Contemporary Strategies to Preserve Renal Function During Cardiac and Vascular Surgery

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Mortality rates associated with perioperative acute renal failure (ARF) range from 60% to 90%. The major causes of ARF are prerenal factors that decrease renal blood flow; intrarenal factors that have a direct effect on tubules, interstitium, or glomeruli; and postrenal factors that obstruct urine outflow. Current strategies to provide perioperative renal protection include maintaining adequate renal O_2 delivery, suppressing renovascular vasoconstriction, renovascular vasodilatation, maintaining tubular flow, decreasing renal cellular O_2 consumption, and attenuating reperfusion injury. A study of patients undergoing elective repair of a thoracoabdominal aortic aneurysm (TAAA) found that the use of the selective dopamine-1 receptor agonist fenoldopam was associated with reductions in mortality, dialysis requirements, and lengths of stay in the hospital and intensive care unit. The study authors suggest that the improved patient outcomes and hospital-utilization data resulting from the use of fenoldopam were directly related to the protection of renal function during surgery and a reduction of postoperative renal complications.

[Rev Cardiovasc Med. *2003;4(suppl 1):S21–S28*]

Key words: Acute renal failure • Perioperative renal protection • Cardiovascular surgery • Thoracoabdominal aortic aneurysm • Selective dopamine-1 receptor agonist • Fenoldopam

Over the past several decades—despite advances in cardiac hemodynamic monitoring, intensive care management, and dialysis techniques—the mortality rate from perioperative acute renal failure (ARF) has remained high. A review of the published literature demonstrates that ARF is associated with mortality rates ranging from 60% to 90%.[1-3]

Table 1
Mortality and Hospital Resource Utilization in Patients Secondary to Renal Impairment

	Mortality (%)	ICU stay (days)	Length of stay (days)
Normal	0.9	3.1	10.6
Renal dysfunction	19.0	6.5	18.2
Acute renal failure	63.0	14.9	28.8

Adapted from Mangano et al.[3]

Perioperative ARF, regardless of etiology, increases morbidity, mortality, and health care costs.[3,4] Patients with perioperative renal failure have morbidity and mortality related to both renal and—even more importantly—nonrenal complications.[3] Mangano and colleagues[3] demonstrated that even small changes in renal function carry an independent risk for complications after coronary artery bypass graft (CABG) surgery. Their findings showed that in patients with normal renal function the in-hospital mortality rate was 0.9%, the intensive care unit (ICU) stay was 3.1 days, and the overall length of stay (LOS) was 10.6 days. This contrasted with patients who developed acute renal dysfunction: their in-hospital mortality was 19.0%, their ICU stay was 6.5 days, and their overall LOS was 18.2 days. Those patients who developed ARF fared even worse: their in-hospital mortality was 63.0%, their ICU stay was 14.9 days, and their overall LOS was 28.8 days (Table 1).

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A review by Aronson and Blumenthal[4] showed the impact that renal dysfunction has on nonrenal morbidity; patients who developed renal failure had higher incidence of gastrointestinal bleeding, respiratory infections, and sepsis. Further, Levy and associates[2] demonstrated the enormous impact that radiocontrast nephropathy (RCN) has on in-hospital mortality. In their review, the authors reported that the mortality odds ratio increased to 5.5 in patients who developed RCN versus those who did not develop RCN.[2]

A unified standard for what constitutes renal insufficiency needs to be agreed upon in order to standardize analysis.

It is not universally appreciated that the morbidity in patients who develop exacerbations of renal dysfunction is related more to nonrenal than to renal complications, including increased rates of respiratory failure, central nervous system dysfunction, sepsis, and gastrointestinal hemorrhage. These complications place a further economic burden on the health care system, as health care costs increase because of longer lengths of stay, more numerous laboratory tests, and more intense interventions, including dialysis.

