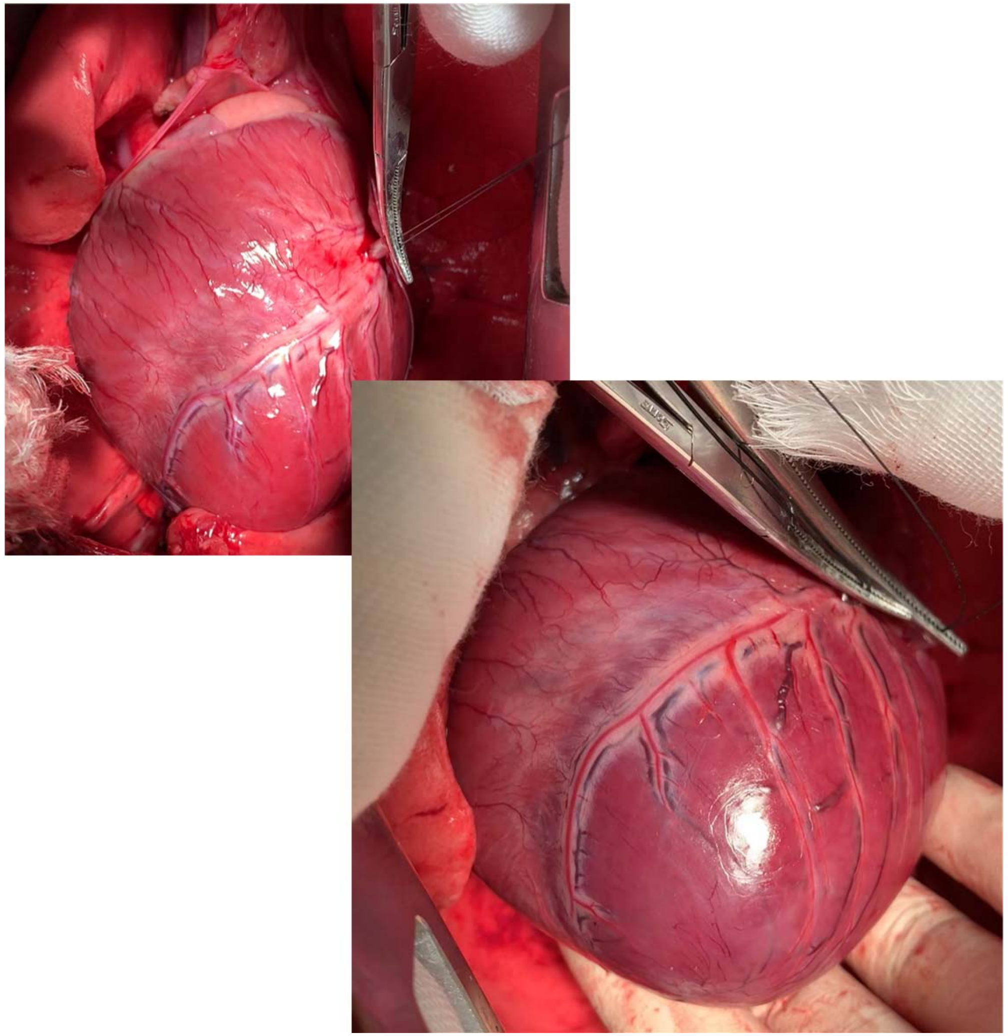


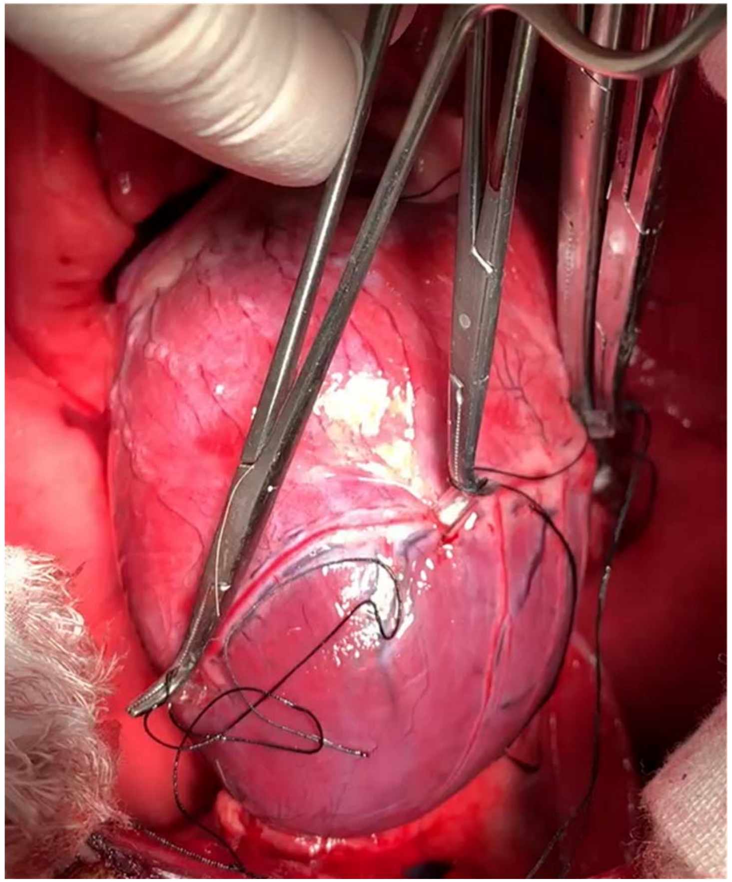
Increasing in heart failure after MI



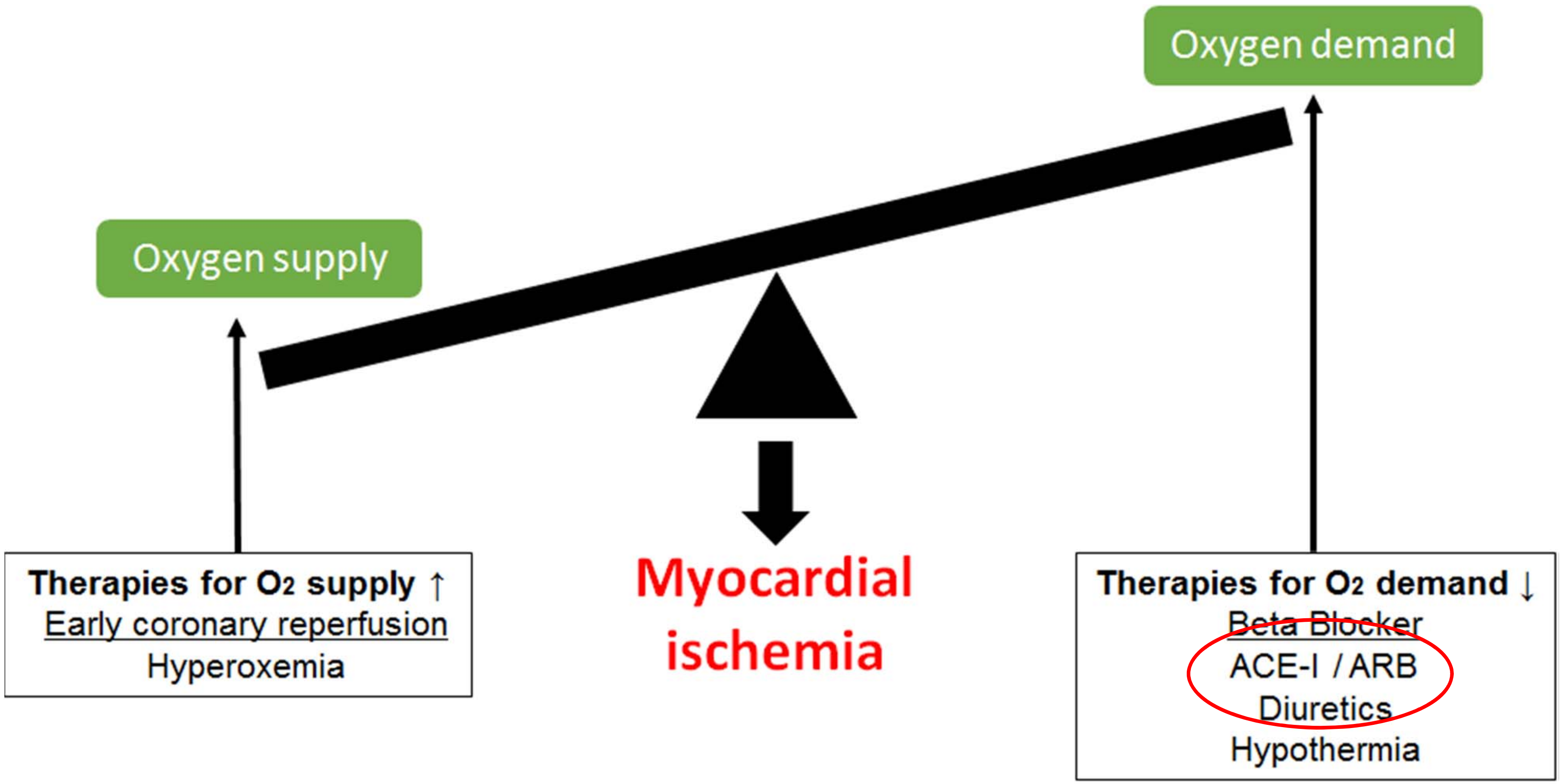
Ischemia-reperfusion

