2020-06-04 (Thu.) 대한흉부외과학회 전공의 연수교육

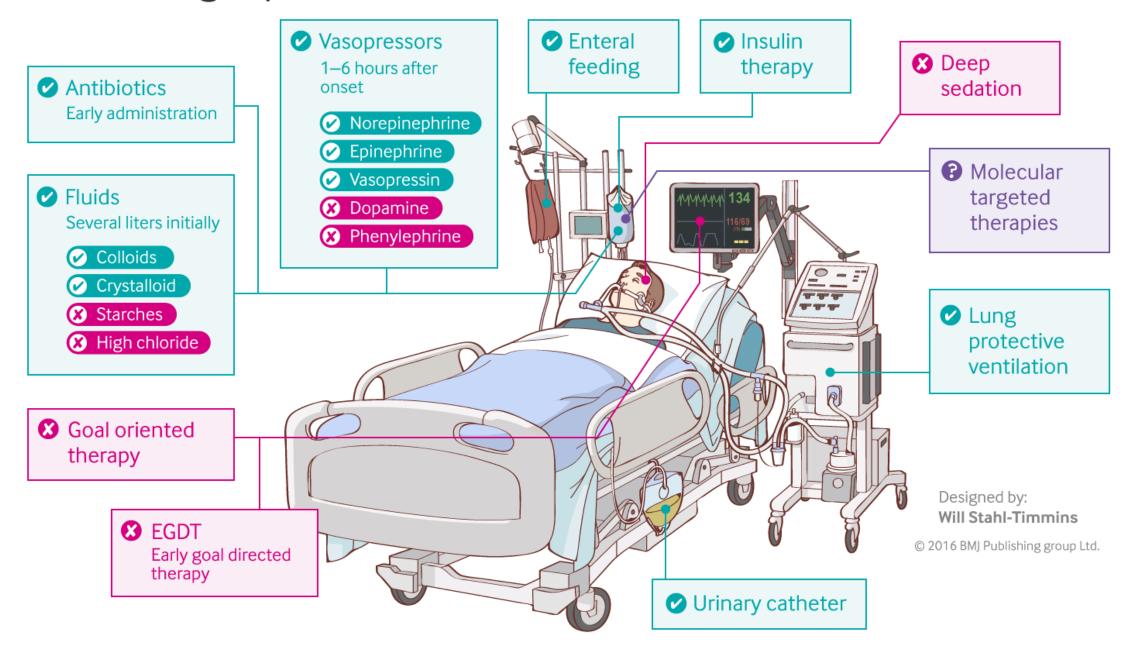
Monitoring at ICU and Cardiovascular Management

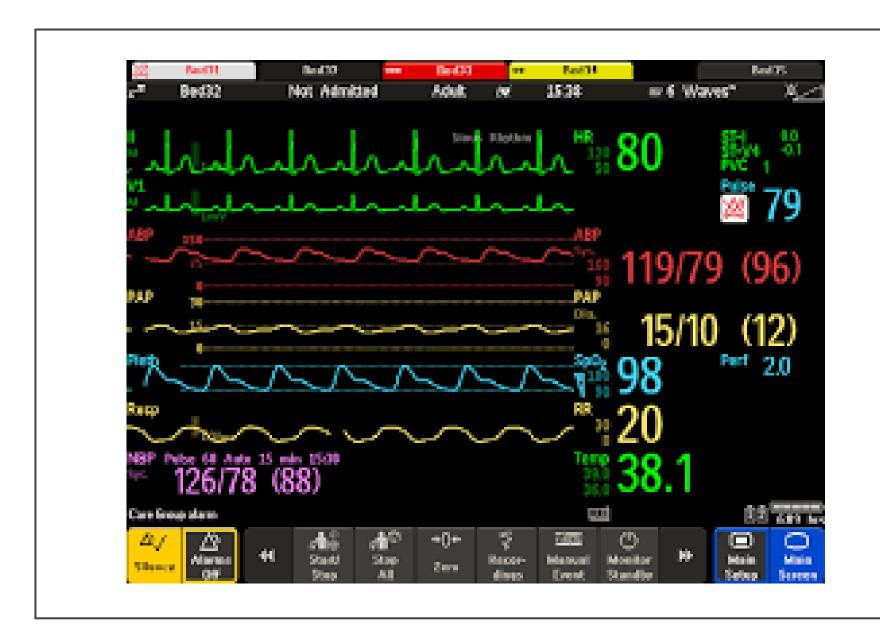
INSEOK JEONG. MD, PhD.

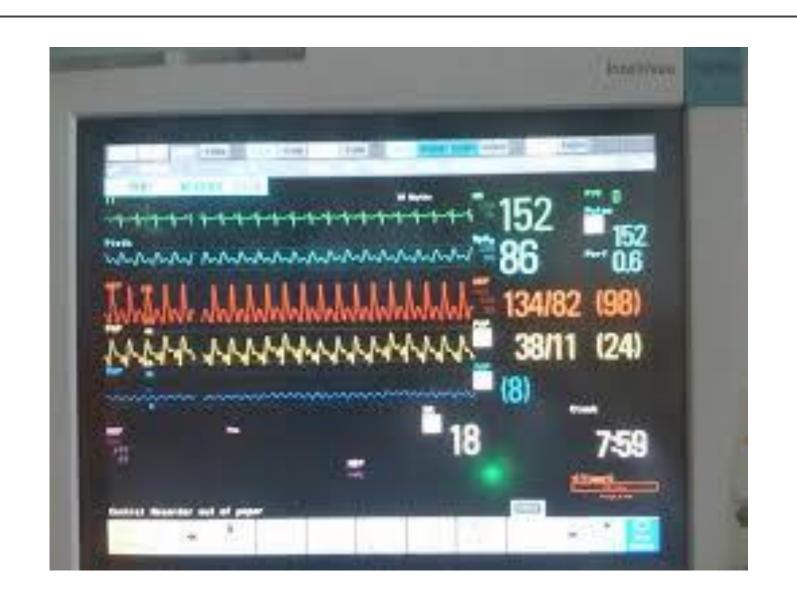
Department of Thoracic and cardiovascular surgery Chonnam National University Hospital and Medical School