Definition of Acute Renal Failure (ARF)

In light of the impact associated with increases in renal impairment, clinical investigators and clinicians need to reach a consensus on the definition of ARF. The variety of definitions present in the medical literature[1] has led to a large variability in the reported incidence of renal insufficiency. Although all clinicians agree that renal insufficiency may be defined as the inability of the kidney to remove nitrogenous waste, a range of laboratory criteria is used to define ARF. Some investigators define acute renal insufficiency as an increase in serum creatinine of > 0.5 mg/dL from baseline. Others use a definition that relies on an increase in serum creatinine of > 50% from baseline. Even the definition of renal insufficiency lacks consistency; some use a predetermined value of the glomerular filtration rate, whereas others use any serum creatinine value above 1.5 mg/dL.[5] Because of this variability in definition, there is also bound to be a corresponding variability in the reported incidence of perioperative renal insufficiency. Clearly, a unified standard for what constitutes renal insufficiency needs to be agreed upon in order to standardize analysis.

Physiology of Perioperative Renal Dysfunction

At first glance it is difficult to understand why the kidney, a highly vascular organ that receives 20% of the cardiac output, should be prone to

developing perioperative dysfunction. It is important to understand the multifactoral nature of renal insults and appreciate the precarious nature of the intrarenal blood distribution in order to clarify the mechanisms of perioperative renal dysfunction.

The major causes of renal failure are usually divided into three broad categories[6]: 1) prerenal factors; 2) intrarenal factors; and 3) postrenal factors.

Prerenal etiologies are those that decrease either global or regional renal blood flow. Some examples include low cardiac output, renovascular vasoconstriction, atheromata, emboli, contrast dye, cyclosporine, and vascular clamps. Intrarenal etiologies include factors that have a direct effect on the tubules, interstitium, or glomeruli. Examples include trauma, toxins (free Hg), and drugs such as aminoglycosides. Postrenal etiologies are those that cause obstruction to urine outflow. These include nephrolithiasis, ureteral kinks, prostatic hypertrophy, and obstructed bladder catheters.

In the surgical patient, the cause of perioperative renal dysfunction is often multifactoral. With the use of the selective dopaminergic receptor agonist, fenoldopam, we may be able to have an impact on certain elements contributing to renal blood flow.

The most common etiology of ARF is from acute tubular necrosis (ATN).[1,7] In ATN, an ischemic insult occurs predominantly in the medullary portion of the nephrons.[8] This area of the kidney is particularly vulnerable to injury as the medulla receives only 5% of the renal blood flow compared to the cortex, which receives 95%. In addition, the cells in the medulla are in a constant low-oxygen environment (PaO_2 8 mm Hg) versus the cortex (PaO_2 50 mm Hg). Injury to the medulla causes cellular injury, followed by an inflammatory cascade. This inflammatory cascade propagates further cellular injury, eventually leading to cell death. Notably, renal vasodilators that have not proven to be renoprotective (ie, atrial natriuretic peptide and dopamine) do not increase medullary blood flow and, in fact, may divert blood from the ischemic medulla into the relatively well-perfused cortex. In contrast, fenoldopam increases both medullary and cortical blood flow.[9] In addition, by directly inhibiting sodium transport in the medullary thick ascending limb, fenoldopam reduces the oxygen demand of this region of the nephron that is most susceptible to ischemic ATN. The combined effect of improving medullary oxygen supply and reducing medullary oxygen demand predicts that fenoldopam would be renoprotective in ischemic ATN. In order to prevent renal damage, it would be useful to identify patients at risk and target therapy to specific renal-protection strategies.

Although multiple risks factors have been entertained, the most consistent preoperative risk factors for developing renal insufficiency are preexisting renal insufficiency, type 1 diabetes, age > 65 years, major vascular surgery, prolonged cardiopulmonary bypass (> 3 hours), and recent exposure to nephrotoxic agents (eg, contrast dye).[10,11]

Renal Protection Strategies

Current strategies in perioperative renal protection can be divided into the following approaches:

1. Maintaining adequate renal O_2 delivery
2. Suppressing renovascular vasoconstriction
3. Renovascular vasodilatation
4. Maintaining tubular flow
5. Decreasing renal cellular O_2 consumption
6. Attenuating reperfusion injury

A comprehensive, detailed review of the specific agents and modalities that have been applied to find the "Holy Grail" of renal protection is beyond the scope of this article. However, various renoprotective therapeutic approaches are briefly reviewed below.

Maintenance of Adequate Renal O_2 Delivery

This is primarily accomplished by ensuring an adequate cardiac output (via preload augmentation and appropriate inotropic support). In addition, adequate oxygen-carrying capacity, hemoglobin, and proper saturation of hemoglobin or other O_2-carrying substrate is essential.