Ischemia → Reperfusion

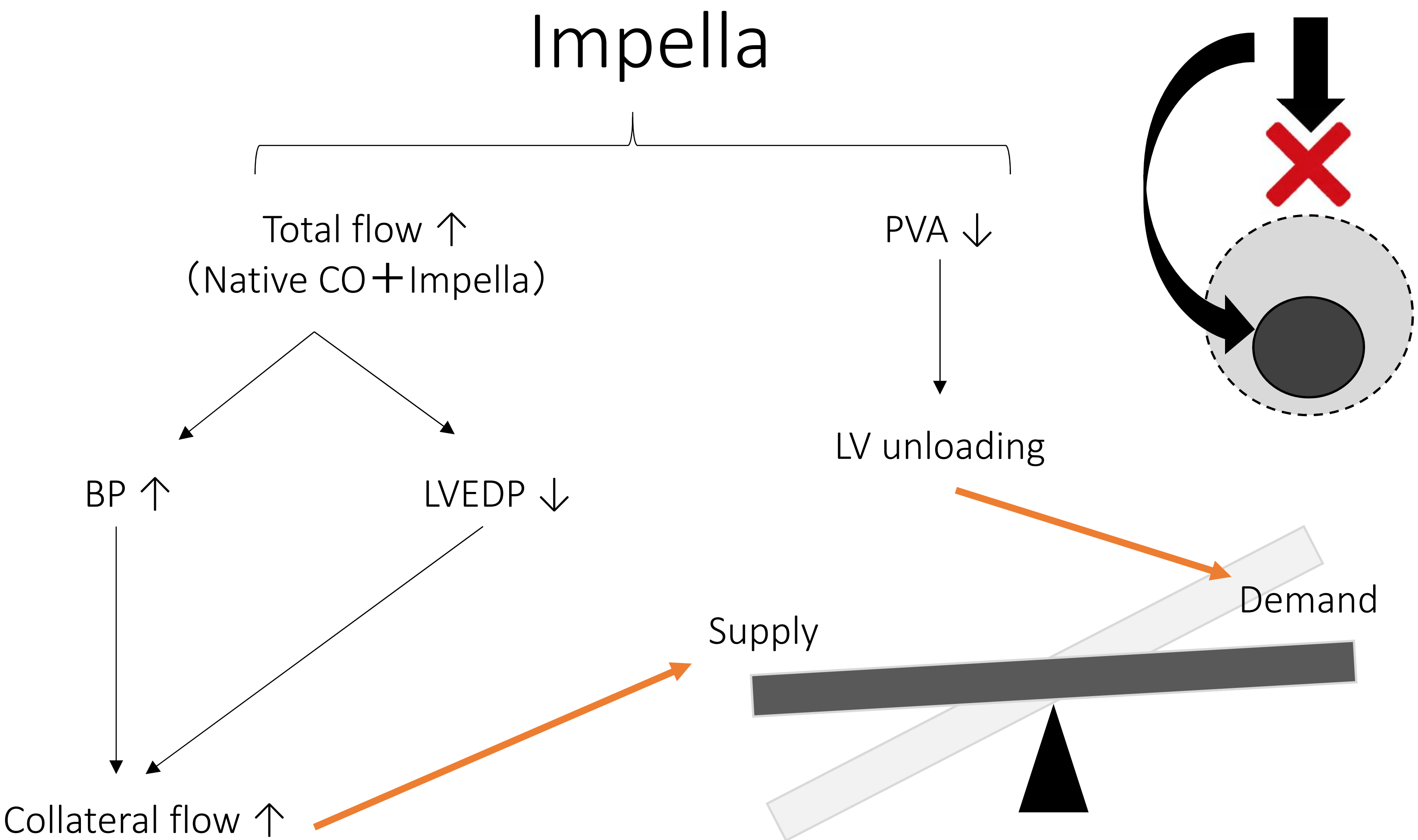




Imbalance between supply and demand



Impella effects during ischemia



Acute unloading in MI is “Functional reperfusion”.

