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The microcirculation

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The microcirculation is a network of complex vascular structures consisting of arterioles, capillaries, and venules unique to each organ it supports. It is essential for the delivery of oxygen and nutrients to cells and the removal of waste for eventual metabolism and excretion.

The microcirculation's anatomical complexity is matched by its numerous physiological functions, which are not limited to its role in the inflammatory response, neurotransmitter functions, and coagulation. With the advancement of technology, we have come to appreciate this unique network and its influences on multiple systems. Its effects on perfusion can now be monitored and visualised to influence decision-making and alter clinical judgement continuously throughout any intervention or management. The need to monitor it independently from the macrocirculation has also been established, as certain disease states can lead to a lack of coherence in the two networks.

Although we have learnt much about the microvascular network and its influence on the anaesthesiologist's management of patients, we are yet to determine if closer monitoring of the microvasculature will lead to better patient outcomes.

Keywords: microcirculation, complex vascular structures

Introduction

History

The description of microcirculation goes back as far as the 16th century when Janssen invented the compound microscope.[1] By then, the microcirculation was already at the centre of inflammatory response discussions.[1] The 20th century proved to be the time of greatest development in the understanding of the microcirculation.[1] During this period, the microcirculation was depicted in vivo and was investigated for its role in inflammation and coagulation.[1]

Description

The microcirculation consists of arterioles, capillaries, and venules (Figure 1).[2] It has the largest endothelial surface area in the body.[2] These endothelial cells are teeming with receptors that allow communication within and across organs.[2] The vessels involved can span from 5 to 200 micrometres in diameter.[2] The vessels in this network are embedded in organs.[2] As such, the architectural structure of the microcirculation is unique to each organ and its requirements.[2]

The surrounding lymphatic network is also depicted in Figure 1, as well as the supporting vascular smooth muscles and nerve fibres associated with the microvasculature in many organs.[3]

The microcirculation and its role in physiology

Arterioles are the smooth and skeletal muscle-containing component of the microcirculation.[2] This anatomy allows them to regulate blood flow and monitor vascular wall shear stress.[2] Sympathetic nerve fibres cue the vasoconstriction and vasodilation of arterioles with the release of neurotransmitters (norepinephrine) that act on vascular smooth muscle.[2] Coordinated constriction and dilatation is made possible by gap junction communication across endothelial cells.[2] The Hagen-Poiseuille law allows us to appreciate the significance of the change in the radius of this vessel network and its influence on blood flow to tissues.[2] Therefore, it is not surprising to learn that this network of vessels is responsible for 80% of pressure drop in the body.[2]

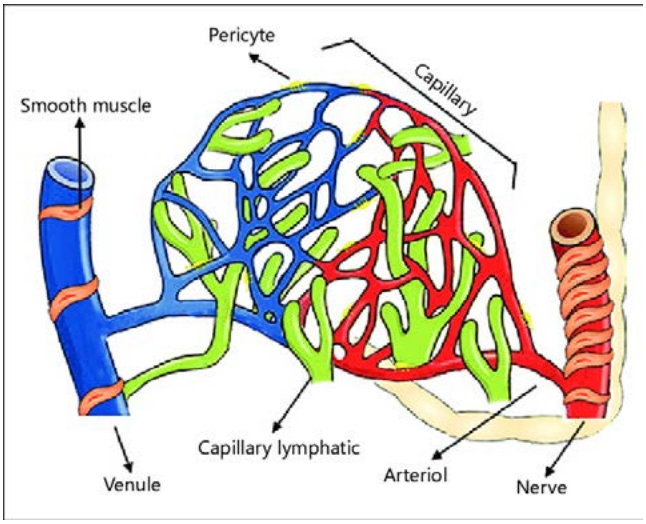

Figure 1: Illustration of the microvascular network consisting of arterioles, venules, and capillaries

The arteriole tone is regulated by myogenic, neurohormonal, and metabolic mechanisms.[3] Meanwhile, capillaries are central to the diffusion of cell nutrients to the interstitial tissue and gaseous exchange.[2] Because they lack smooth muscle, they cannot constrict and dilate.[2] The capillary surface area is approximately 70 m^2 in an adult human.[3] The capillary wall houses the endothelial glycocalyx on the luminal side.[2] The glycocalyx consists of proteoglycans, glycoproteins, and glycosaminoglycans.[3] The glycocalyx is involved in homeostasis, solute transport, immunological mechanisms, and haemostasis.[3] Venules smaller than 50 micrometres in diameter also do not contain smooth muscle or skeletal muscle tissue.[2] Instead, they contain receptors that partake in ligand binding to rheological cell lines.[2]

The microcirculation ultimately plays a significant role in oxygen transport by convection of oxygen-carrying red blood cells and oxygen diffusion.[2] It is also central to nutrient delivery, solute exchange and diffusion of hormones and neurotransmitters, and waste removal.[2] Given the significant function it fulfils in multiple systems and organs, it is an important component to monitor.