Suppression of Renovascular Vasoconstriction

Attenuation of renal vasoconstriction is often best achieved by ensuring adequate renal preload. In addition, various agents such as mannitol, calcium channel antagonists (CCAs), and angiotensin-converting enzyme inhibitors (ACEIs) may play a role in the prevention of vasoconstriction.

Renovascular Vasodilatation

Another strategy to improve or maintain renal blood flow is to vasodilate the renal arterial vessels. Several agents are under investigation. These include dopaminergic agents, prostaglandins, and atrial natriuretic peptide (ANP).

Maintenance of Tubular Flow

Obstruction to tubular flow from shed casts or other intraluminal debris can result in cellular swelling, ischemia, and death. The use of loop diuretics and mannitol is thought to maintain or promote tubular flow.

Decreased O_2 Demand

It has been proposed that if the metabolic demand of the kidney

were reduced, then the cells would be able to better tolerate an ischemic insult. Both loop diuretics and mild cooling of the kidney play independent roles in decreasing renal metabolic demand, whereas mannitol can increase renal metabolic demand. Conclusive results demonstrating the efficacy of reducing the kidney's metabolic demand is lacking.

Attenuation of Reperfusion Injury

One of the final common pathways of ischemic-related injury involves reperfusion. Upon reperfusion of ischemic cells, oxygen free radicals and Ca ions are released. These substances are toxic to cells and promote cell damage. Agents that buffer free radicals (free radical scavengers) and limit the release of Ca ions may be of benefit in limiting the reperfusion insult.

Renal Protective Effects of Dopamine-1 in Surgery

The focus of this section is on the use of the selective dopamine-1 (DA_1) agonist and the potential role DA_1 has in renal protection in surgery. We (Sheinbaum and associates, unpublished data) studied the effect of a selective DA_1 agonist as a renoprotective strategy during the intraoperative and postoperative period in vascular surgery.

The renal vascular bed is rich in dopamine receptors (DA_1 and DA_2).[10,12] DA_1 receptors are postsynaptic, cause vasodilatation, and increase renal blood flow. DA_2 receptors are presynaptic, cause vasoconstriction, and decrease renal blood flow.[13] Historically, clinicians have advocated the use of low-dose dopamine (so-called "renal-dose" dopamine) in the belief that at doses of 0.05–2.50 μg/kg/min dopamine stimulates renal dopamine receptors and hence improves renal blood flow.[14] More importantly, low-dose dopamine has been advocated as a means of preserving renal function.[14,15] More recently, the use of renal-dose dopamine has been more closely scrutinized. The results have been mixed, with ever-increasing reports of low-dose dopamine providing little, if any, renal benefits.[16] Moreover, some authors report that the use of low-dose dopamine is associated with an increased incidence of cardiac arrythmias and worsening of renal function.[14,17] It is not surprising, however, that the effects of dopamine are varied, as dopamine does not possesses receptor specificity. Dopamine can and does bind to a variety of receptors depending upon the individual receptor affinity as well as on the drug concentration.[13] These properties are in contradistinction to fenoldopam, which is a specific agonist for the DA_1 receptor (Figure 1).

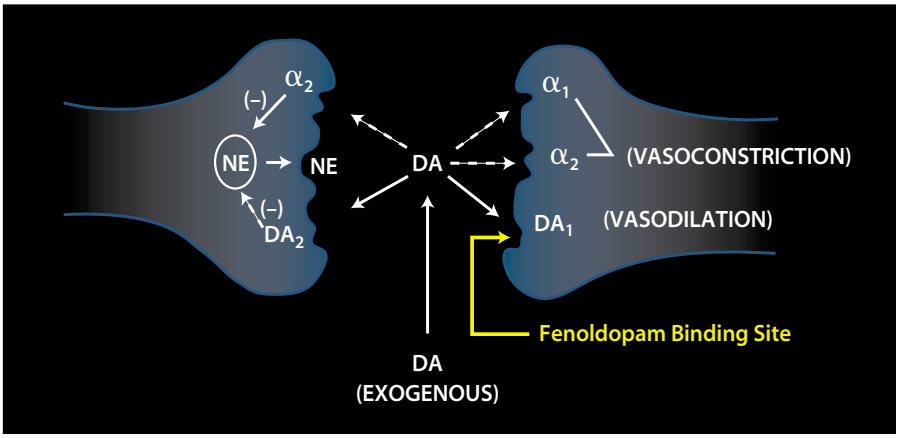


Figure 1. *Nerve ending receptor affinity for fenoldopam versus dopamine. DA, dopamine; DA_1, postsynaptic dopamine receptor; DA_2, presynaptic dopamine receptor; NE, nerve ending.*