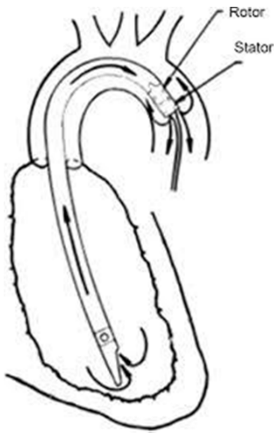
Acute umloading limits infarct size

Hypothesis

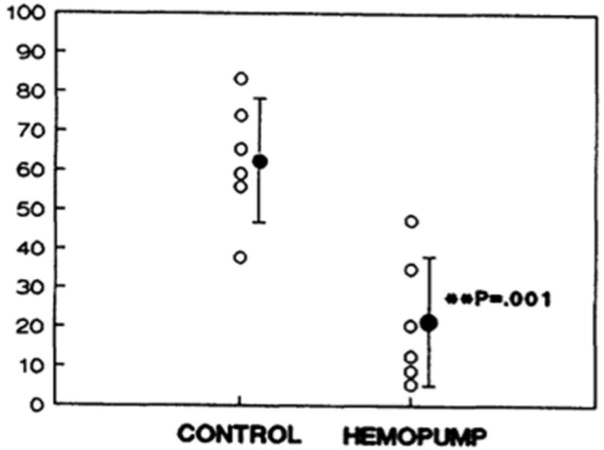
LV mechanical unloading in acute MI (acute unloading) reduces infarct size.

Hemopump reduces MI size

- Dog
- 2 hrs MI and 1 hr reperfusion
- Hemopump



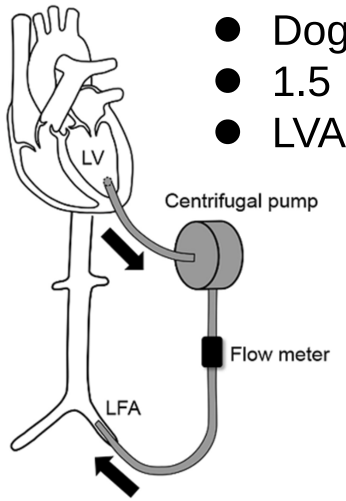
Infarct size (%)

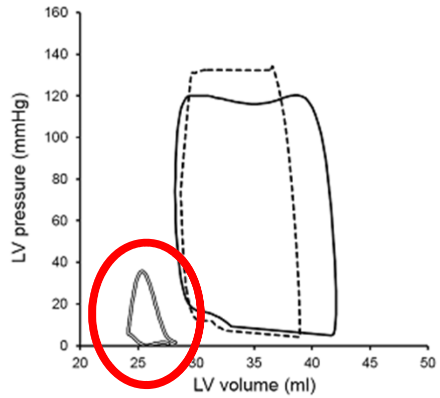


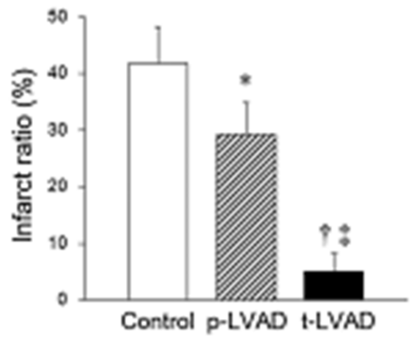
Smalling et al. Circulation 1992.

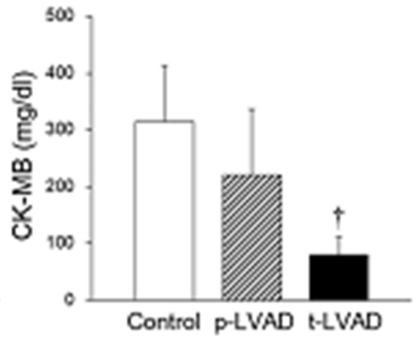
Total LVAD reduces MI size

- Dog
- 1.5 hrs MI and 5 hr reperfusion
- LVAD









Saku et al. Plos one 2015.

Acute Impella limits infarct size

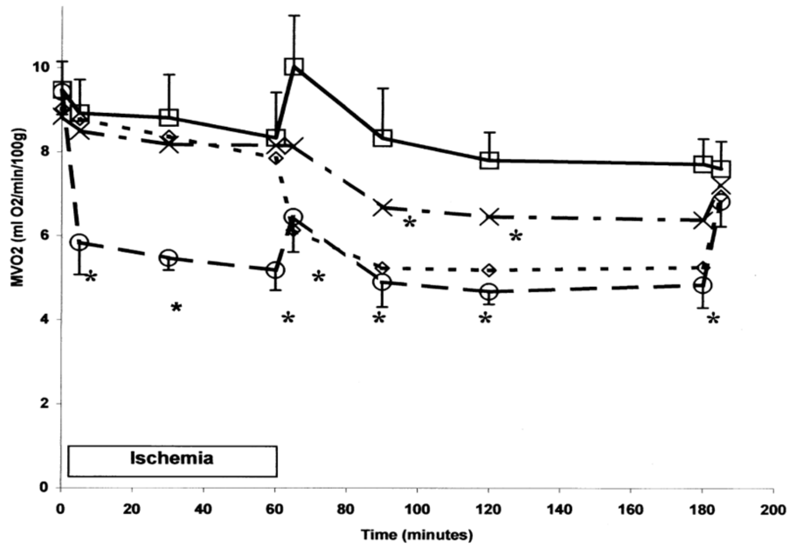
Left Ventricular Support by Catheter-Mounted Axial Flow Pump Reduces Infarct Size

Bart Meyns, MD, PhD, Jarek Stolinski, MD, Veerle Leunens, Erik Verbeken, MD, PhD, Willem Flameng, MD, PhD

