Perioperative renal dysfunction is a well recognized complication in patients undergoing elective repair of abdominal aortic aneurysm (AAA). Postulated mechanisms include diminished preoperative renal function, tubular functional impairment secondary to altered intrarenal circulation, activation of the renin-angiotensin-aldosterone system, reduced distal tubular sodium delivery and atheromatous emboli. Infraaortic aortic cross-clamping per se has been demonstrated to produce profound and sustained alterations in renal haemodynamics (38% reduction in renal blood flow and 75% increase in renal vascular resistance) in the absence of significant changes in cardiac output or systemic vascular resistance. Prolonged aortic cross-clamping, hypotension and large-volume blood transfusion are important risk factors in the development of postoperative renal impairment in this patient population. Acute renal failure (ARF) in this context carries a high mortality rate, and its avoidance is an important goal of postoperative management. Hence, the findings of Girbes and colleagues in a recent issue of British Journal of Anaesthesia that an infusion of dopamine 2–4 μg kg⁻¹ min⁻¹ increased glomerular filtration rate (GFR) and renal blood flow (RBF) in seven haemodynamically stable patients undergoing mechanical ventilation and receiving postoperative extradural analgesia after elective AAA repair merits attention and critical analysis. The authors attributed the dopamine-induced increased GFR and RBF to increased cardiac output and they went on to conclude that “if an increase in RBF and GFR is considered as a goal of treatment, our data indicate that 4 μg kg⁻¹ is the optimal dose of the given doses”. Do the findings of this study support the claims often made by proponents of “renal-dose” or “low-dose” dopamine that such a regimen augments RBF, GFR and/or natriuresis in healthy humans and experimental animals, and limits adenosine triphosphate utilization and oxygen requirements in nephron segments at risk for ischaemic injury, actions that could potentially limit renal injury and accelerate recovery in ARF? Undoubtedly, dopamine infusion induces a dose-dependent increase in RBF, natriuresis and diuresis in healthy experimental animals and humans and improves RBF in patients with chronic renal impairment, renovascular disease and mild to moderate sodium depletion. The mechanisms by which dopamine modulates RBF differ depending on the rate of infusion. At low doses (threshold 0.5, maximum 3.0 μg kg⁻¹ min⁻¹), dopamine augments RBF principally by DA1 receptor-induced intrarenal vasodilatation and possible contributory engagement of DA2 receptors on presynaptic sympathetic nerve terminals with inhibition of noradrenaline release. Intermediate doses of dopamine (threshold 3.0, maximum 10 μg kg⁻¹ min⁻¹) are thought to augment renal perfusion by increasing cardiac index via cardiac β₁-adrenoreceptor stimulation. Higher doses of dopamine administration (threshold 5.0, maximum 20 μg kg⁻¹ min⁻¹) may produce systemic vasoconstriction via α-adrenoreceptor stimulation. An important caveat worthy of note is that the above-mentioned dopamine dose–response relationships were advanced after studies in normovolaemic healthy subjects. Do they apply to the potentially hypovolaemic and hypothermic patient, with coexisting ischaemic heart disease, hypertension or diabetes in the immediate postoperative period? In this uncontrolled, small scale study of relatively normovolaemic, normothermic patients without coexisting cardiac or renal impairment, infusion of dopamine 2–4 μg kg⁻¹ min⁻¹ increased urine output, GFR and RBF. What was/were the mechanism(s) involved? The mechanisms by which dopamine exerts its renal effects are complex and might include: β-adrenoceptor-mediated increase in cardiac output; DA1 and DA2 receptor-mediated vasodilatation and increased RBF; increased delivery of diuretics to the distal tubule; decreased renin–angiotensin–aldosterone activation; or direct effects on tubular function. Increased cardiac output and RBF were the most striking findings in the study by Girbes and colleagues. Plasma renin activity was essentially unchanged, while plasma aldosterone concentrations were reduced significantly when an infusion of dopamine 8 μg kg⁻¹ min⁻¹ was given. Dick, Dasta and Choban, in a study of oliguric, critically ill surgical patients, reported that an infusion of dopamine 2–5 μg kg⁻¹ min⁻¹ for 6 h decreased serum aldosterone concentration with increased urine output and sodium excretion. Do the results of this study suggest a role for prophylactic low-dose dopamine in this clinical context? The authors make no such claim based on their observations. Moreover, several recent editorials have strenuously urged abandonment of low-dose dopamine therapy in the treatment of ARF. Paul and colleagues observed no clinically important benefit from intraoperative administration of mannitol and dopamine compared with extracellular fluid volume expansion with saline alone in the prevention of changes in renal function associated with aortic cross-clamping. Studies assessing the efficacy of “renal” or low-dose dopamine in the prevention of ARF in high-risk clinical situations—major cardiac surgery, vascular or biliary surgery, renal and liver transplantation, and exposure to contrast material—have been challenged on the basis of patient numbers and study methods. In a prospective, randomized controlled study of 37 patients undergoing elective abdominal aortic surgery, 24-h infusion of dopamine 3 μg kg⁻¹ min⁻¹ in the postoperative period did not improve creatinine clearance or reduce serum creatinine concentrations measured after 1 and 5 days, respectively. Two postoperative deaths occurred in the dopamine
group (from renal failure and myocardial infarction). Four patients had myocardial infarction, three of whom received dopamine.

In examining the potential therapeutic effects of low-dose dopamine, it is necessary to perform a risk–benefit analysis regarding deleterious side effects. This process is essential when the treatment is of questionable benefit. Girbes and colleagues reported no major changes in heart rate in the seven patients studied. None the less, dopamine is a potent catecholamine, with positive inotropic and chronotropic activity, even in the low doses used in the study. Apart from the obvious potential problems with tachycardia and increased myocardial oxygen consumption, dopamine may depress hypoxic respiratory drive and, in a porcine shock model, was reported to divert blood flow away from the gut mucosa. Administration of dopamine warrants central venous cannulation, and drug extravasation adjacent to an artery may provoke distal ischaemia and gangrene.

There is no doubt that dopamine in low doses in healthy kidneys leads to an increase in urine output, accompanied by natriuresis and kaliuresis. Low-dose dopamine, as used by Girbes and colleagues, appeared to function as a “diuretic” with perhaps some inotropic and renal vasodilator properties. This diuresis would be a dubious blessing if it were to mask or even cause hypovolaemia and subsequent renal hypoperfusion. The absence of prospective, controlled, large-scale studies confirming reduced incidence of ARF and improved outcome three decades after the first reports of administration of renal protective doses of dopamine remains a concern. Perhaps clinicians and investigators should focus attention on catecholamines such as dobutamine, devoid of diuretic properties, but with the potential to augment cardiac output and renal blood flow?

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References