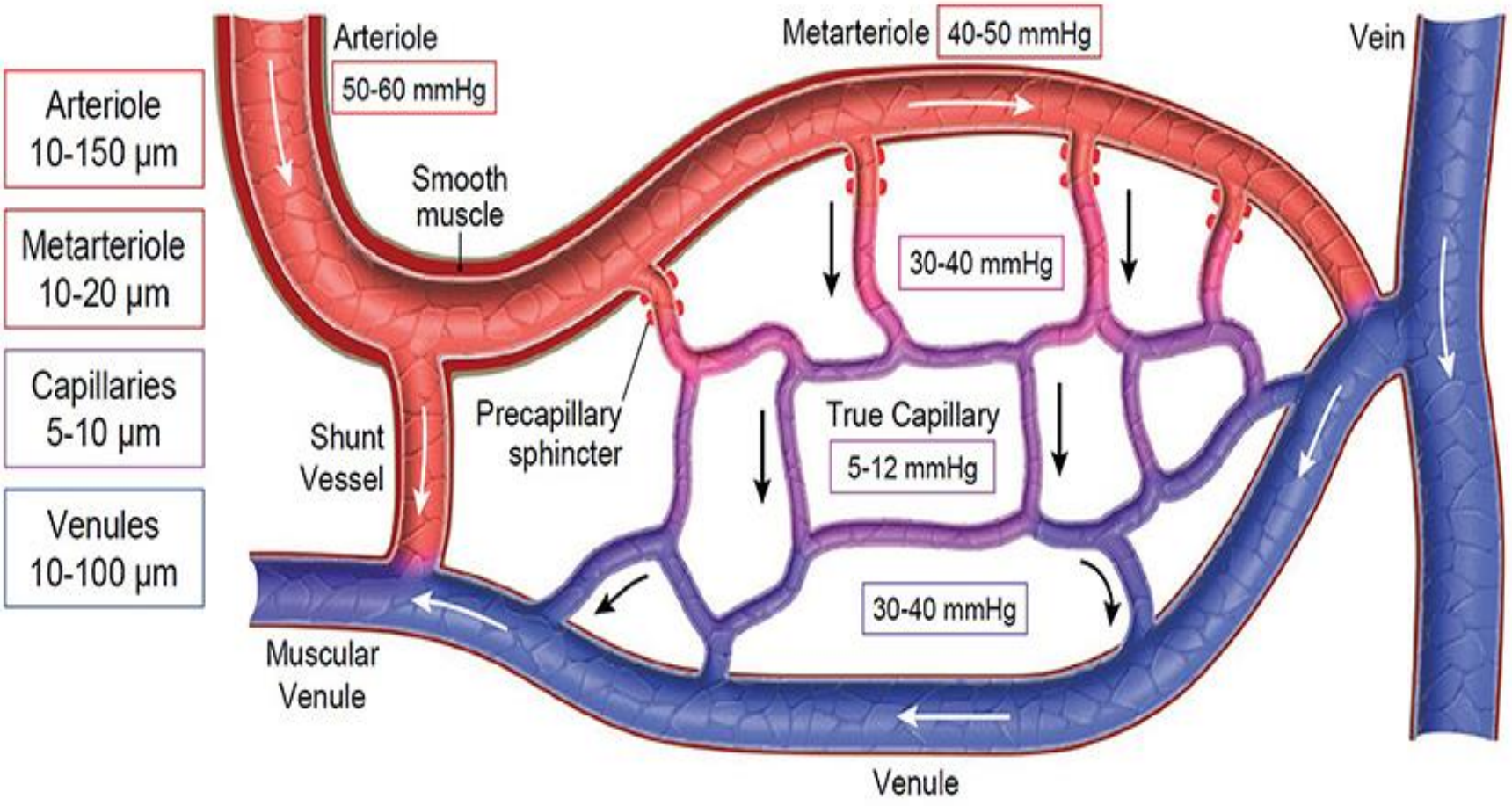
Microcirculation Monitoring

By: A.Noohi
Pediatric Intensivist

Introduction

- Microcirculation is the ultimate organ of the cardiovascular system. Microcirculation is a heterogenous and complex network, *composed by arterioles, capillaries and venules that connect the arterial and venous system.*
- *Oxygen exchange, carbon dioxide and protons removal, transport of hormones, nutrients, drugs and immune response*, occur at a microcirculatory level.