With this in mind, we chose to study the effect the selective DA_1 receptor agonist fenoldopam would have on renal function during vascular surgery. Fenoldopam has been shown to improve creatinine clearance, improve renal blood flow, and reverse the effects of cyclosporine A toxicity.[18,19] Fenoldopam is not an inotrope and therefore has no direct effect on myocardial contractility. In contrast to the lack of myocardial activity, fenoldopam has a protective effect on a variety of arterial vascular beds, including the mesenteric and renal vascular beds.[20] By selective vasodilation of the mesenteric and renal beds, gut and renal perfusion are enhanced in certain hypovolemic states such as hemorrhagic shock. The only adverse effect associated with DA_1 stimulation is a possible increase in intraocular pressure. Mathur and colleagues[21] have shown that there is a dose curve to increasing renal blood flow in the human kidney (Figure 2). At doses as low as 0.03 μg/kg/min they observed increases in renal blood flow, which peaked at about 0.3 μg/kg/min.

Fenoldopam has been shown to improve creatinine clearance, improve renal blood flow, and reverse the effects of cyclosporine A toxicity.

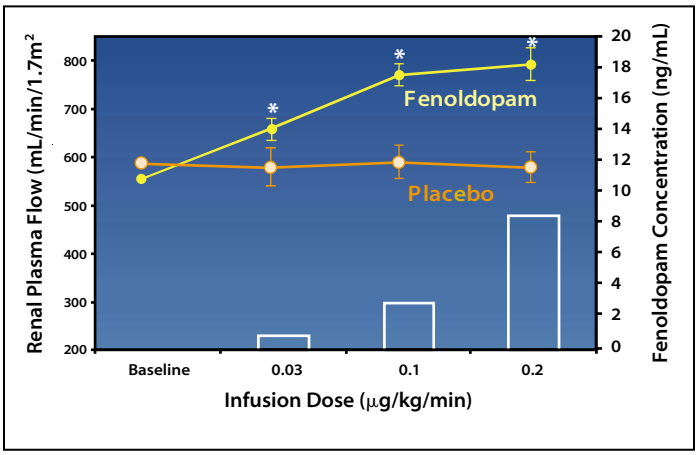


Figure 2. *Comparative dose response of renal blood flow in normotensives. Adapted from Mathur et al.*[21]

Study of Fenoldopam in Vascular Surgery

Study Methods

A total of 58 patients who were undergoing elective repair of a thoracoabdominal aortic aneurysm (TAAA) utilizing single-lung anesthesia, cerebrospinal fluid (CSF) drainage, and distal aortic perfusion were studied. This study was approved by the Institutional Review Board with informed consent obtained. Patients were excluded from the study if the procedure was not elective, if the patients had been on dialysis preoperatively, or if there were any contraindications to receiving fenoldopam. Preoperatively, all patients had a 20-gauge, right radial arterial catheter and a well-functioning peripheral intravenous line inserted. Induction was standardized for all patients and consisted of a narcotic/benzodiazepine/hypnotic/relaxant technique. The agents used were fentanyl 20–25 μg/kg, midazolam 0.05 mg/kg, pancuronium 0.1 mg/kg, and a small, hypnotic dose of propofol (40–70 mg). After induction, central lines were placed. Central access consisted of a Cordis 9 French introducer (Arrow International, Reading, PA) and an Arrow 12 French triple-lumen catheter, both of which were inserted into the right internal jugular vein. An Abbott (Abbott Labs, Abbott Park, IL) oximetric pulmonary artery catheter was then inserted through the Cordis introducer. The patients were placed in the lateral position, with the left side up. A lumbar CSF catheter was then placed at level L2–4.

The study group of 28 patients received a fenoldopam infusion of 0.05 μg/kg/min, which was continued for 24 hours after the induction of anesthesia. The control group of 30 patients did not receive a fenoldopam infusion. The dose of fenoldopam was chosen because renal blood flow was augmented without impact on blood pressure.[21] At higher doses (0.1–0.5 μg/kg/min), fenoldopam produces systemic vasodilatation, corresponding decrease in blood pressure, and mild reflex tachycardia.