Monitoring the microcirculation

Advances in haemodynamic monitoring have assisted anaesthesiologists with macrocirculation management and manipulation. The microcirculation, however, proves difficult to monitor.[4] In certain disease states, the coherence of the macrocirculation and microcirculation is compromised, making it difficult to rely on macrocirculation-based parameters for monitoring.[4]

Handheld vital microscopes

The handheld microscope has a ring of light-emitting diodes, the light wavelength of 530 nm is absorbed by red blood cells allowing one to visualise the flow of red blood cells.[5] This imaging of red blood cells can occur at any mucosal surface that contains microcirculation.[5] There are currently three generations of handheld microscopes, with debulking and changes in image quality improving the technology with each generation.[4] This non-invasive technique has gained popularity in the critical care space and is commercially available.[5]

Studies have demonstrated that sublingual microcirculatory changes mirror changes in the microcirculation of other major organs.[4] This has allowed the extrapolation of the microcirculatory condition using handheld microscopes, viewing sublingual microvasculature.[4] The microvascular images obtained allow quantification of measures, such as microvascular flow index, which looks at the gross impression of red blood cell velocity, perfused vessel density determined by capillary distance, and red blood cell velocity and heterogeneity index, which looks at the heterogeneity of blood flow in different regions.[5]

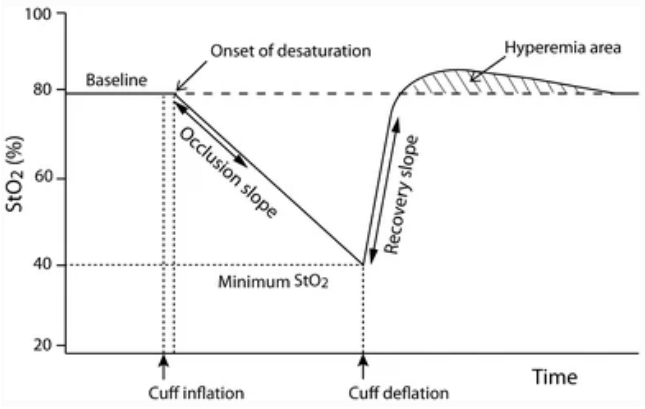

Figure 2: The changes in saturation during vascular occlusion and reperfusion[6]

Vascular occlusion test

The vascular occlusion test uses a pneumatic cuff over the arm to induce transient ischaemia.[5] An oxygen sensor of the thenar muscles monitors changes in tissue oxygen saturation.[5] The parameter changes are then plotted on a graph and the recovery slope, indicating the amount of time it takes for tissue oxygenation to normalise after ischaemia, is used to predict patient outcome after major surgery (Figure 2).[5]

Laser Doppler flowmetry

This technique measures backscattered light that is Doppler-shifted during tissue motion.[5] A two-dimensional image is created from different skin sources.[5] However, this technique is not accurate if there is a lack of vascular heterogeneity, and it is limited in its ability to monitor alterations in microvasculature.[5]

Near-infrared spectroscopy

This non-invasive technique uses the difference in absorption of light at two wavelengths (600 nm and 800 nm) by deoxyhaemoglobin to determine haemoglobin saturation in the tissue under study.[7] This technique can be used alongside a vascular occlusion test to determine the recovery of tissue oxygenation post-ischaemia.[7]

Sublingual capnometry

The partial pressure of carbon dioxide in sublingual tissue can be monitored using a microelectrode sensor.[8] The difference between arterial and tissue carbon dioxide partial pressure is measured.[8] A decrease in the pressure gap suggests an improvement in capillary perfusion.[8] Gastric mucosal-arterial partial pressure carbon dioxide has also been used in a similar way to monitor microcirculation.[8]

Gastric tonometry

Gastric tonometry has been used to measure the condition of the splanchnic circulation.[9] Decreased perfusion leads to increased partial pressure of carbon dioxide in gastric mucosa, which in turn leads to a reduction in gastric pH.[9] A semipermeable balloon

is attached to a nasogastric tube and inserted into the stomach.[9] The balloon is filled with saline and the carbon dioxide is allowed to diffuse across the membrane.[9] The partial pressure of carbon dioxide in the saline is then measured and the Henderson-Hasselbalch equation is used to quantify the pH.[9] The difference between the gastric mucosal-arterial pH is used to demonstrate the degree of gastric ischaemia.[9]

Anaesthesia and the microcirculation

Anaesthetists have a special interest in manipulating microcirculatory properties in their physiological and pathological states to influence the flow of blood to tissue for resultant oxygenation. Administered anaesthesia also alters the microcirculation, potentially influencing patient outcomes. The discussion below explores the various influences disease and anaesthesia have on microcirculation.