Arteriole 10-150 µm
Metarteriole 10-20 µm
Capillaries 5-10 µm
Venules 10-100 µm
Arteriole
50-60 mmHg
Smooth muscle
Metarteriole
40-50 mmHg
Vein
30-40 mmHg
Precapillary sphincter
Shunt Vessel
True Capillary
5-12 mmHg
30-40 mmHg
Muscular Venule
Venule

Continue

- Redistribution of blood flow among tissues involves **extrinsic** and **intrinsic** factors. Extrinsic regulation is accomplished by neural (autonomic) and humoral (hormones) mechanisms.
- For instances, *α-adrenergic receptor*-mediated vasoconstriction is a main determinant of blood flow redistribution.

Continue

- Since the main goal of shock resuscitation is the normalization of tissue perfusion and oxygenation, ***the classic approach based on the correction of blood pressure and cardiac output might fail to correct tissue hypoxia and hypoperfusion.***

CONTINUE….

- During the resuscitation of shock, two different responses have been described.
- *Hemodynamic coherence,* which implies that the correction of systemic cardiovascular variables results in a parallel improvement in tissue perfusion. **Conversely**,
- *Hemodynamic incoherence*:*the normalization of systemic hemodynamics is* ***unable*** *to correct tissue perfusion and oxygenation.*

CONTINUE....

- Septic shock is the paradigm of this form of dissociation. But any type of shock might evolve to this condition, due toof persistent inflammatory response.
- ***Microcirculatory shock*** can be defined as a situation in which microvascular flow is insufficient to maintain tissue oxygenation *despite* of normalized systemic hemodynamics.
- ***Indeed, available evidence strongly suggests that the principal motor of sepsis is microcirculatory dysfunction.***

Therefore,

- *Monitoring of microcirculation during resuscitation seems necessary to detect patients at higher risk of worse outcome, to guide therapy as a target of resuscitation, to monitor the response to therapy, and to unmask persistent shock in apparently well-resuscitated patients.*

Continue

- The two main determinants of the microcirculation for oxygen transport are:
- ***Convection***: *the flow of oxygen-carrying RBC*.
- **Diffusion**: *the distance oxygen must travel from the RBC to the cells*.
- Parameters related to the convective (e.g., RBC flow rate) and diffusive (e.g., functional capillary density) capacity of the microcirculation are used to quantify the functional state of the microcirculation.

Continue

- The loss of coherence between the macrocirculation and the microcirculation is predictive of organ failure and unfavorable outcomes .

- For example, the diffusive capacity of the microcirculation may be compromised during fluid therapy *if increased RBC flow cannot compensate for dilution of RBC mass and if tissue edema induces increased diffusion distances between RBC and tissue cells,.*

Continue

- *Another risk is to over-optimize the macrocirculation in relation to the needs of the microcirculation and to end up with fluid overload or overuse of vasopressors that is often harmful in terms of tissue oxygenation*.
- **Clinicians are currently blind to what is happening in the microcirculation of organs, (the black box) which prevents them from individualizing resuscitation by targeting the microcirculation.**