INTRODUCTION

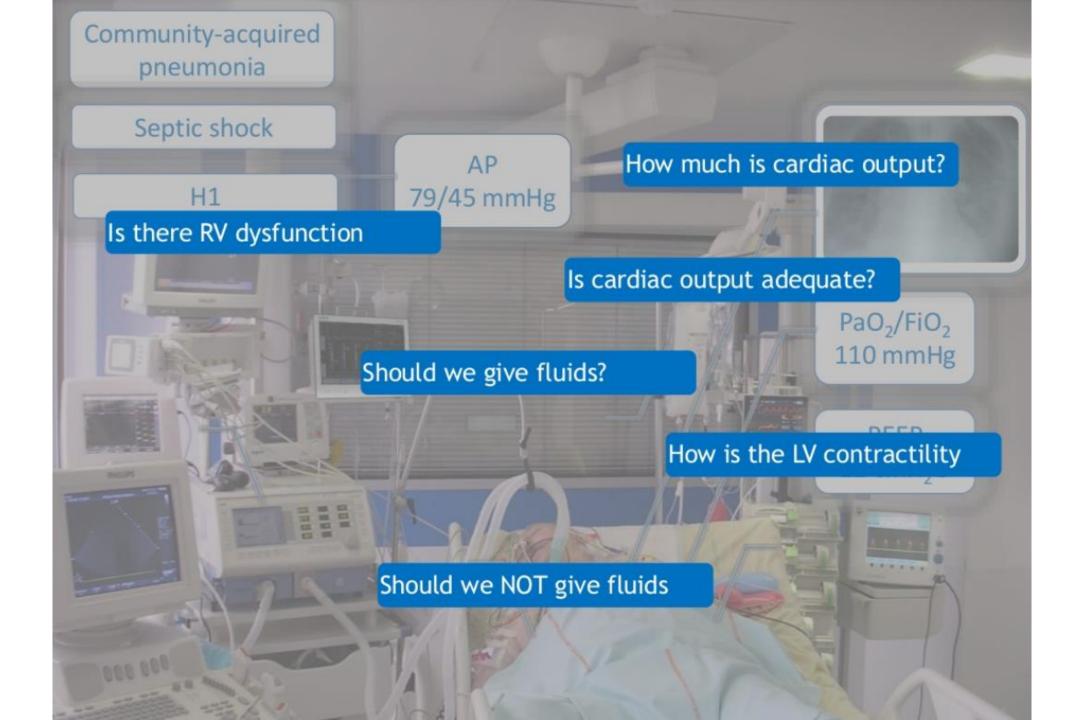
Treating sepsis: the latest evidence







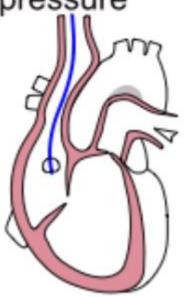




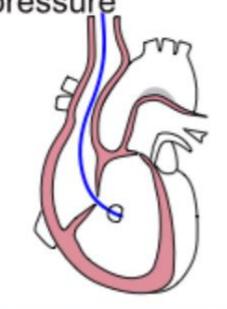
- Central venous and pulmonary artery catheters (PAC) are invasive tools that have traditionally been used for hemodynamic monitoring in patients who present with shock.
- However, these tools have drawbacks and inaccuracies.
- Thus, several, less invasive, novel technologies are available or being investigated for use to assess parameters such as cardiac output, intravascular volume status, responsiveness to intravenous fluid administration, and tissue perfusion.
- They can potentially be used in the emergency department, intensive care unit, and operating room when caring for patients with shock or hypovolemia.

GENERAL PRINCIPLES

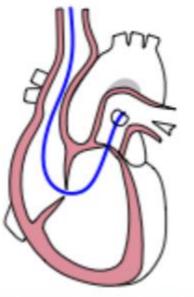
Right atrial pressure

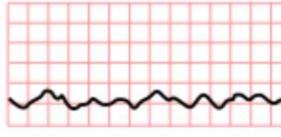


Right ventricular pressure

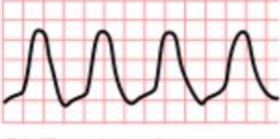


Pulmonary artery pressure





RAP = 0 - 6 mm Hg

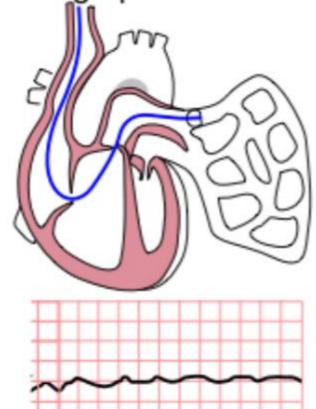


RVP = 15 - 250 - 8 mm Hg



PAP = 15 - 25 8 - 10 mm Hg Mean PAP = 10 - 20 mm Hg

Pulmonary capillary wedge pressure



PCWP = 8 - 12 mm Hg

• Central venous and pulmonary artery catheterization (PAC), the traditional tools used for hemodynamic monitoring of patients who present with shock, <u>are invasive and frequently</u> inaccurate.

CVP and PAC monitoring suffer from the following inadequacies:

- 1. Inconsistent prediction of fluid responsiveness
- 2. Complications associated with invasiveness
- 3. Difficult data interpretation

Inconsistent prediction of fluid responsiveness

- 1. Both CVP and pulmonary alveolar occlusion pressure have been shown to have poor predictive value for predicting fluid responsiveness (arbitrarily defined as an increase of at least 15 percent in cardiac output [CO] in response to a 500 mL bolus fluid challenge, as measured by PAC).
- 2. Furthermore, CVP is affected by a number of other physiologic derangements, including valvular regurgitation, right ventricular dysfunction, pulmonary hypertension, and variation in intrathoracic pressure with respiration.

Complications associated with invasiveness

 CVCs and PACs require central venous access and have been associated with a number of complications, including arrhythmias, injury to vascular or cardiac structures, catheter-associated bloodstream infection, pneumothorax, and venous thromboembolism.

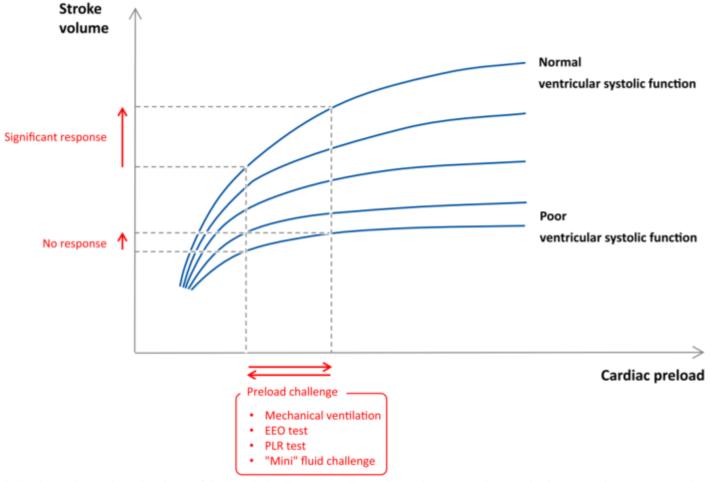


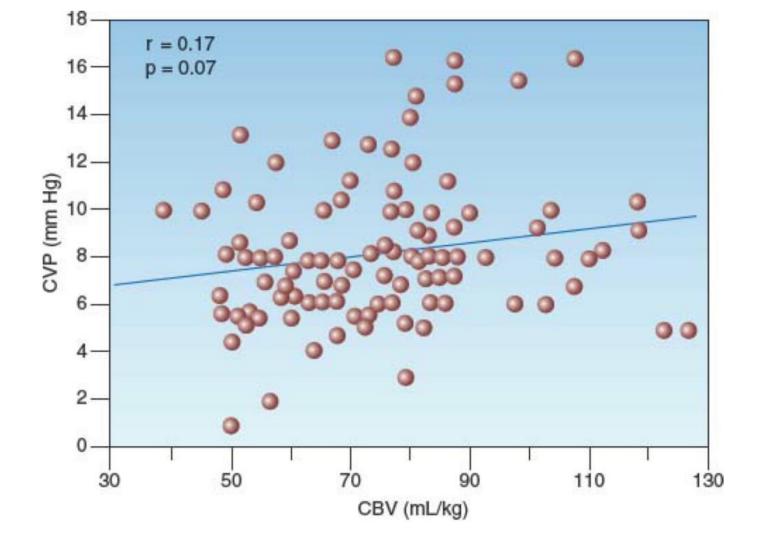
Fig. 1 Frank–Starling relationship. The slope of the Frank–Starling curve depends on the ventricular systolic function. Then, one given level of cardiac preload does not help in predicting fluid responsiveness. By contrast, dynamic tests include a preload challenge (either spontaneous, induced by mechanical ventilation or provoked, by passive leg raising, end-expiratory occlusion or fluid infusion). Observing the resulting effects on stroke volume allows for the detection of preload responsiveness. *EEO* end-expiratory occlusion, *PLR* passive leg raising