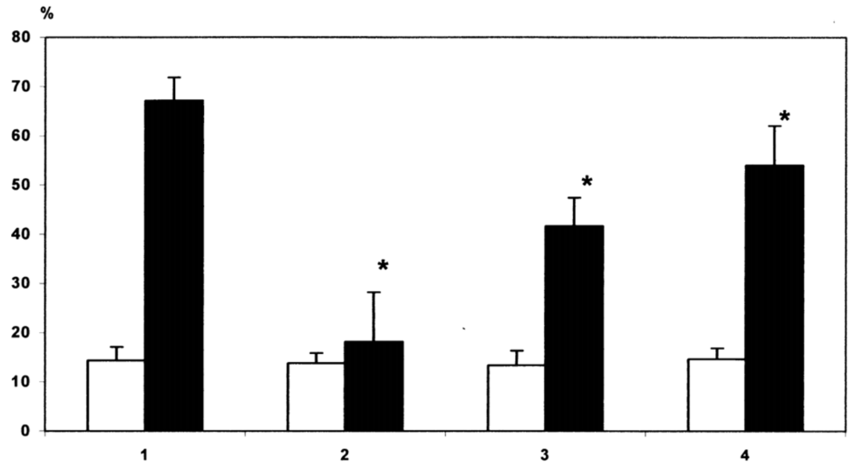
- Swine
- 1 hr MI and 3 hrs reperfusion

Group 1 : Control group
Group 2 : Maximum Impella entire exp.
Group 3 : Maximum Impella during reperfusion
Group 4 : Partial Impella during reperfusion

<u>Changes in MVO_2</u>



<u>MI size (%)</u>

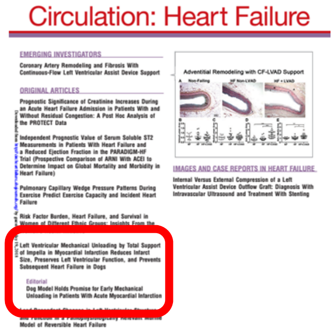


Meyns et al. JACC 2003.

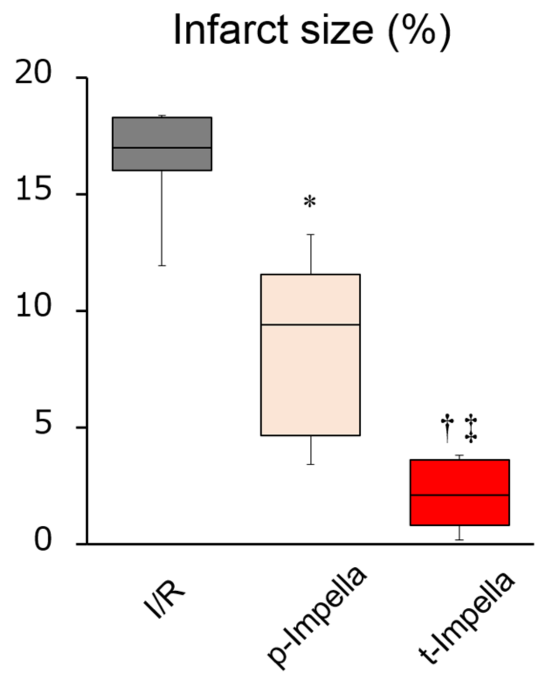
Total Impella support limits infarct size and prevents heart failure

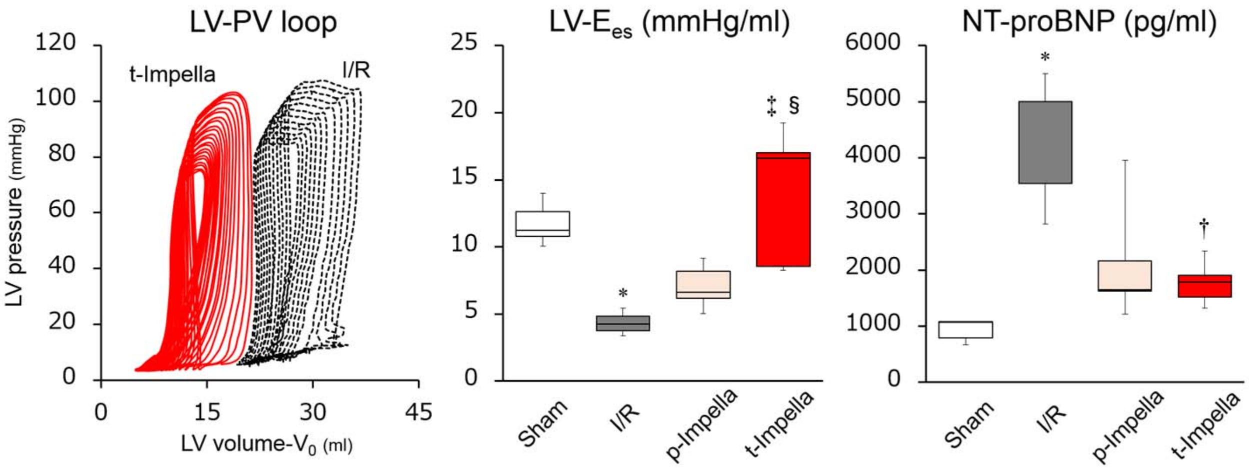
ORIGINAL ARTICLE

Left Ventricular Mechanical Unloading by Total Support of Impella in Myocardial Infarction Reduces Infarct Size, Preserves Left Ventricular Function, and Prevents Subsequent Heart Failure in Dogs