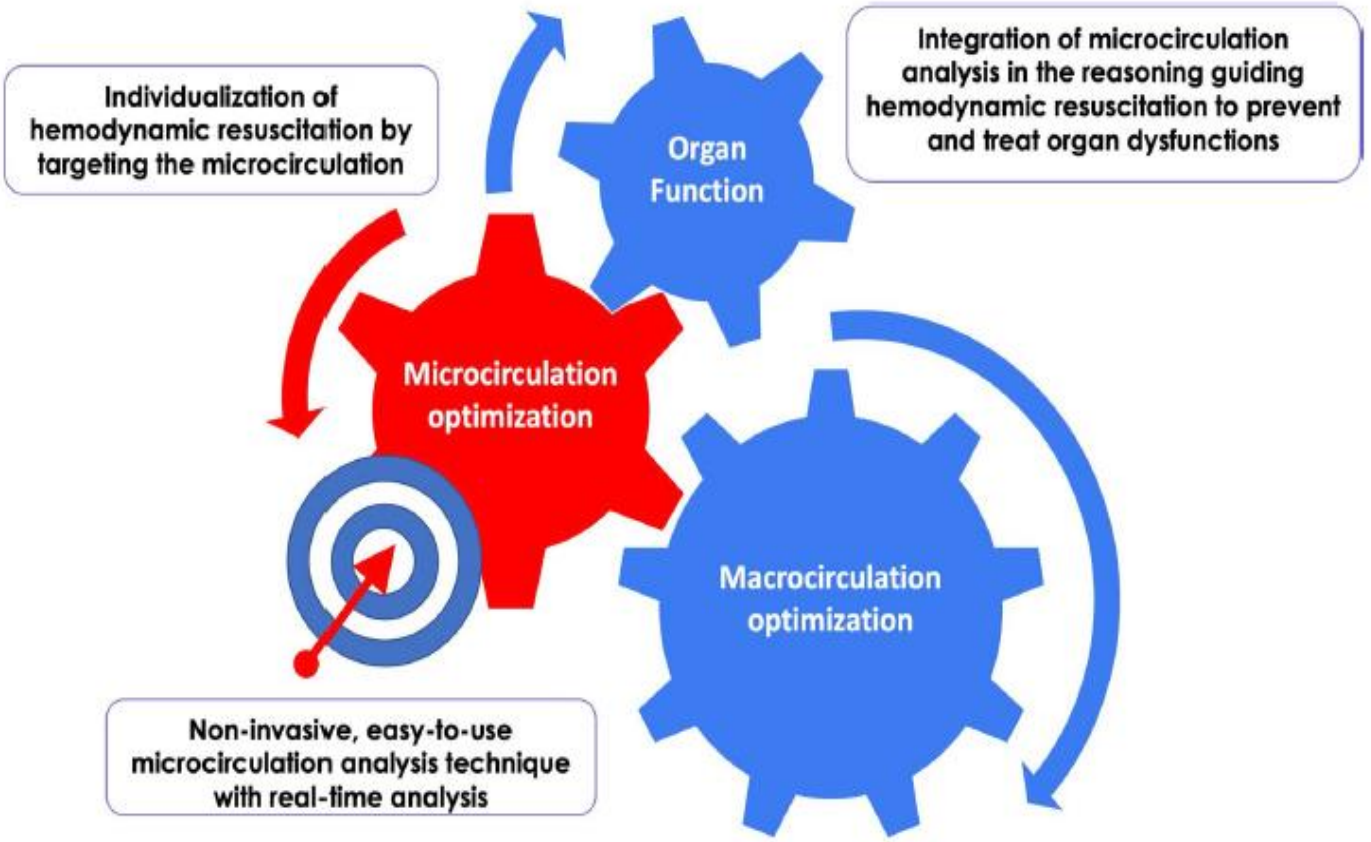


Fig. 3 The challenge for the future of microcirculation monitoring in ICU

Continue

- Harrois et al. found significant ***differences*** in renal cortical microcirculation recovery in patients with septic shock after macrovascular hemodynamic optimization.

- Watchorn et al. showed that the severity of AKI was related to the degree of renal cortical hypoperfusion independently of macrovascular optimization in patients in septic shock.