Table 1 Summary of methods predicting preload responsiveness with diagnostic threshold and limitations

Method	Threshold	Main limitations
Pulse pressure/stroke volume variations [22]	12%	Cannot be used in case of spontaneous breathing, cardiac arrhythmias, low tidal volume/ lung compliance
Inferior vena cava diameter variations [44]	12%	Cannot be used in case of spontaneous breathing, low tidal volume/lung compliance
Superior vena caval diameter variations [44]	36%*	Requires performing transesophageal Doppler Cannot be used in case of spontaneous breathing, low tidal volume/lung compliance
Passive leg raising [55]	10%	Requires a direct measurement of cardiac output
End-expiratory occlusion test [75]	5%	Cannot be used in non-intubated patients Cannot be used in patients who interrupt a 15-s respiratory hold
"Mini"-fluid challenge (100 mL) [84]	6%**	Requires a precise technique for measuring cardiac output
"Conventional" fluid challenge (500 mL) [81]	15%	Requires a direct measurement of cardiac output Induces fluid overload if repeated

^{*} Thresholds from 12 to 40% have been reported

^{** 10%} is more compatible with echography precision. Citations indicate the most important reference regarding the test



Monnet, et al. Prediction of fluid responsiveness: an update. Ann Intensive Care. 2016 Dec;6(1):111. Epub 2016 Nov 17.

Indications

• A plethora of techniques aimed at overcoming the deficiencies associated with standard hemodynamic monitoring tools have been developed, many of which use complex imaging technology and computer algorithms to estimate the following:

1. Fluid responsiveness and volume status

(see 'Volume tolerance and fluid responsiveness' below)

2. Cardiac output

(see 'Cardiac output' below)

3. Tissue perfusion

(see 'Measurement of tissue oxygen saturation' below and 'Measurement of microcirculatory blood flow' below and 'Tissue perfusion' below)

- While no large randomized trials of resuscitation guided by noninvasive hemodynamic monitors have been conducted, a systematic review of 13 trials enrolling over 1600 subjects found that such practice was associated with reduced mortality, ICU length of stay, and duration of mechanical ventilation.
- A sub-analysis of the ANDROMEDA-SHOCK trial suggests that assessment of fluid responsiveness was possible in 80 percent of patients.
- Fluid responsive patients received lower fluid volumes, exhibited less positive fluid balances, and received more vasopressors, but had no difference in mortality or organ failure.
- These findings will likely only increase the interest in use of these tools in critically ill patients.

Physiologic principles

- Upstream versus downstream monitors
- A greater understanding of tissue and cellular hypoxia as a cardinal feature of shock has led to the concept of "upstream" and "downstream" indicators of organ perfusion [11].



Upstream Industry

- Geological Surveys
- Mining and Drilling
- Manufacturing



Midstream Industry

- Storage
- Transportation (Pipelines, Rail, Truck)



Downstream Industry

- Distribution
- Retail Outlets



Physiologic principles: Upstream

- "Upstream" ("macro") markers assess flow and pressure in the heart, vena cava, pulmonary artery, and aorta and are the traditional variables that have been used to assess the hemodynamic status of critically ill patients.
- The majority of existing hemodynamic monitors are upstream monitors.

Physiologic principles: Downstream

- Shock with end-organ dysfunction occurs at the capillary and tissue levels [12].
- Tools have been developed that follow alterations in tissue oxygenation and microvascular blood flow.
- These techniques are known as the "downstream" (or "micro") markers of resuscitation.

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High versus Low Blood-Pressure Target in Patients with Septic Shock

Pierre Asfar, M.D., Ph.D., Ferhat Meziani, M.D., Ph.D., Jean-François Hamel, M.D., Fabien Grelon, M.D., Bruno Megarbane, M.D., Ph.D., Nadia Anguel, M.D., Jean-Paul Mira, M.D., Ph.D., Pierre-François Dequin, M.D., Ph.D., Soizic Gergaud, M.D., Nicolas Weiss, M.D., Ph.D., François Legay, M.D., Yves Le Tulzo, M.D., Ph.D., Marie Conrad, M.D., René Robert, M.D., Ph.D., Frédéric Gonzalez, M.D., Christophe Guitton, M.D., Ph.D., Fabienne Tamion, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Pierre Guezennec, M.D., Thierry Van Der Linden, M.D., Antoine Vieillard-Baron, M.D., Ph.D., Eric Mariotte, M.D., Gaël Pradel, M.D., Olivier Lesieur, M.D., Jean-Damien Ricard, M.D., Ph.D., Fabien Hervé, M.D., Damien du Cheyron, M.D., Ph.D., Claude Guerin, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Jean-Louis Teboul, M.D., Ph.D., and Peter Radermacher, M.D., Ph.D., for the SEPSISPAM Investigators*

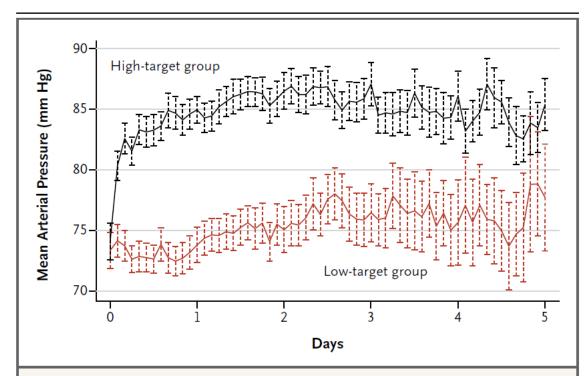


Figure 2. Mean Arterial Pressure during the 5-Day Study Period.

Mean arterial pressures were significantly lower in the low-target group than in the high-target group during the 5 protocol-specified days (P=0.02 by repeated-measures regression analysis), although the values exceeded the target values of 80 to 85 mm Hg in the high-target group and 65 to 70 mm Hg in the low-target group. The I bars represent 95% confidence intervals.

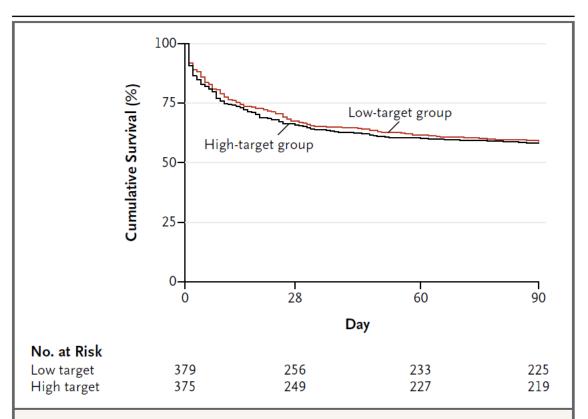


Figure 3. Kaplan-Meier Curves for Cumulative Survival.

Data for the survival analysis, which was performed in the intention-to treat population, were censored at 90 days. There was no significant difference in survival between the high-target group and the low-target group (P=0.57 at 28 days; P=0.74 at 90 days).