Surgical access was accomplished via a left thoracoabdominal incision. Upon dissection and exposure of the aneurysm and administration of heparin, an atrial-femoral bypass was established via the left upper pulmonary vein and left femoral artery. A BioMedicus centrifugal pump was used to control the distal aortic perfusion flow rate.

While patients were on single-lung ventilation, they were placed on 100% oxygen. Before the application of the aortic cross clamp, the mean arterial blood pressure was maintained between 75–95 mm Hg and the mean central venous pressure was kept between 8–13 mm Hg. Upon application of the aortic cross clamp, the BioMedicus flow rate was adjusted to maintain a mean arterial blood pressure of 65–80 mm Hg. Flow rates were maintained at 1.5–2.5 L/min by the administration of vasodilators or inotropes, as required.

After replacing the aneurysm with a graft and unclamping the clamp to reestablish pulsatile flow to the kidneys, indigo carmine was administered parenterally to indicate the return of renal blood flow. The time from injection of the dye until the appearance of blue dye in the urine was measured. On completion of the procedure, patients were transferred directly to the cardiovascular intensive care unit.

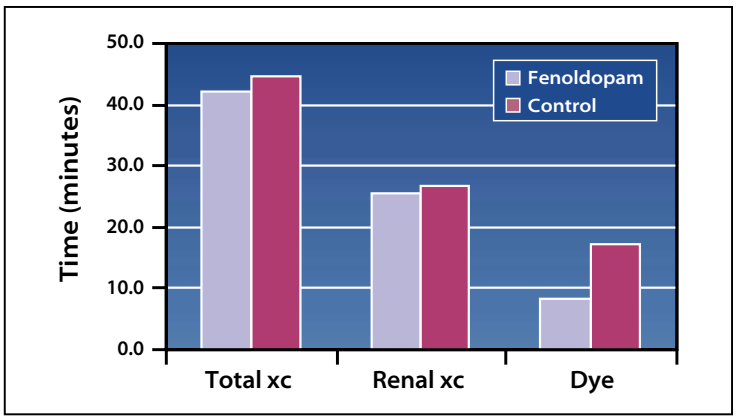


Figure 3. *Effect of fenoldopam on cross clamp and renal dye transit times. xc, excretory cystogram.*

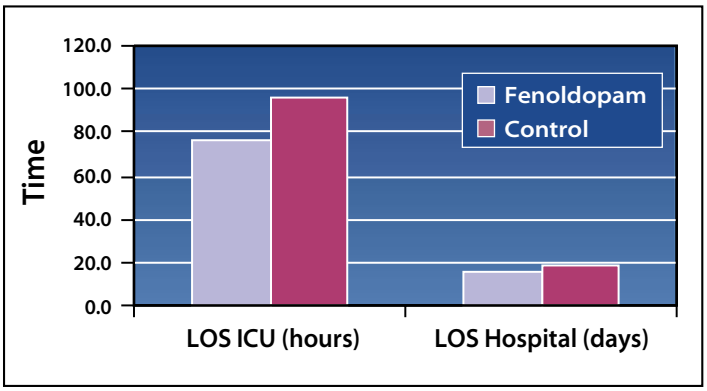


Figure 4. *Effect of fenoldopam on in-hospital recovery time. LOS, length of stay.*