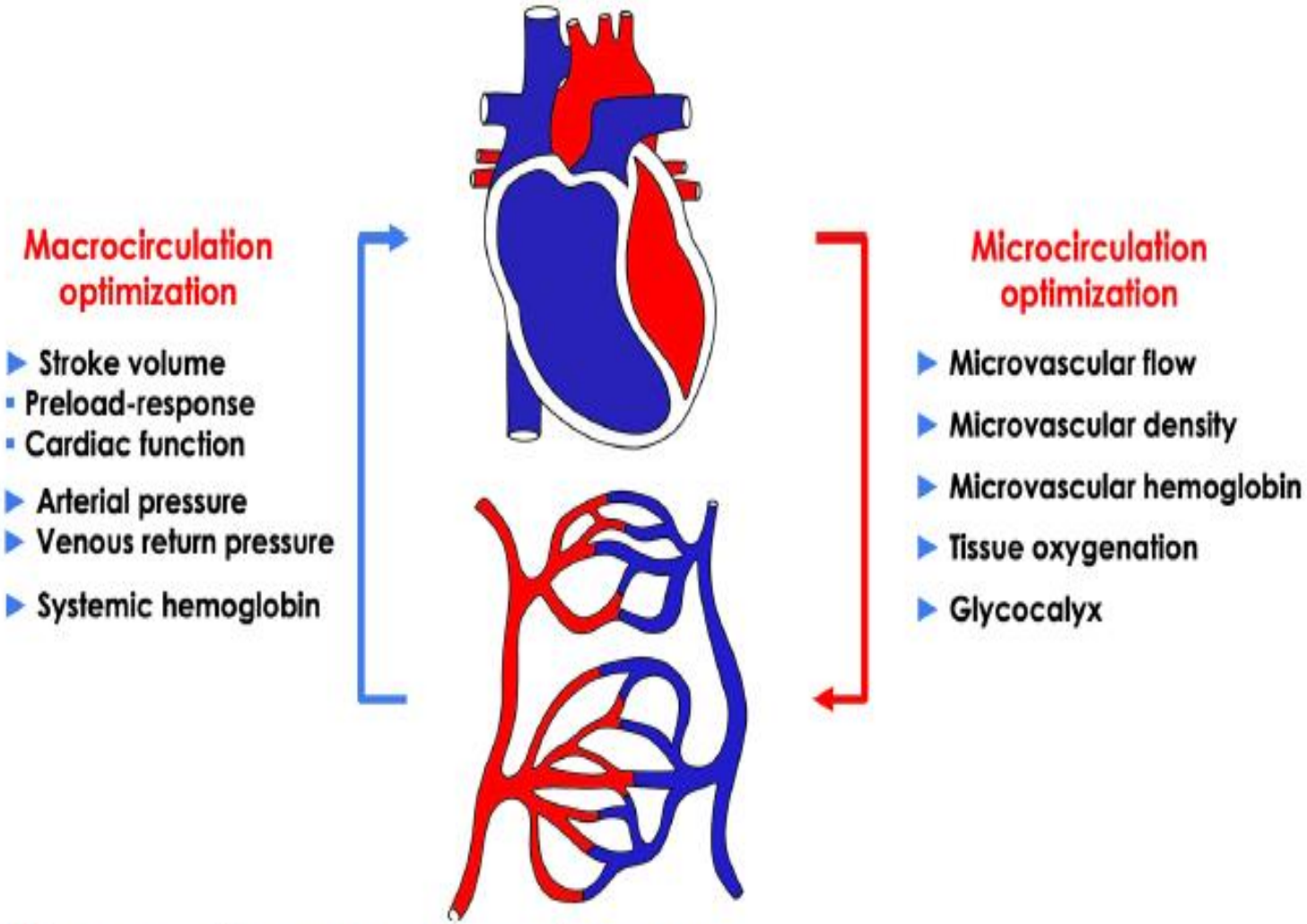


Fig. 1 Different parameters of macrocirculation and microcirculation optimization

Microcirculation assessment in ICU in the future.

- The most suitable window, for microcirculation monitoring has been the direct assessment of the subligual capillaries by means of *videomicroscopy.*
- The technique consists of a handheld microscope (HVM) that emits polarized light in the wavelength of the spectrum absorption of the hemoglobin. The device has a light guide and a disposable sterile lens at the tip, which can be placed on the tissues (eg, sublingual or intestinal mucosa).

Development of Clinical Handheld Videomicroscopy(HVM)

- Orthogonal polarization spectral (OPS) imaging device
- Side stream dark Field(SDF), a better capillary contrast and quality visualization
- Incident Dark Field (IDF) illumination technique with higher resolution optic lens and autofocusing mechanism

Different techniques exist to assess the microcirculation

TABLE 1 Types of microcirculation assessment devices.

Technical device	Device	Anatomical site	Characteristics
Handheld Vital Microscopy (HVM) -Orthogonal polarization	OPS	Sublingual	Pressure artifacts can distort the image
-Sidestream dark field	SDF	Buccal mucosa	
-Incident dark field	IDF	Skin Ear	
Laser doppler perfusion imaging (20)	Flowmetry Perfusion		Non-contact measurements Sensitive to motion artifacts
Laser speckle contrast imaging			Non-contact measurements Sensitive to motion artifacts
Capillaroscopy		Nailbed	
SDF software (GlycocCheck©) (21)	Measures Glycocalyx	Sublingual	Measures endothelial glycocalyx thickness Microvascular vessel density Red blood cell filling percentage Reported as perfused boundary region (PBR)

Adapted from (20) and (21)

What are we looking for in videomicroscopy?