ASAIO Journal 2019 Adult Circulatory Support

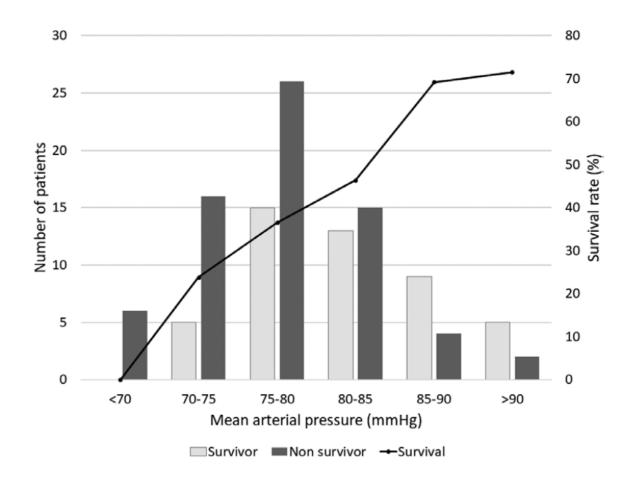
What Is the Optimal Blood Pressure on Veno-Arterial Extracorporeal Membrane Oxygenation? Impact of Mean Arterial Pressure on Survival

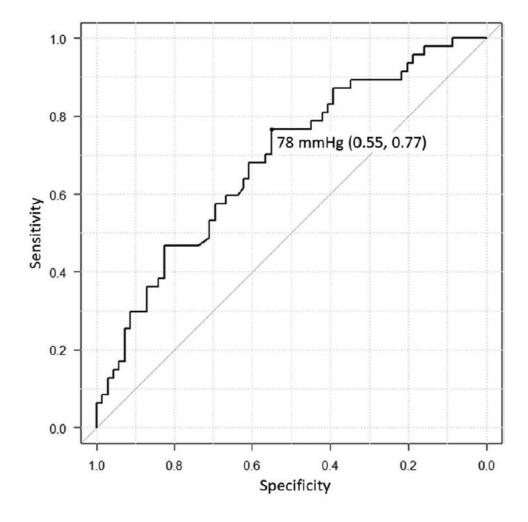
Daizo Tanaka, Shogo Shimada, Megan Mullin, Kristin Kreitler, Nicholas Cavarocchi, and Hitoshi Hirose

- 116 patients with VA ECMO (2010.9 2016.3)
- Mean MAP: significantly higher in survivors
- $(82 \pm 5.6 \text{ vs. } 78 \pm 5.5 \text{ mm Hg, p} = 0.0003).$
- There was a positive association between MAP and survival.
- Higher MAP: not affect the probability of strokes or bleeding complications,
- Higher MAP: a lower incidence of kidney injury (p = 0.007).

ASAIO Journal 2019; 65:336–341.

Thomas Jefferson University, Philadelphia, Pennsylvania





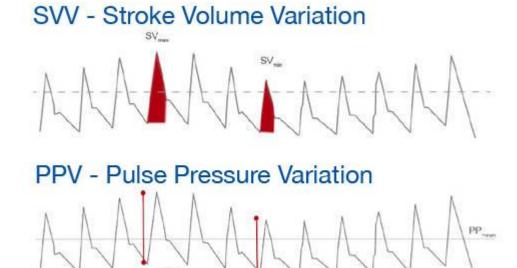
VOLUME TOLERANCE AND FLUID RESPONSIVENESS

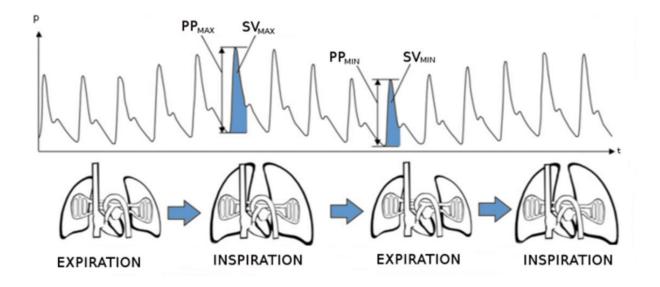
Pulse contour analysis (fluid responsiveness)

- 1. Pulse pressure variation (PPV)
- 2. Stroke volume variation (SVV)
- 3. Oximetric waveform variation

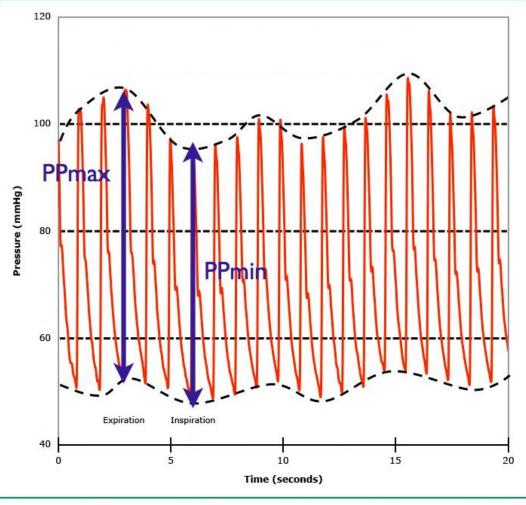
Pulse pressure variation (PPV)

- Numerous studies have demonstrated that a PPV of at least 13 to 15 percent is strongly associated with volume responsiveness.
- As an example, one systematic review of 29 studies reported a higher area under the receiver operating characteristic curve (AUROC) for PPV compared with CVP (0.94 versus 0.55) as an indicator of fluid responsiveness (sensitivity and specificity were 0.88 each).





Calculating pulse pressure variation



Pulse pressure variation (PPV). Pulse pressure is the difference between systolic and diastolic blood pressure. The phases of respiration, denoted by positive (expiration) and negative (inspiration) deflections, reflect those for patients on mechanical ventilation (these would be different if the patient was spontaneously breathing and can vary depending upon the mode of ventilation). PPV can be calculated as follows: $PPV = 100 \times (PPmax - PPmin) / ([PPmax + PPmin] / 2)$.

PPmax: maximum pulse pressure; PPmin: minimum pulse pressure.

Reproduced from: ProfBondi. Available at: https://commons.wikimedia.org/wiki/File:Pulse pressure variation.ipg (accessed on August 10, 2016).