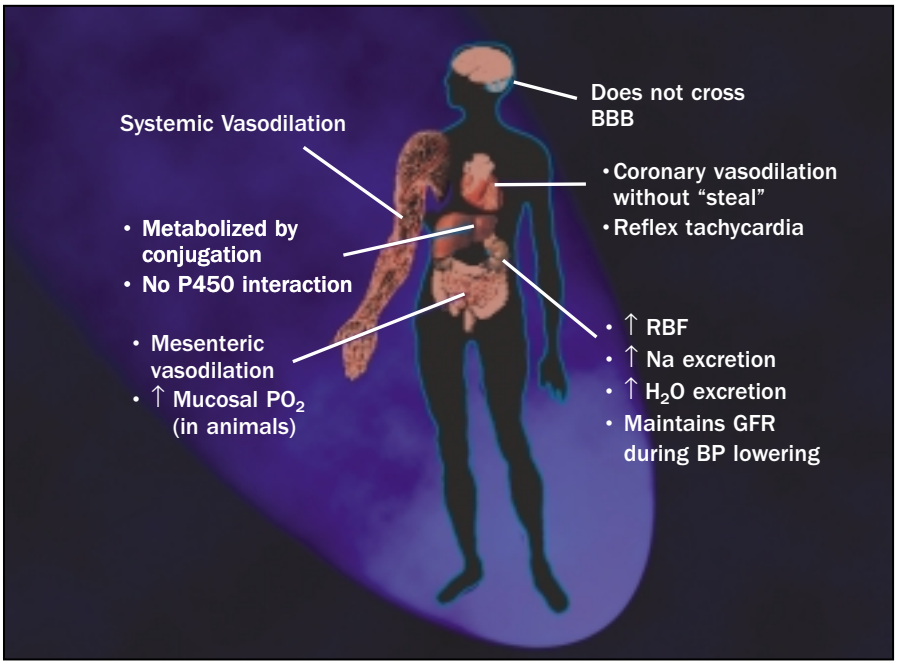
Categorical variables were tested using chi-square. Continuous variables were tested with paired or unpaired *t* tests or with comparable nonparametric tests, if distributions were not normal.

Study Results

We analyzed the fenoldopam and control groups for renal risk factors, mortality, postclamp return of renal blood flow, dialysis requirements, and length of stay in the ICU and overall in the hospital. We assessed the return of postclamp renal blood flow by injecting indigo carmine dye after unclamping the visceral cross clamp and measuring the time required for the blue dye to appear in the urine. Following are the results:

1. The groups were compared for the preoperative risk factors known to predict the occurrence of perioperative acute renal failure: ie, age > 70 years, preoperative serum creatinine ≥ 1.2 mg/dL, radiocontrast administration within 5 days of surgery, peripheral vascular disease, congestive heart failure, complexity of surgery, and reoperation. The fenoldopam group had higher baseline risks than the control group had. The mean age in the fenoldopam group was 69.8 years versus 64.1 years in the control group (P = .05). The fenoldopam group also had a mean of 2.28 renal risk factors compared with 1.80 in the control group (P = .05). Gender distribution and preoperative creatinine were similar in both groups.
2. The fenoldopam group had improved (shorter) clearance time of the dye (a mean of 8.4 minutes versus 17.2 minutes; P = .005), indicating a more rapid return of renal blood flow. See Figure 3.
3. The fenoldopam group had a very strong trend towards a relative reduction in the mortality rate of 65% (2 [7%] of 28 patients in the fenoldopam group versus 6 [20%] of 30 patients in the control group; P = .1).
4. The fenoldopam group had a strong trend in the relative reduction in dialysis requirements of 21% (3 [11%] of 28 patients in the fenoldopam group versus 4 [13%] of 30 patients in the control group; P = .1).
5. The fenoldopam group had shorter ICU stays than the control group (a mean of 76.0 hours versus 96.5 hours, respectively).
6. The fenoldopam group had shorter lengths of stay in the hospital than the control group (a mean of 15.7 days versus 18.8 days, respectively). See Figure 4.

Figure 5. *Secondary physiologic effects of fenoldopam. BBB, blood-brain barrier; BP, blood pressure; GFR, glomerular filtration rate; RBF, renal blood flow.*



Discussion

Our study shows that the use of

fenoldopam in TAAA is associated with reductions in mortality, dialysis requirements, and lengths of stay in the hospital and ICU. Because the fenoldopam group had more risk factors than the control group for ARF, including age, the actual differences in mortality, dialysis, and resource utilization between the two groups could be even larger than that noted in our study. The mechanisms behind the reduced mortality and resource utilization found in the fenoldopam group are likely mediated in part through fenoldopam's augmentation of renal perfusion, which we demonstrated intraoperatively using the transit time for dye. The improved renal perfusion may have prevented ARF, which is known to predict mortality. Even in our relatively small study, we noted strong trends in reducing the need for dialysis in patients receiving fenoldopam.