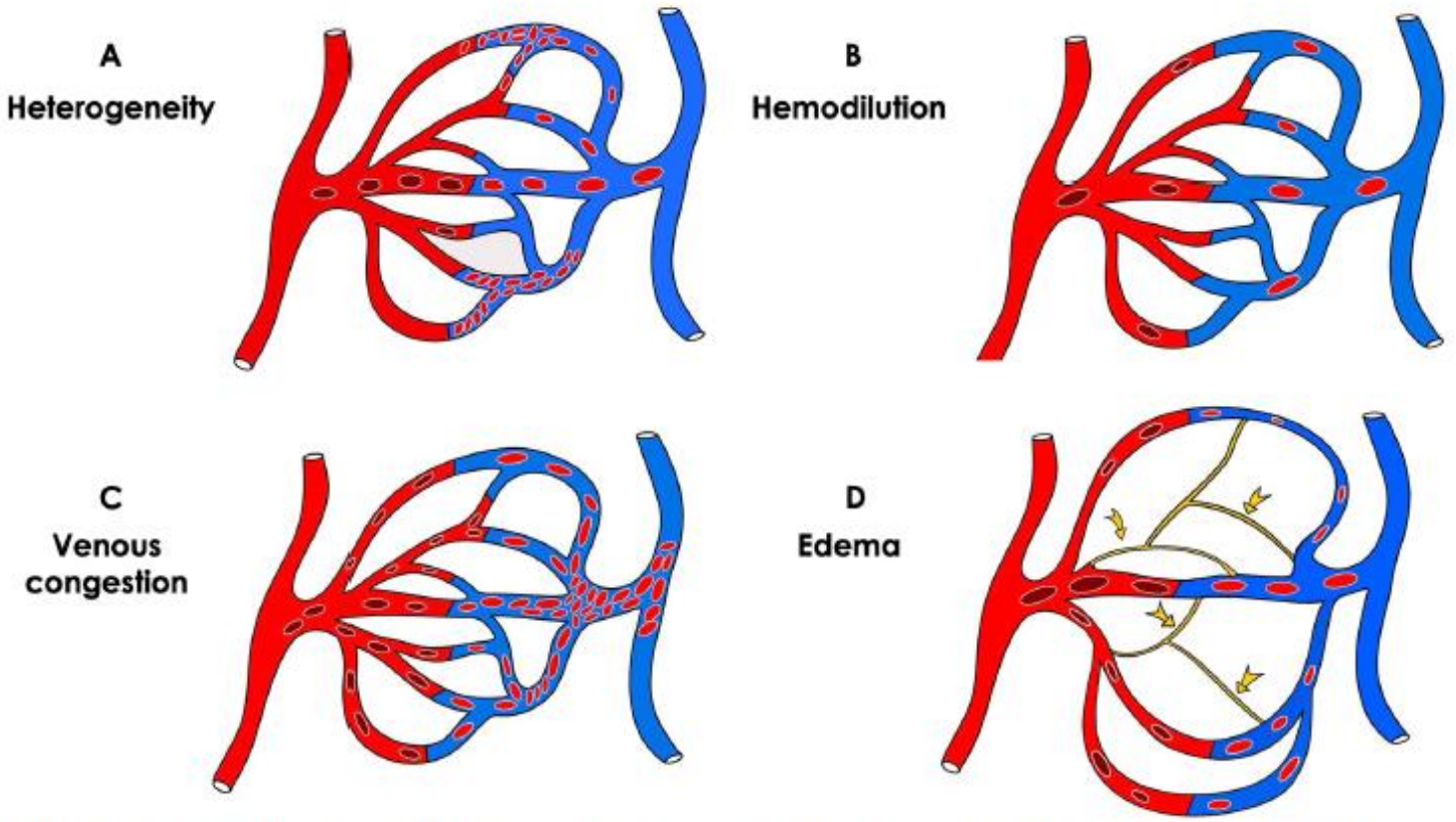
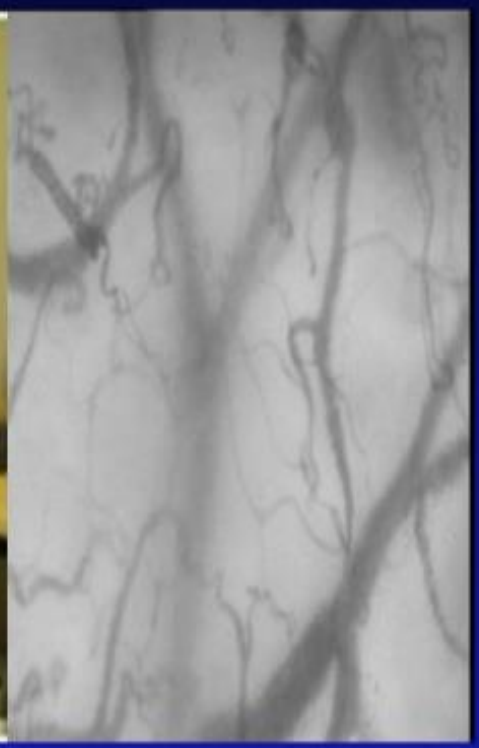