Conditions where pulse pressure and stroke volume variations are less reliable

Spontaneous breathing

Cardiac arrhythmias

Low Vt/low lung compliance

Open chest

Increased intra-abdominal pressure

Very high respiratory rate (HR/RR < 3.6)

Right heart failure*

British Journal of Anaesthesia, 118 (3): 298–310 (2017)

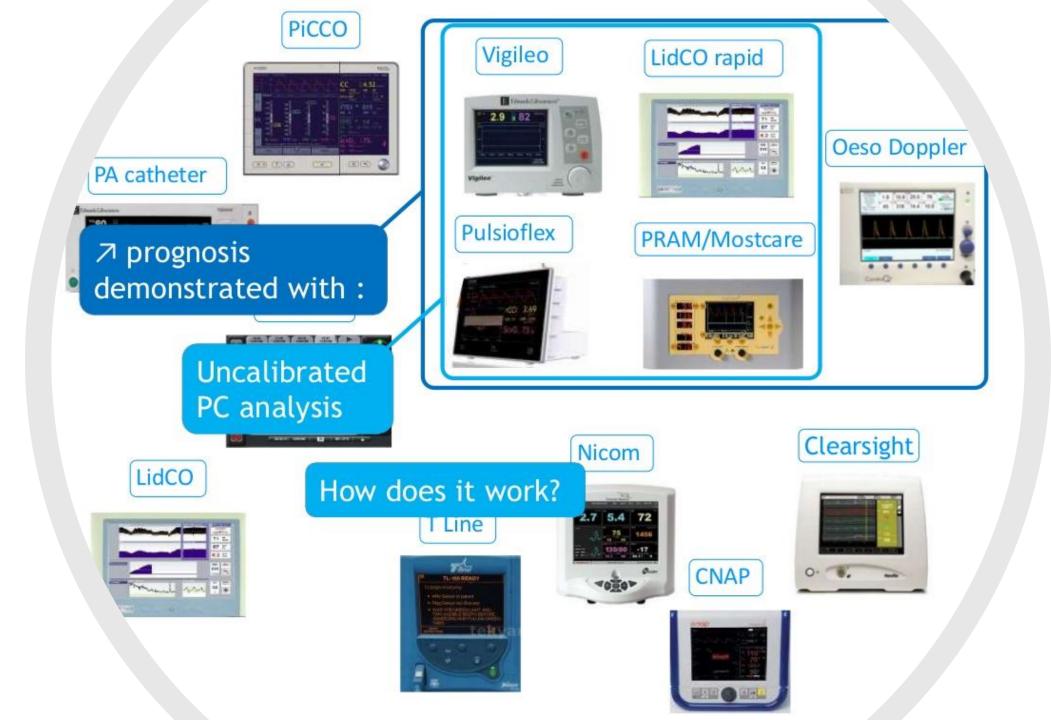
BJA

doi: 10.1093/bja/aew461 Review Article

REVIEW ARTICLE

Accuracy and precision of non-invasive cardiac output monitoring devices in perioperative medicine: a systematic review and meta-analysis[†]

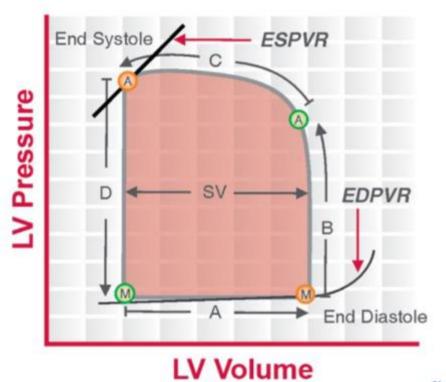
- A. Joosten^{1,*}, O. Desebbe², K. Suehiro³, L. S.-L. Murphy⁴, M. Essiet⁵,
- B. Alexander⁶, M.-O. Fischer^{7,8}, L. Barvais¹, L. Van Obbergh¹,
- D. Maucort-Boulch⁹ and M. Cannesson¹⁰



Editor's key points

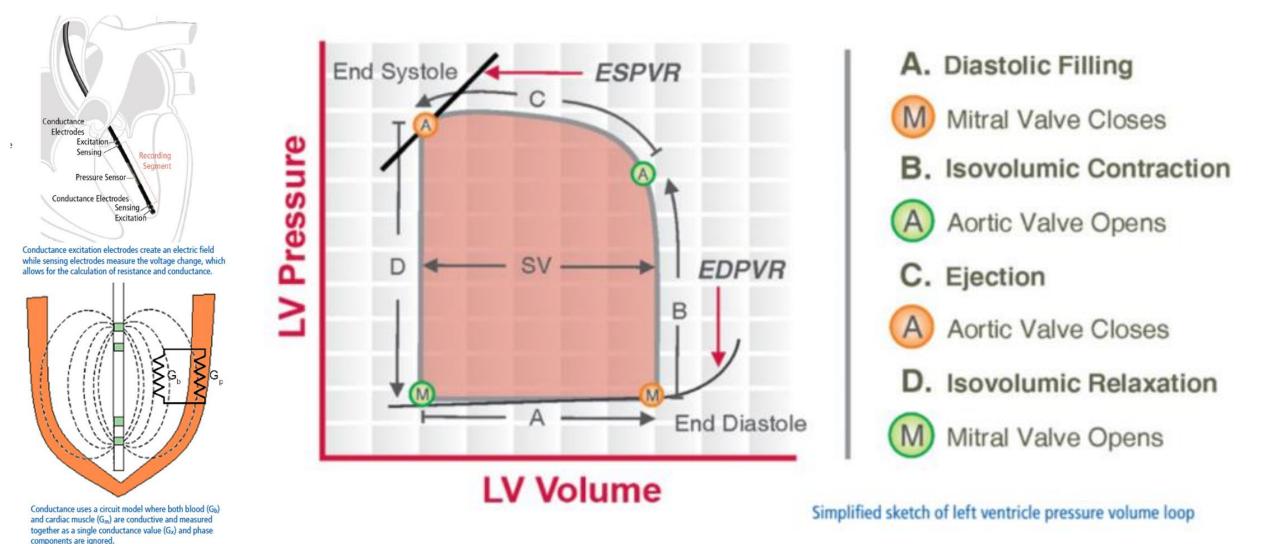
- Advances in non-invasive cardiac output technologies offer simpler perioperative monitoring, but their accuracy is questioned.
- This meta-analysis found modest agreement and inadequate percentage error for most technologies.
- Novel non-invasive cardiac output technologies are typically developed in relatively healthy populations; their internal algorithms may thus be inappropriate to major surgery or critical illness.
- Percentage error and trending are important variables in the evaluation of non-invasive cardiac output technologies.

TISSUE PERFUSION

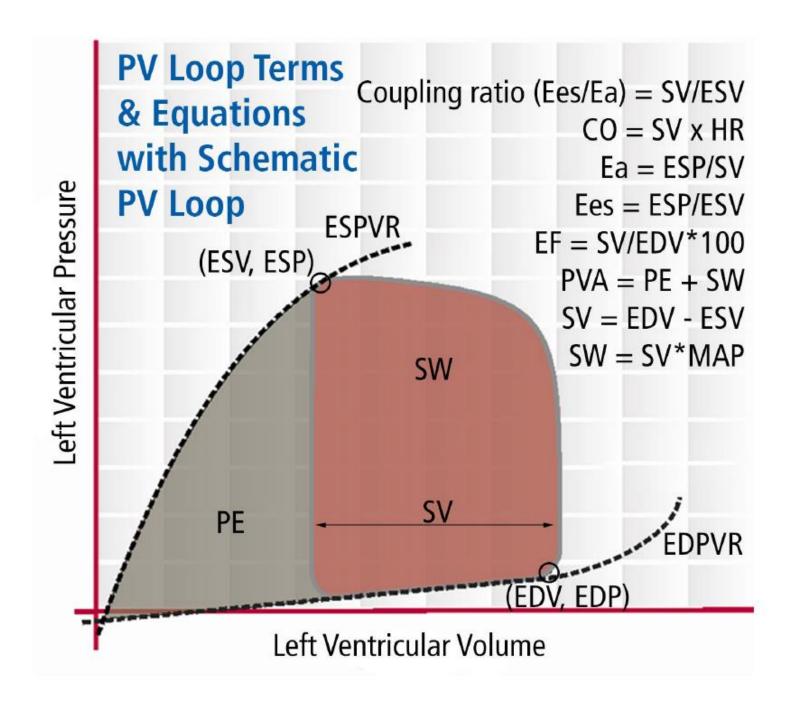


- A. Diastolic Filling
- Mitral Valve Closes
- B. Isovolumic Contraction
- A Aortic Valve Opens
- C. Ejection
- A Aortic Valve Closes
- D. Isovolumic Relaxation
- Mitral Valve Opens

Simplified sketch of left ventricle pressure volume loop



Basics of Pressure-Volume Loop



Definition of Shock

- Shock is defined as a state of cellular and tissue hypoxia due to reduced oxygen delivery, increased oxygen consumption, inadequate oxygen utilization, or a combination of the three.
- "Undifferentiated shock" refers to the situation where shock is recognized but the cause is unclear.