- Dog
- 3 hrs MI and reperfusion
- Assessment in a month after MI
- Impella CP

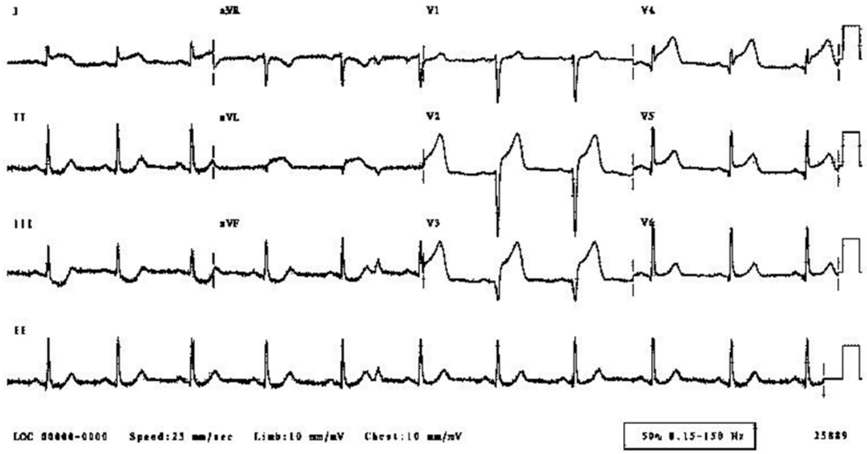


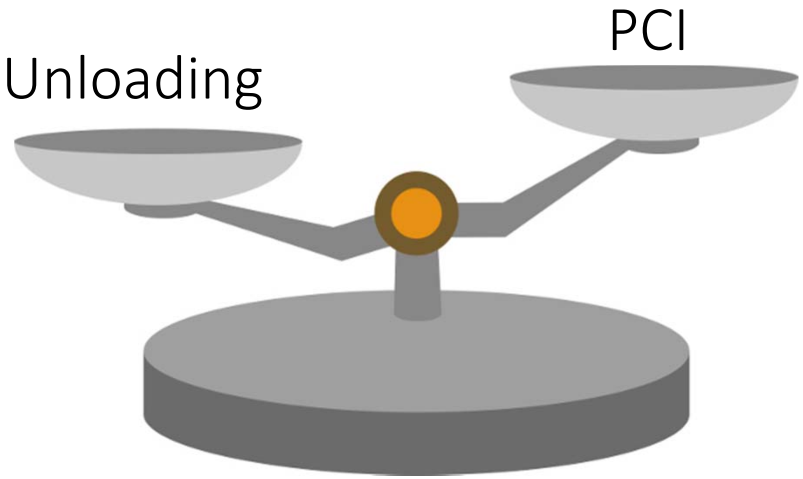


Saku et al. Circ Heart Fail 2018.

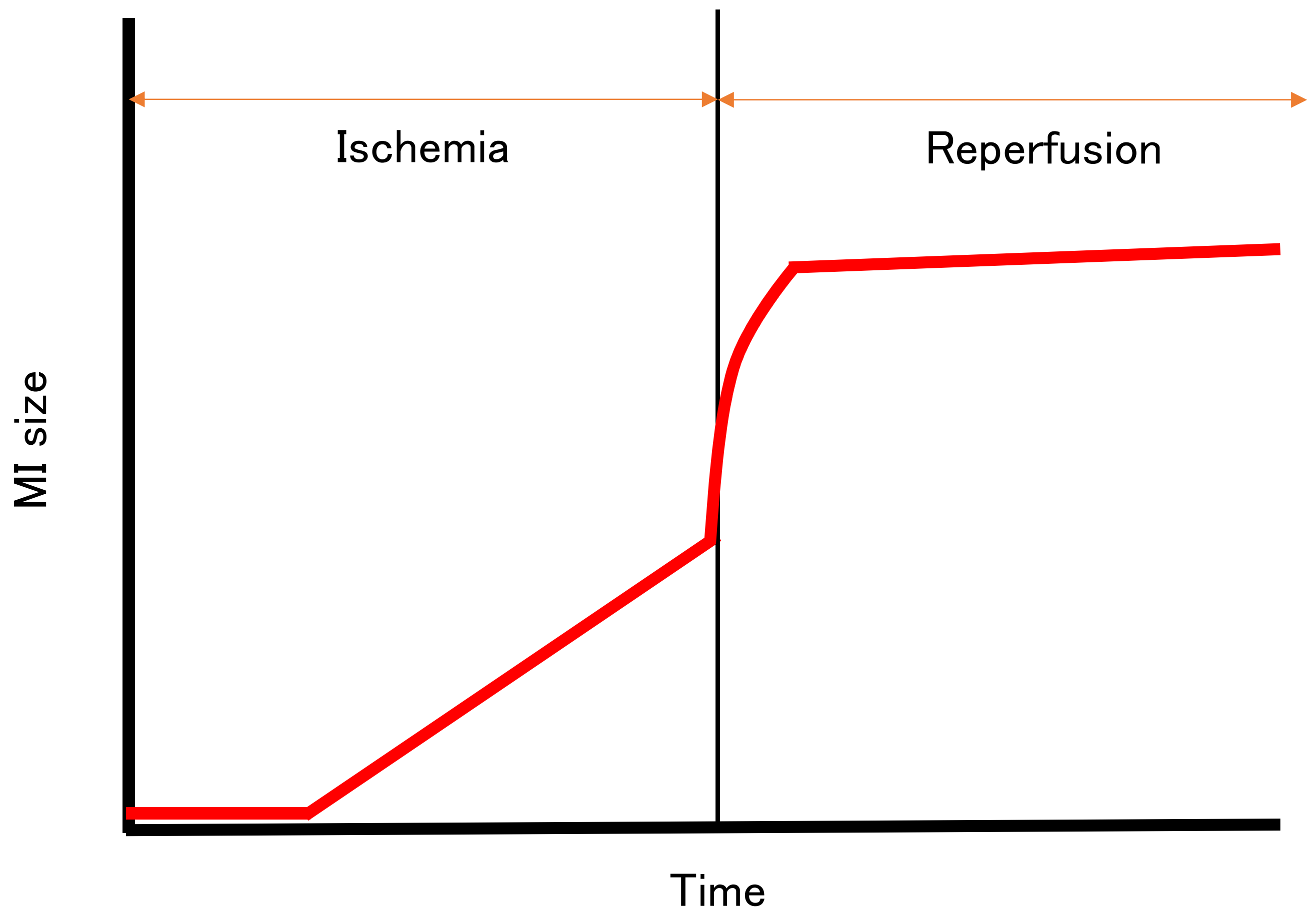
Clinical scenario of AMI

Sixty-two years old man with multiple CV risk factors.
Chest pain evoked 2 hrs before admission.
Tachycardia, Stable hemodynamics, Positive for troponin, ECG ST elevation

