

INVITED COMMENTARY

When the Vicious Circle Begins...

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In their study, van Schaik *et al.*¹ showed that cold renal perfusion during a simulation of juxtarenal aortic aneurysm repair preserved renal function and had beneficial effects on sigmoid integrity by preserving microcirculatory flow, as well as reducing oxidative stress and leucocyte infiltration.

Per-operative measures to preserve renal function are still a matter of debate during open juxtarenal aortic aneurysm repair. Critics of preservation techniques state that total ischaemia times are increased by these extra procedures, thereby increasing the risk of harming post-operative renal function. However, experimental studies have demonstrated that renal hypothermia can preserve renal function through reduced oxygen consumption and per-operative measures with cooling have already been applied in humans with beneficial effects on post-operative renal function.² According to the European Society for Vascular Surgery guidelines, a strategy to preserve renal function by means of cold crystalloid renal perfusion may therefore be considered in patients undergoing open repair of juxtarenal abdominal aortic aneurysm.³ Enrichment of crystalloid solution with mannitol has also been proposed, since mannitol decreases blood viscosity, induces renal vasodilatation, and produces an osmotic diuresis. Moreover, mannitol may contribute to reducing oxidative stress related to ischaemia reperfusion because it is a reactive oxygen species scavenger.⁴ However, there is no compelling evidence in favour of pharmacological protection of renal function, since only limited data from underpowered studies are available.³

Interestingly, van Schaik *et al.*¹ investigated the remote effects of renal cooling measures. Sigmoid damages following aortic cross clamping proximal to the renal arteries could not be attributed to the temporary exclusion of the inferior mesenteric artery, because animals were expected to have patent visceral vasculature. Accordingly, sigmoid damage was related to the remote effects of renal ischaemia reperfusion injury and consecutive oxidative stress. This is an important notion: the kidney should not be considered as a passive bystander but rather as a driving force of a detrimental spiral that can lead to multiple organ failure.⁵ In fact, acute renal injury frequently occurs in combination with other organ dysfunction, such as lung injury, decreased cardiac function, or sepsis. There is therefore increasing evidence that ischaemia reperfusion injury can lead to a substantial cross talk between different organs and that acute renal injury by itself can cause deterioration of other organ's function, and thereby result in multi-organ failure.⁵

The mechanisms underlying the renal cooling conferred remote protection deserve further studies. Oxidative stress related to ischaemia reperfusion and the activation of inflammatory pathways, being largely mediated by cytokines such as interleukin 1, interleukin 6, and tumour necrosis factor- α , have been shown to be responsible for post-operative complications in abdominal aortic aneurysm repair.⁶ However, the link between oxidative stress and inflammatory pathways is poorly understood. Moreover, controversy still exists over which particular tissues are most susceptible to ischaemia reperfusion and which tissues are most likely to be responsible for the initial inflammatory response. The gastrointestinal tract (which has been investigated by the authors) and the muscle mass of the lower limbs seem implicated as the potential origin of the inflammatory response in abdominal aortic aneurysm repair.⁶ Identifying the origin of inflammation and multi-organ failure in patients undergoing abdominal aortic aneurysm repair, as well as identifying the protective pathways is therefore a very important goal, as it may enable the development of targeted therapy with the aim of reducing the mortality and morbidity of surgical procedures.

In conclusion, methods for attenuating ischaemia reperfusion injury and the subsequent inflammatory responses in patients undergoing juxtarenal aortic aneurysm repair are needed. The study of van Schaik *et al.* suggests a need to protect the kidneys beyond renal preservation itself, since acute renal injury might be a promoter or at least an amplifier of systemic inflammatory response. However, future research is needed in order to allow evidence based recommendations for assisting physicians in their practice.

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