Classifications of Shock

- Four types of shock are recognized. However, many patients have a combination of more than one of the forms of shock listed below (table 1):
- Distributive shock: septic shock, SIRS (ex.pancreatitis), neurogenic shock, anaphylactic shock, toxin-related shock, and endocrine shock (ex. adrenal crisis).
- Cardiogenic shock: cardiomyopathic (ex. AMI), arrhythmia (ex. sustained VT/Vf), mechanical abnormality (ex. acute valvular rupture).
- 3. Hypovolemic shock: hemorrhagic (ex. trauma) or non-hemorrhagic fluid losses (ex. diarrhea).
- 4. Obstructive shock: pulmonary vascular related (ex. pulmonary embolism) or due to a mechanical cause of reduced preload (ex. tension pneumothorax, pericardial tamponade).

Hemodynamic profiles of shock on pulmonary artery catheter in adults

Physiologic variable	Preload	Pump function	Afterload	Tissue perfusion
Clinical measurement	Pulmonary capillary wedge pressure	Cardiac output*	Systemic vascular resistance	Mixed venous oxyhemoglobin saturation¶
Hypovolemic	↔ (early) or ↓ (late)	↔ (early) or ↓ (late)	1	>65% (early) or <65% (late)
Cardiogenic	1	ţ	1	<65%
Distributive	↔ (early) or ↓ (late)	↑ or ↓ (occasionally)	1	>65%
Obstructive				
PE, PH, tension pneumothorax	↔ (early) or ↓ (late)	↔ (early) or ↓ (late)	Ť	>65%
Pericardial tamponade [∆]	†	ţ	†	<65%

PE: pulmonary embolus; PH: pulmonary hypertension; PAC: pulmonary artery catheter.

 Δ Equalization of right atrial, right ventricular end-diastolic and pulmonary artery wedge pressures is classic in pericardial tamponade and distinguishes it from primary cardiogenic shock.



^{*} Cardiac output is generally measured using the cardiac index.

[¶] Mixed venous oxyhemoglobin saturation cutoff measured on PAC is 65%, but on triple lumen catheter is 70%.

- In compensated shock, macro-circulatory measures such as arterial pressure and cardiac output (CO) may be normal in the face of markedly abnormal oxygen delivery and utilization.
- Devices have been developed to measure indices of shock at the tissue level.

Measurement of tissue oxygen saturation (StO2)

- StO2 measurement using near-infrared spectroscopy (NIRS) has been proposed as a downstream hemodynamic monitoring tool to survey the micro-circulation and assess the balance of oxygen delivery and consumption at the tissue level.
- StO2 is measured transcutaneously using NIRS via a number of commercially available devices that measure tissue absorbance values in a defined range of wavelengths.
- StO2 with VOT has been shown to predict outcome and organ dysfunction in patients with sepsis and congestive heart failure in two small studies, and preliminary studies have demonstrated its usefulness in trauma patients.

Measurement of tissue oxygen saturation (StO2)

- However, the value of StO2 value is limited because StO2 remains within normal range until shock is quite advanced.
- The addition of a dynamic ischemic challenge such as the <u>vascular</u> <u>occlusion test</u> (VOT; application of a tourniquet or sphygmomanometer above systolic arterial pressure for brief, defined intervals) <u>may improve the predictive ability</u> of StO2 to identify tissue hypoperfusion.

Measurement of microcirculatory blood flow

- There is considerable interest in shock-induced microcirculatory dysfunction, most notably in the case of sepsis.
- The sublingual mucosa is the preferred means to evaluate the microcirculation in critically ill patients because it shares embryological origin with the splanchnic circulation and can be easily accessed at the bedside.
- Imaging of the sublingual microvasculature is typically obtained using advanced microscopy techniques, such as sidestream dark field imaging, or by near-infrared spectroscopy (NIRS).
- Early studies demonstrated alterations in microvascular flow in patients with sepsis and cardiogenic shock.
- Multiple subsequent studies have demonstrated that alterations in sublingual microcirculatory blood flow are associated with poor outcome among patients with septic shock.

Fingernails Nail Blanch Test



Pressure is applied to nail bed until it urns white

Blood returned to tissue



*ADAM.

capillary refill time of nail plate <3 seconds





Pressure is applied to nail bed until it turns white

Blood returned to tissue



@ ADAM, Inc.







Pressure is applied to nail bed until it turns white

Blood returned to tissue



@ ADAM, Inc.

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE 2019



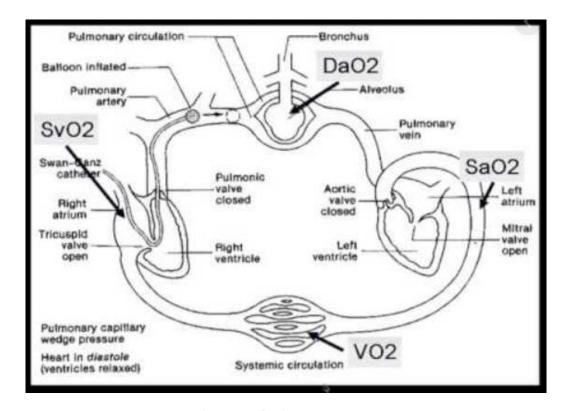
William G. Sir Peter J. Gregg L. Kaelin Jr. Ratcliffe Semenza

"for their discoveries of how cells sense and adapt to oxygen availability"

THE NOBEL ASSEMBLY AT KAROLINSKA INSTITUTET







- SaO2: arterial saturation
- SvO2: mixed venous saturation
- CaO2: arterial oxygen contents
- DaO2: oxygen delivery (supply)

 DO_2 (cc/min)

=Cardiac output (L/min)×arterial CO₂ (cc/dL)×10

 CO_2 (cc/dL)

- =Hemoglobin bound O₂+dissolved O₂
- =(Hemoglobin [g/dL]×saturation [%]×1.36 cc/g)+(pO₂ [mmHg]×0.0031 cc/mmHg/dL)

DO2: CO / Hgb / SaO2

- DaO2: oxygen delivery (CO, Hgb, SaO2)
- CaO2: oxygen contents (Hgb bound oxygen + dissolved oxygen)
- VO2: oxygen consumption in tissue (tissue metabolism)
- SvO2: mixed venous oxygen saturation (not utilized oxygen, measured in pulmonary artery)
- DO2 / VO2 ratio = 4 ~ 5 (normal condition)

• SvO2 = DO2 - VO2 = 60 ~ 80 (%) (normal condition)

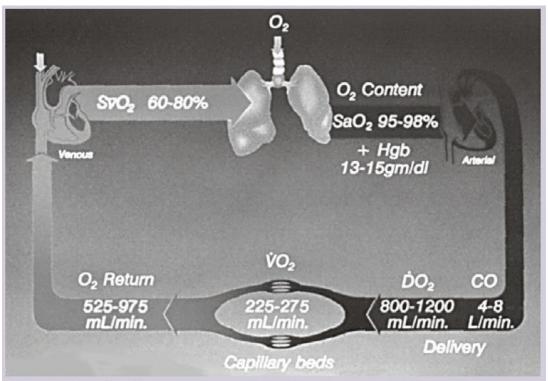


Figure 2 Cardiopulmonary system including the normal values of tissue oxygenation parameters. Mixed venous oxygen saturation (Svo₂) reflects the adequacy of oxygen delivery (Do₂) in meeting oxygen demand. As shown, cardiac output (CO), hemoglobin (Hgb), and arterial oxygen saturation (Sao₂) make up delivery. Oxygen consumption (Vo₂) is a reflection of oxygen demand.