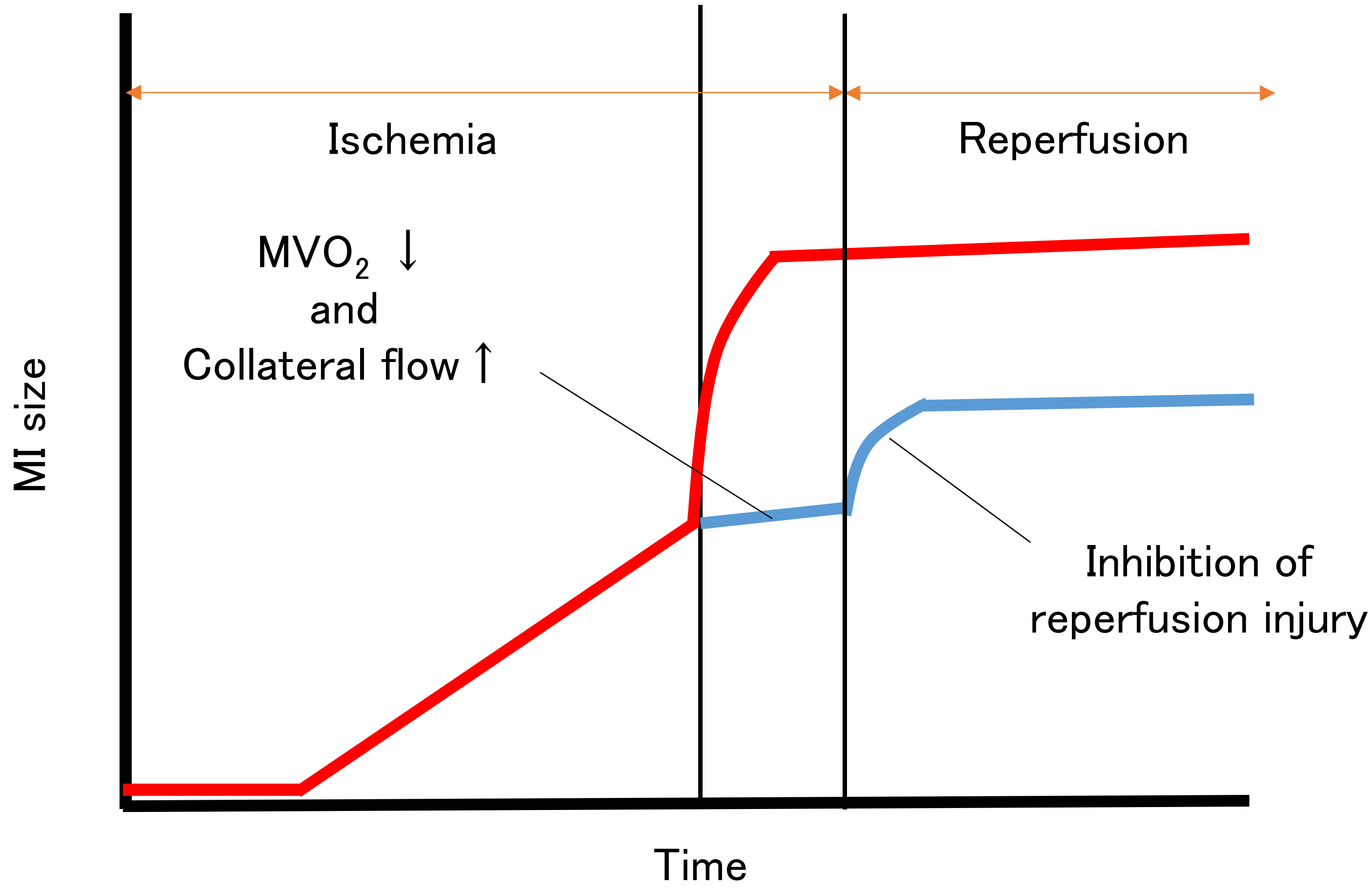




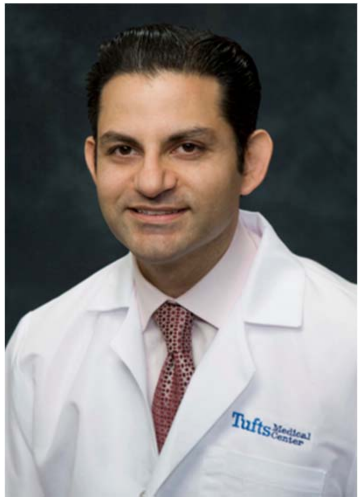
Door to unload



Door to unload



STEMI-DTU trial



Navin K. Kapur, MD

Tufts University

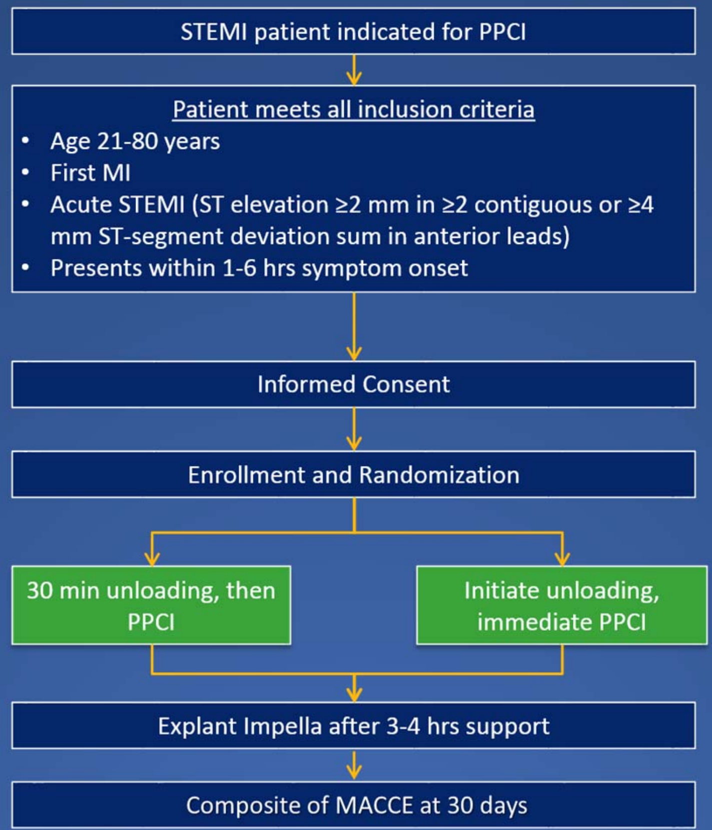
Circulation

American Heart Association

Mechanically Unloading the Left Ventricle Before Coronary Reperfusion Reduces Left Ventricular Wall Stress and Myocardial Infarct Size
Navin K. Kapur, Vikram Paruchuri, Jose Angel Urbano-Morales, Emily E. Mackey, Gerard H. Daly, Xiaoying Qiao, Natesa Pandian, George Perides and Richard H. Karas

While, the contemporary strategy of treating AMI is dominated by a quest to achieve rapid coronary recanalization in AMI (Door to Balloon Time), we now propose that first mechanically reducing LV preload (Door to Unload) and then delaying coronary reperfusion will promote RISK pathway activation and significantly reduce myocardial infarct size.