Fig. 2 Illustration of the different types of microvascular alterations occurring despite macrovascular optimization of the macrocirculation. **A** Heterogeneous distribution, with perfused capillaries next to non-circulating capillaries, observed mainly in inflammatory and/or severe septic states. **B** Dilution of red blood cells occurring during hemodilution (for example in hemorrhagic shock during fluid resuscitation) and anemia. **C** Congestion due to increased venous pressure. **D** Tissue edema with increased oxygen diffusion distances

- *Heterogeneity* of microcirculatory flow, with the presence of occluded capillaries next to perfused capillaries, inducing microcirculatory shunting responsible for the decreased oxygen extraction capacity, has been demonstrated in COVID-19.
- Items measured by capillary videomicroscopy:
  - Total vascular density (TVD)
  - Proportion of perfused vessels (PPV)
  - MFI is computed as the average of the predominant flow as (absent = 0, intermittent = 1, sluggish = 2, and normal = 3)



Handheld Video Capillary Microscope (KK Research Technology, UK) interfaced with a computer running the GlycoCheck software (GlycoCheck BV, Maastricht, The Netherlands).

Quality of IDF

- A recent multicenter study, in which the investigators were previously trained in video acquisition.
- 20% of the time points lacked of images of suitable quality for analysis. Insufficient quality was mainly explained by *pressure* (40%) and *artifacts* (30%).

CONTINUE…

- Actually, the most striking difference between healthy volunteers and patients with septic shock, as well as between survivors and nonsurvivors, was in ***heterogeneity flow*** index.
- **The most sensitive microvascular bed seems the kidney.** In experimental models of hemorrhagic and septic shock, renal peritubular capillaries are more severely disrupted than sublingual and villi microcirculation.

Microcirculatory Response to Resuscitation

- FLUIDS
- Fluids can improve convective microvascular flow due to increases in cardiac output and blood pressure. Nevertheless, an excess in intravascular volume expansion can reduce diffusional microvascular oxygen transport because of the development of tissue edema.
- Edema increase the diffusional distance and a lower viscosity might reduce capillary flow and hematocrit.

CONTINUE…

- *Another important issue is the selection of patients who might benefit from volume administration.*
- The timing of solution administration is a key factor. In sepsis, the early administration (<24 h) improve sublingual microcirculation but the delayed indication (>48 h) is ineffective.
- **The effects of fluid resuscitation also depend on the basal state of microcirculation**. In patients with an MFI <2.6, there were improvements in microcirculation and organ perfusion.In contrast, no benefits arose with MFI ≥2.6.

Microcirculatory Response to Resuscitation–Vasopressors

- The aim of vasopressors is to reach a perfusion pressure above the lower limit of autoregulation that allows tissue perfusion, while avoiding excessive vasoconstriction.
- In patients with septic shock, increases in mean arterial pressure (MAP) from 60 to 90 mm Hg by means of norepinephrine improved systemic oxygen delivery and skin perfusion increased without detrimental effects on the sublingual microcirculation.

CONTINUE…

- A more detailed analysis shows that when MAP increased from 70 to 90 mm Hg, there were falls in the MFI, of about 10%.

- *The key result, however, was that the highly variable effects were strongly dependent on the basal state of the microcirculation.*

- *The clinical implication is that the optimal MAP might be selected according to microcirculatory status.*

Microcirculatory Response to Resuscitation–Inotropes

- An observational study found that an infusion of 5 μg/kg/min of dobutamine improves the PPV from 58% to 75%, *regardless of the changes in cardiac output or MAP*. In contrast, we found that increasing doses of dobutamine do not increase microvascular in patients with septic shock.
- These conflicting responses to dobutamine might be explained again to the different microvascular states at **baseline.**

What are the future therapies targeting microcirculation in critical care?

- In experimental septic shock, favorable results have been reported with the administration of *L-arginine* and tetrahydrobiopterin (BH4) (cofactor of nitric oxide synthases)
- *ilomedin* (a prostacyclin analogue with vasodilatory and antithrombotic properties)
- Due to antioxidant properties, *albumin* is also an interesting therapeutic option to limit glycocalyx alterations and preserve endothelial function in intensive care patients

Conclusion

- Hemodynamic management requires **individualization** of macrovascular and microvascular parameters.
- Challenge for the future is to have noninvasive, easy-to-use equipment for reliable assessment and immediate quantitative analysis of the microcirculation at the patient's bedside. Use of automatic analysis and the future possibility of introducing artifcial intelligence into the analysis software make it possible to eliminate observer bias and provide orientation of therapeutic options coupled with an analysis of the microvascular responses to the applied interventions.