Reprinted with permission from Abbott Critical Care Systems, Mountain View, Calif.

Increase SvO2 (DaO2 ↑, VO2 ↓)

Decrease in oxygen consumption Use of analgesics and anesthetics

Neuromuscular blockade or use of paralytics

Use of β -antagonists

Hypothermia Hypothyroidism

Sepsis (dysoxia, shunting)

Cyanide poisoning

Sleep or rest

Increase in oxygen saturation
Increase in fraction of inspired oxygen or hyperoxia

Intracardiac shunt or arteriovenous fistula

Severe mitral valve regurgitation

Distal migration of a pulmonary artery catheter

Increase in cardiac output Optimal preload

Use of inotropic agents

Use of mechanical-assist devices

Decrease SvO2 (DaO2 ↓ , VO2 ↑)

Decrease in cardiac output Hypovolemia or cardiac tamponade

Shock

Myocardial infarction

Arrhythmias

Increases in positive end-expiratory pressure

Decrease in oxygen saturation Pulmonary edema

Adult respiratory distress syndrome

Decrease in inspired oxygen

Decrease in hemoglobin level Anemia

Hemorrhage

Dysfunctional hemoglobin

Increase in oxygen consumption Pain

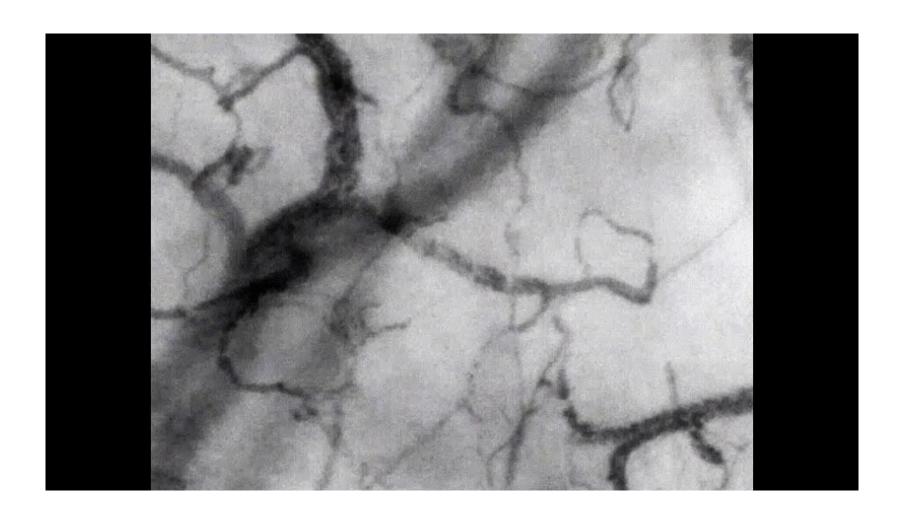
Anxiety or fear

Agitation or restlessness Hyperthermia or burns

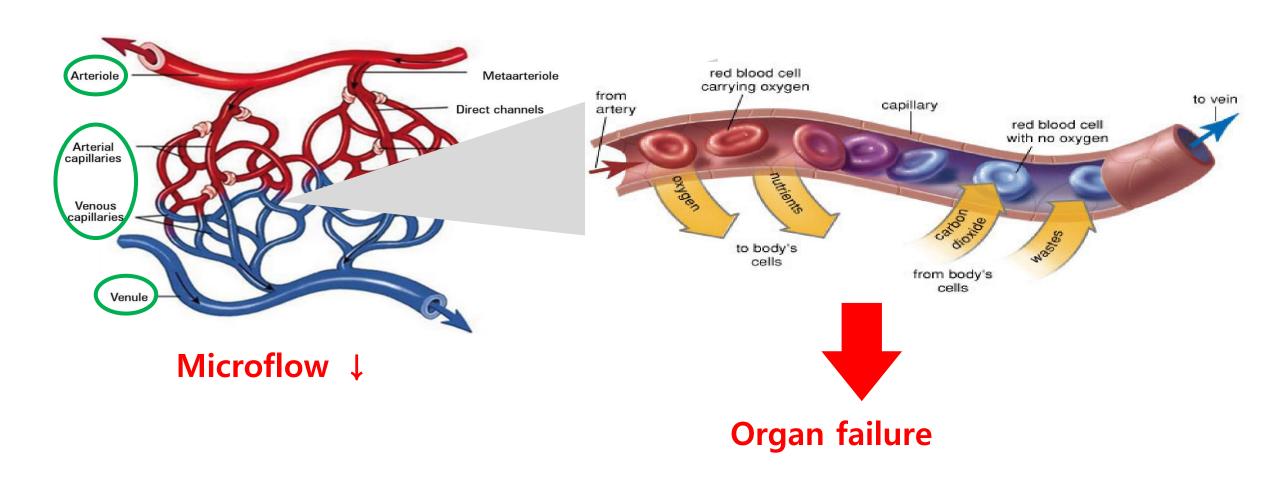
Tachycardia Shivering

Activity (positioning, suctioning)

- If <u>DO2</u> is severely decreased, there is <u>insufficient oxygen</u> to meet metabolic demands, anaerobic metabolism occurs, and, finally, <u>lactic acidosis and shock</u> occur.
- Since SvO2 reflects this ratio accurately, it is one of the most important considerations when monitoring and managing critically ill patients.
- VA ECMO can be an option for the treatment of various types of shock because it can increase CO2 and systemic blood flow and eventually increase DO2.
- Hence, the goal of VA ECMO is as follows: to restore organ blood flow and adequate tissue oxygenation while awaiting recovery.