STEMI DTU
Safety & Feasibility Study

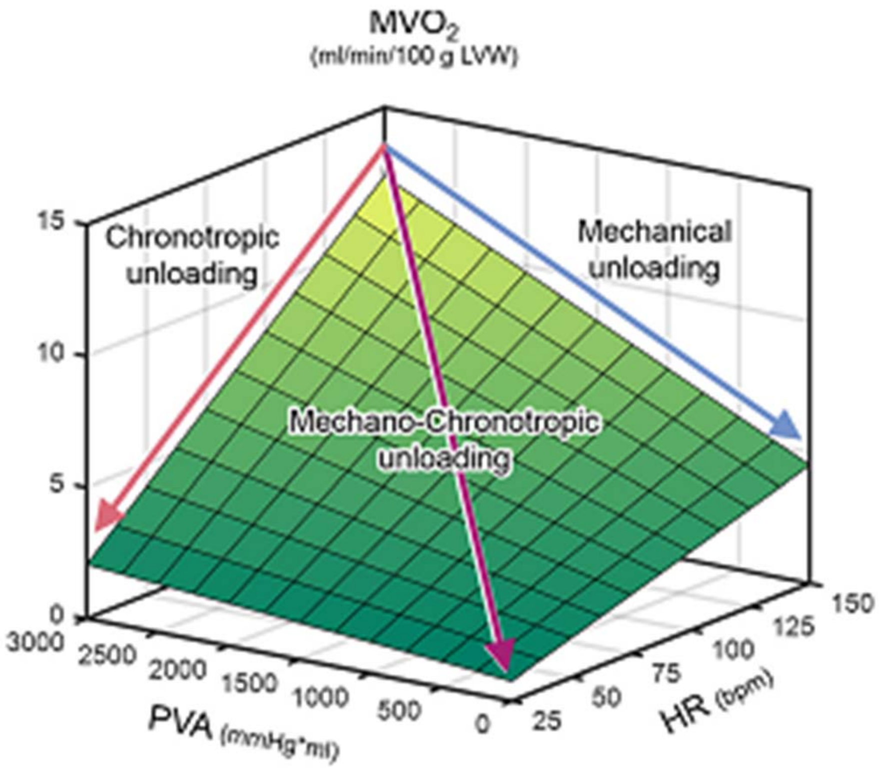


A pivotal trial assessing the impact of LV unloading in anterior STEMI is planned to begin in 2019.

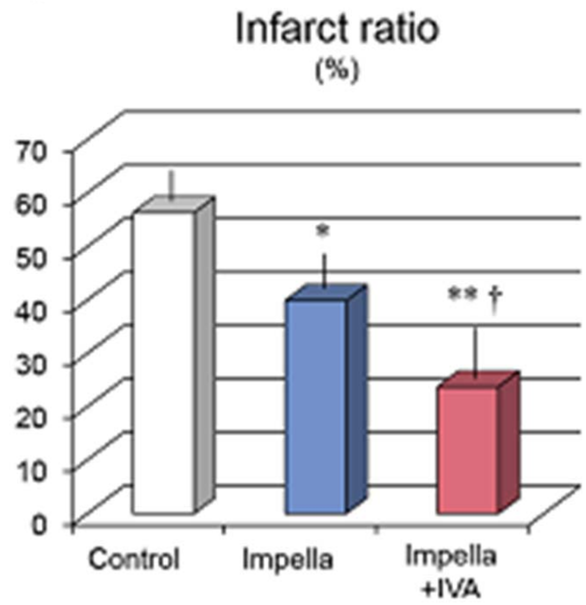
Impella+Ivabradine

Mechano-chronotropic Unloading During the Acute Phase of Myocardial Infarction Markedly Reduces Infarct Size via the Suppression of Myocardial Oxygen Consumption

Genya Sunagawa[1] · Keita Saku[2] · Takahiro Arimura[1] · Takuya Nishikawa[1] · Hiroshi Mannoji[1] · Kazuhiro Kamada[1] · Kiyokazu Abe[3] · Takuya Kishi[2] · Hiroyuki Tsutsui[1] · Kenji Sunagawa[4]



- Dog
- 3 hrs MI and 3 hrs reperfusion
- Treatment started from 1 hr after MI
- Partial support with Impella CP



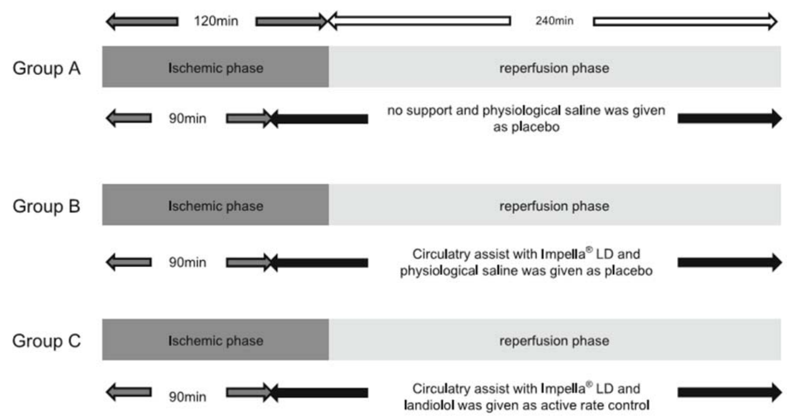
Sunagawa et al. JCTR 2018.

