

Endothelial dysfunction in the peri-operative setting

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Learning objectives

- To provide a brief synopsis of endothelial (dys)function.
- To explore the pathophysiology of endothelial dysfunction in the peri-operative period.
- To explore strategies for modulation of endothelial function.

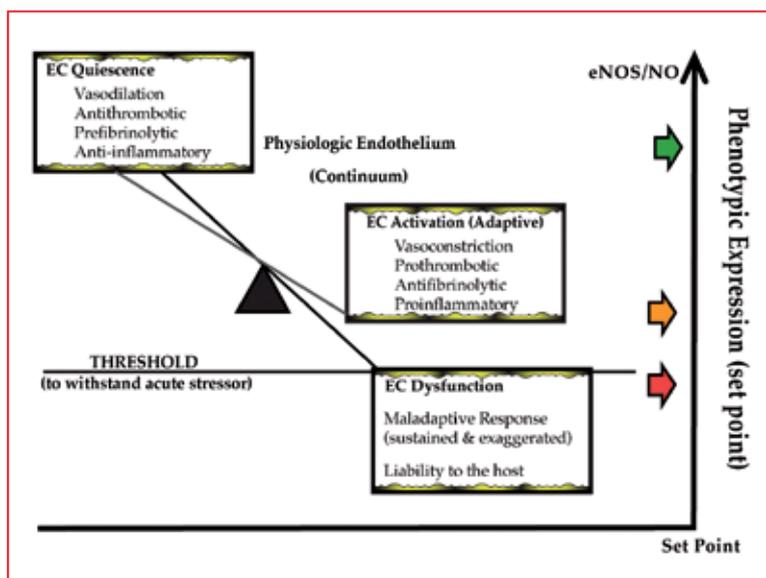
While peri-operative macrovascular events (e.g. myocardial infarction, stroke, etc) are readily evident, their absolute incidence remains relatively low. In contrast, microvascular dysfunction and its role in peri-operative morbidity is not readily appreciated nor easily measured. Given the ubiquitous presence of endothelium in all organs, microvascular dysfunction is likely to have a greater impact, through impaired perfusion, on non-cardiovascular complications (e.g. wound healing and end organ failure) than that which is readily appreciated.

The endothelium is a highly responsive organ, with its phenotypic expression (set point) determined by host (genetic) and the

extracellular (environmental triggers) milieu. This set point — whether it resides in a quiescent, activated or dysfunctional state — reflects the health of the endothelium. Triggers such as inflammation and oxidative stress disrupt endothelial homeostasis, thereby decreasing the bioavailability of nitric oxide and other physiologic mediators. This predisposes blood vessels to vasoconstriction, inflammation, leukocyte adhesion, thrombosis — an adaptive physiologic response (transient endothelial activation) to an acute stressor such as surgery or critical illness. However, when this response is maladaptive (persists or is exaggerated, termed endothelial dysfunction), it contributes to peri-operative events at both the macro- and microvascular level. Such a maladaptive response can exist in the pre-operative comorbidities, or accompany the acute phase reaction to surgery or critical illness. The maladaptive response may also reduce the "critical threshold" of endothelial function needed to sustain microvascular perfusion.

Additionally, a reparative bone marrow response, most likely mediated through the paracrine effects of endothelial progenitor cells at the injured site, offsets tissue injury. Impaired mobilisation of endothelial progenitor cells is associated with impaired recovery from injury (e.g. acute lung injury, sepsis) and poorer survival.

Figure 1: The endothelium as a highly adaptive organ fluctuating between a state of quiescence and activation. Co-morbidities result in a maladaptive response that reduces endothelial function. A "physiologic threshold" may exist, below which injury (e.g. postoperative complications) to the host is likely. The set point (proteomic expression) is determined by the host genome, co-morbidities and changes in the extracellular milieu.



Assessment of the microvascular function reflects upon the concerted interactions of the endothelial, inflammatory and thrombotic cascades. As the clinical utility of noninvasive methods that assess pre-operative endothelial/microvascular (dys)function, and that of bone marrow reserve, continues to expand, we anticipate improved risk stratification, thereby allowing opportunity for timely peri-operative optimisation. In this regard, there is increasing recognition of the need for peri-operative strategies that maintain the integrity of the endothelial-inflammatory-coagulation/fibrinolytic (hemostatic) cascades — and for strategies that repair or modulate endothelial function, including promising cell-based (progenitor) therapy.

Current clinical strategies applicable to the peri-operative setting that improve microvascular health

include pre-operative exercise therapy, pharmacologic interventions (e.g. statins, newer β -blockers) and attempts to stimulate mobilisation and homing of bone marrow-derived endothelial progenitor cells. Many of these strategies are still in their infancy, and large prospective trials that investigate the impact of these therapeutic options on postoperative outcome are eagerly awaited.

Key references

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