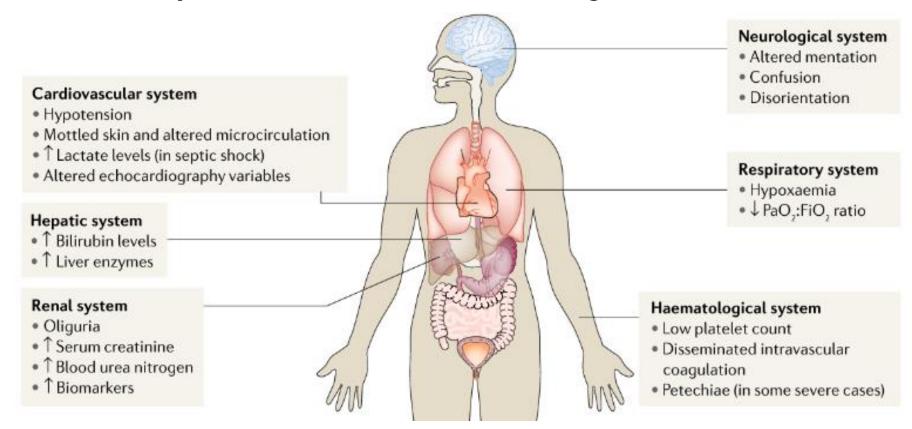


Tissue Perfusion



Microcirculatory dysfunction

- transudation of fluids in the perivascular region → tissue pressure ↑
 - → alters viscosity within the vessel lumen
 - ⇒ microcirculatory alterations (in or around the organs)



Evaluation of microcirculation

Table 1. Selected modalities to investigate the microcirculation in cardiogenic shock

Assessment of the micro-circulation	Advantages	Disadvantages	
Indirect methods			
Blood pressure	Monitored in every CS patient, no costs	Questionable correlation to organ perfusion	
Central venous pressure	Available in most patients	Only one of various variants determining organ microcirculation	
Capillary refill	Easy available, no costs	Influenced by extremity perfusion, interobserver and intraobserver variability	
Mottling score	Easy available and reproducible	Comparable low correlation to organ microcirculation	
Serum lactate	Easy available	Influenced by other parameters and conditions, not on-line with delayed response	
Various serum parameters	Sensitive and specific markers available for different organs in research contexts	Not available within a reasonable time frame	
(Contrast) Ultrasound/ Echocardiography	Good organ resolution	Moderate correlation to organ failure	
(Contrast) MRI	Good organ resolution	Not applicable in CS patients	
Gas tomography	Reflects organ metabolism	Direct or indirect organ access necessary, low correlation to organ failure	
Direct methods			
Capillaroscopy (nail-fold)	Good reproducibility under standardized conditions	Limited availability, low correlation to organ perfusion, dependent on body temperature	
Intravitalmicroscopy [SDF (imaging), IDF (imaging)]	Good reproducibility, good correlation to organ failure, outcome prediction validated, on-line available	Limited availability	

CS, cardiogenic shock; IDF, incident dark-field; SDF, sidestream dark-field.

ASAIO Journal 2017 Case Reports

Ejection Fraction May Not Reflect Contractility: Example in Veno-Arterial Extracorporeal Membrane Oxygenation for Heart Failure

Philippe Morimont,* Bernard Lambermont,* Julien Guiot,* Vincent Tchana Sato,* Christophe Clotuche,*

Jonathan Goffoy,* and Jean-Olivier Defraigne‡

RESEARCH Open Access



Functional evaluation of sublingual microcirculation indicates successful weaning from VA-ECMO in cardiogenic shock

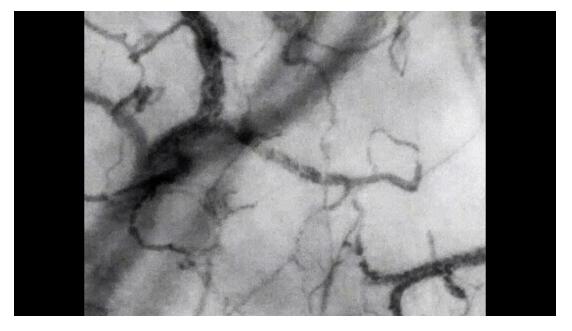
Sakir Akin^{1,2*}, Dinis dos Reis Miranda¹, Kadir Caliskan², Osama I. Soliman², Goksel Guven^{1,2}, Ard Struijs¹, Robert J. van Thiel¹, Lucia S. Jewbali^{1,2}, Alexandre Lima¹, Diederik Gommers¹, Felix Zijlstra² and Can Ince¹

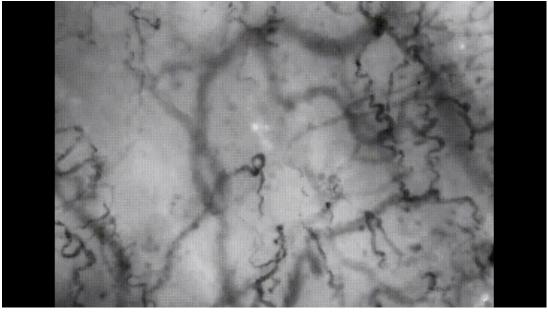
Microcirculatory image on VA-ECMO weaning trial



successful weaning

unsuccessful weaning







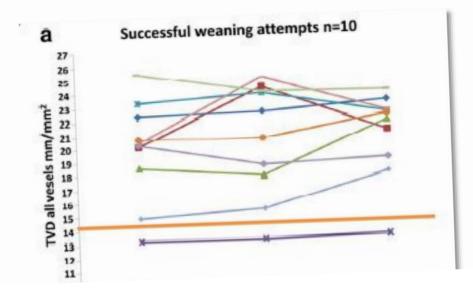


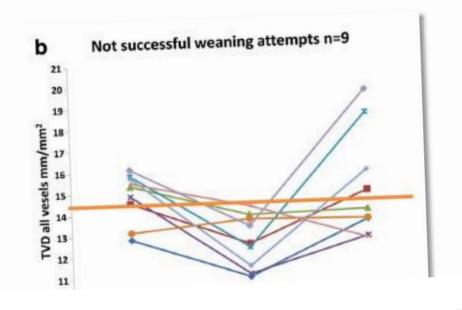


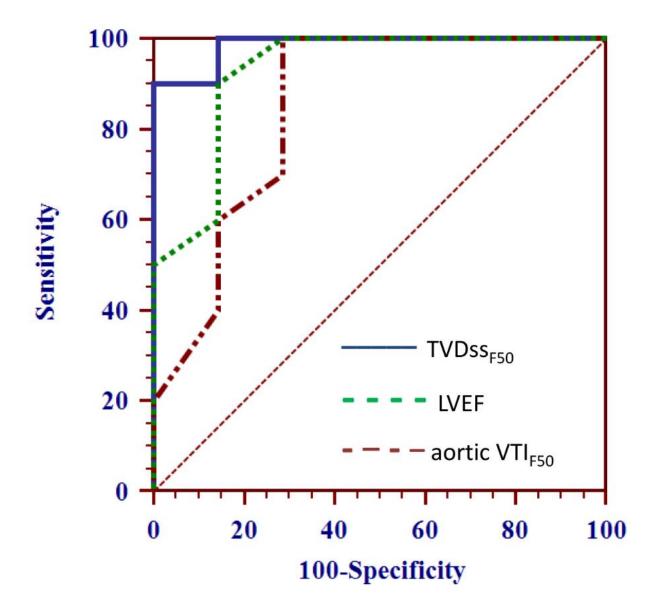
Functional evaluation of sublingual microcirculation indicates successful weaning from VA-ECMO in cardiogenic shock

Sakir Akin^{1,2*}©, Dinis dos Reis Miranda¹, Kadir Caliskan², Osama I. Soliman², Goksel Guven^{1,2}, Ard Struijs¹, Robert J. van Thiel¹, Lucia S. Jewbali^{1,2}, Alexandre Lima¹, Diederik Gommers¹, Felix Zijlstra² and Can Ince¹

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감사합니다. (isjeong1201@gmail.com)