Impella+beta-blocker

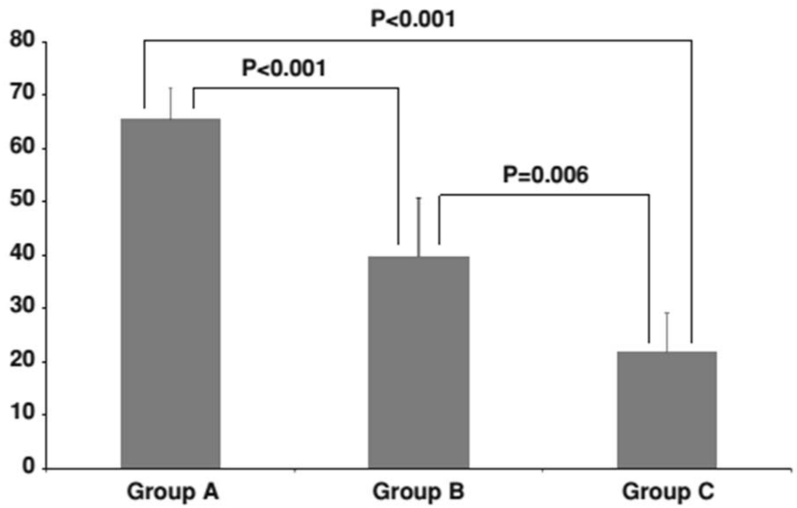
The effect of combined treatment with Impella® and landiolol in a swine model of acute myocardial infarction

Isamu Yoshitake · Mitsumasa Hata · Akira Sezai · Satoshi Unosawa · Shinji Wakui · Haruka Kimura · Kin-ichi Nakata · Hiroaki Hata · Motomi Shiono

- Swine
- 2 hrs MI and 4 hrs reperfusion
- Impella LD and landiolol 0.5 mg/kg/min

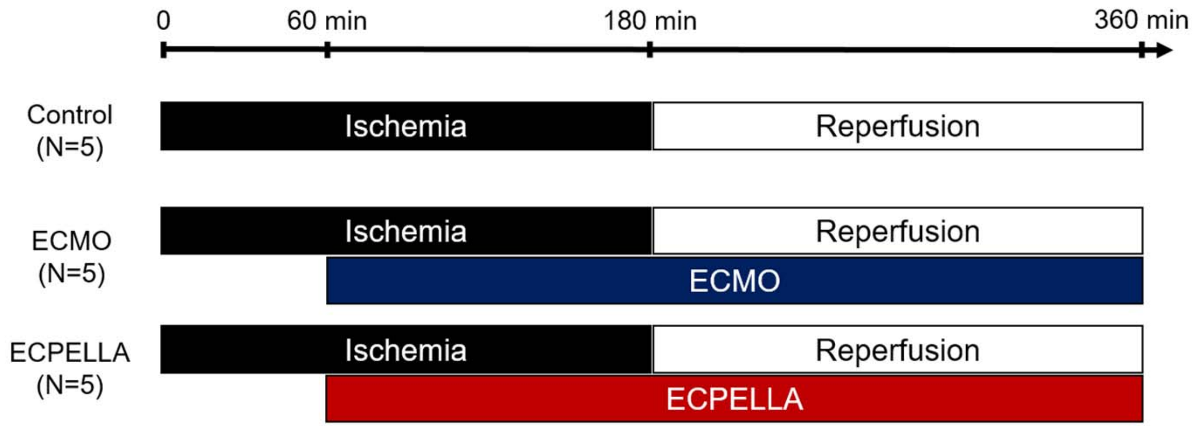


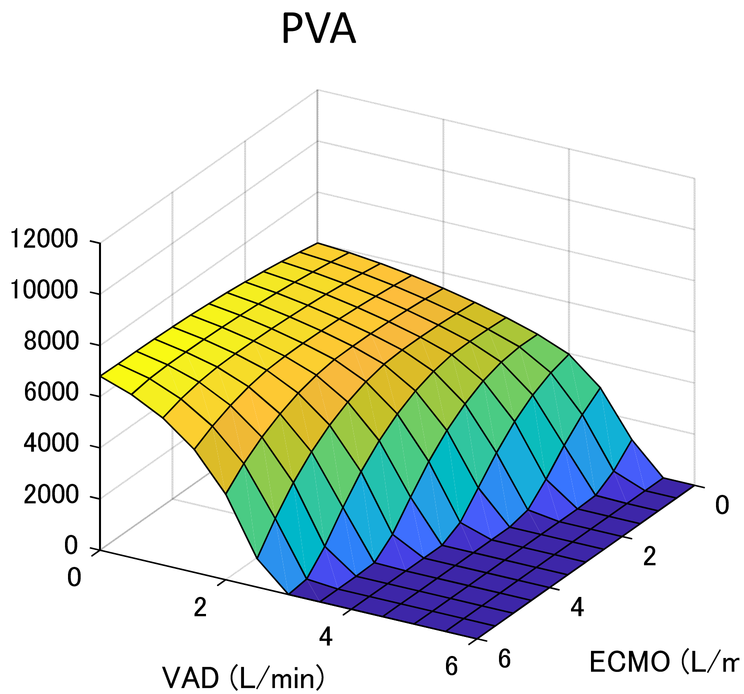
MI size (%)

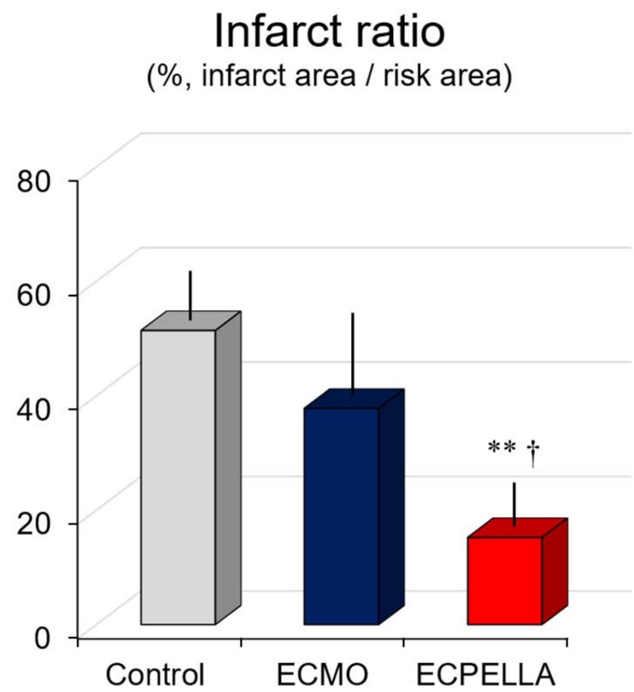


Yoshitake et al. J Artif Organs 2012.

ECMO+Impella







Conclusion

- Impella increases total cardiac output, thereby reducing LVEDP.
- Impella support effect depends on native LV systolic function because Impella shifts CO curve by LVEF × Impella flow.
- Impella reduces PVA, thereby reducing MVO_2.
- Impella unloading effect may contribute to the limitation of infarct size (STEMI-DTU trial).