The microcirculation and fluid administration

Fluid administration has long been identified as an essential part of resuscitation for many states of shock. Early fluid administration in sepsis and patients with a microvascular flow index of less than 2.6 has been found to improve the flow index in the microcirculation.[10] However, in patients where the microvascular flow index was greater than 2.6, there was no improvement in flow index and therefore no advantage in fluid administration.[10]

The microcirculation in sepsis

Sepsis is defined as a life-threatening organ dysfunction due to a dysregulated host response to infection.[11] It results in microcirculatory dysfunction due to endothelial dysfunction, shedding of the glycocalyx, and abnormal secretion of neurotransmitters involved in vasodilation and vasoconstriction.[4] Not only is there a compromise in nutrient tissue delivery, but the tissue itself also has a reduced ability to extract and utilise oxygen and nutrients appropriately.[11] The microvascular changes that precede these events are changes in capillary wall density, blood flow shunts, and rheological changes leading to microthrombi.[11] Sepsis is recognised as a disease state where the macrocirculation and the microcirculation are uncoupled.[11] Consequently, the monitoring of microcirculation in sepsis has grown popular.[11] This improved monitoring is yet to prove more useful at bettering outcomes in septic patients.

The microcirculation in non-cardiac surgery

Surgical response

A meta-analysis has shown that there are significant changes in microcirculatory flow immediately after surgery using microvascular flow index and perfusion vessel density as monitored parameters.[12]

Intravenous induction agents

Propofol, thiopentone, and ketamine cause vasodilation by inhibiting L-type gated calcium channels.[13] Propofol has been shown to induce a reduction in microvascular density and capillary perfusion in ASA 1 patients through vasodilation.[13] Propofol has also been shown to have anti-inflammatory effects in humans by altering the balance of cytokine and anti-inflammatory interleukins.[13] A small study also showed improvement in vascular occlusion test recovery time as a result of peripheral vasodilation after induction of anaesthesia with a total intravenous technique, suggesting that microcirculation monitoring may be a poor indicator of microvascular status at induction.[14] These changes are yet to be correlated with patient outcomes.[12]

Inhalation agents

Volatile agents cause dose-dependent smooth muscle tone reduction in the arterioles.[15] This causes a change in blood flow across microcirculatory vasculature.[15] These agents also contribute to blocking sympathetic outflow and preventing an appropriate adrenergic response to reduction in cardiac output.[15] Sevoflurane, isoflurane, and desflurane have been shown to reduce the amount of pro-inflammatory cytokines and tumour necrosis factor production in humans.[13]

Neuraxial technique

Thoracic epidural anaesthesia has been shown to improve splanchnic blood flow, thereby improving gastric mucosal pH.[13] However, epidural anaesthesia limited to the lumber region has been shown to cause splanchnic vasoconstriction due to the compensatory increase in sympathetic outflow at the thoracic level.[13]

Vasopressors

In a pathological state such as sepsis, loss of macrovascular and microvascular coherence is common.[16] The use of vasopressors, such as norepinephrine, can increase macrovascular parameters, such as mean arterial pressure, left and right ventricular stroke work indices, and cardiac index while failing to improve the sublingual microvascular flow index.[16]

The microcirculation in cardiac surgery

There are many changes in the microcirculation as a result of cardiac surgery and all it entails.[17] Cardiopulmonary bypass, hypothermia and ischaemic reperfusion can all contribute to microvascular dysfunction leading to microthrombi formation, poor oxygen delivery, and changes in neurohormonal activity that regulates vessel wall size and red blood cell convective flow across the vessels.[17] The above results in poor microcirculatory flow and possibly, poor tissue perfusion.[17]

Conclusion

The microcirculation is a complex network involved in all organ systems. It is key to many physiological functions and is significantly affected by anaesthesia. The anaesthetist's awareness of its complexity and monitoring options may be the key to improved patient outcomes. The use of various drugs targeted at improving macrocirculation might have limited use in improving microcirculation in disease states that lead to the uncoupling of these vascular networks. It is prudent to identify the patients at risk of this uncoupling and adjust the targeted monitoring and treatment accordingly.

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