It is important to note, however, that one or more of fenoldopam's other nonrenal physiologic effects may have contributed to the observed reduction in mortality and resource utilization (Figure 5). Unlike dopamine, fenoldopam does not agonize β-adrenergic receptors; therefore, it is not likely to be arrhythmogenic like dopamine.[22] Furthermore, in animal models, fenoldopam increased gut mucosal oxygenation,[23] increased coronary blood flow, without causing "steal" from ischemic myocardium,[24] and reduced gastric ulceration directly. In human CABG trials, fenoldopam reduced afterload and pulmonary pressures and was not associated with intrapulmonary shunting.[25] In a previous study involving 234 patients undergoing TAAA repair, Safi and colleagues[10] reported the incidence of ARF as 18% (41 out of 234 patients). In this same cohort, the incidence of acute perioperative renal failure requiring dialysis was approximately 15% (36 out of 234 patients). Of the patients who developed ARF, 50% (20 out of 41 patients) died.

Because the fenoldopam group had more risk factors than the control group for ARF, including age, the actual differences in mortality, dialysis, and resource utilization between the two groups could be even larger than that noted in our study.

The infusion dose chosen in our study (0.05 μg/kg/min) was based on the dose-response characteristics of the drug and our personal observation that when fenoldopam is used at higher doses (> 0.1 μg/kg/min), blood-pressure effects are more common. At these higher doses, fenoldopam can produce vasodilatation and a dose-dependent reflex tachycardia.[20,21] In order to minimize the hemodynamic variables in these complex procedures, we chose a dose of the drug that would produce a desired renal benefit with minimal hemodynamic effects.

Conclusions

Surgical repair of TAAA is a complex, high-risk, but necessary, endeavor. One of the poorest prognostic indicators is the development of perioperative renal insufficiency.[10] The results of the study reported here support the use of the DA_1 agonist fenoldopam for renal protection in patients undergoing TAAA repair. Of particular significance are the

Main Points

- Despite advances in cardiac hemodynamic monitoring, intensive care management, and dialysis techniques, perioperative acute renal failure (ARF) is associated with mortality rates ranging from 60% to 90%.
- The major causes of ARF are usually divided into three broad categories: prerenal factors that decrease renal blood flow; intrarenal factors that have a direct effect on tubules, interstitium, or glomeruli; and postrenal factors that obstruct urine outflow.
- Current strategies in perioperative renal protection include maintaining adequate renal O_2 delivery; suppressing renovascular vasoconstriction; renovascular vasodilatation; maintaining tubular flow; decreasing renal cellular O_2 consumption; and attenuating reperfusion injury.
- A study of the effects of an infusion of the selective DA_1 receptor agonist fenoldopam on patients undergoing elective repair of a thoracoabdominal aortic aneurysm found that the use of fenoldopam was associated with reductions in mortality, dialysis requirements, and lengths of stay in the hospital and intensive care unit.
- The study authors suggest that the improved patient outcomes and hospital-utilization data resulting from the use of fenoldopam were directly related to the maintenance of renal function and a reduction of postoperative renal complications.

improved patient outcomes and hospital-utilization data. We believe that these benefits are directly related to the maintenance of renal function and a reduction of postoperative renal complications. It remains to be determined if using a higher dose of fenoldopam for a longer duration of infusion would translate into greater benefits. The ability to generalize these study results in patients undergoing other surgical and percutaneous vascular interventions could have profound effects on reducing both risk and costs. ■

References

1. Sladen RN, Prough DS. Perioperative renal protection. *Probl Anesth*. 1997;9:314–331.
2. Levy EM, Viscoli CM, Horowitz RI. The effect of acute renal failure on mortality: a cohort analysis. *JAMA*. 1996;275:1489–1494.
3. Mangano CM, Diamondstone LS, Ramsay JG, et al. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischemia Research Group. *Ann Intern Med*. 1998;128:194–203.
4. Aronson S, Blumenthal R. Perioperative renal dysfunction and cardiovascular anesthesia: concerns and controversies. *J Cardiothorac Vasc Anesth*. 1998;12:567–586.
5. Godet G, Fleron MH, Vicaut E, et al. Risk factors for acute postoperative renal failure in thoracic or thoracoabdominal aortic surgery: a prospective study. *Anesth Analg*. 1997;85:1227–1232.
6. Wilkes BM, Mailloux LU. Acute renal failure: pathogenesis and prevention. *Am J Med*. 1986;80:1129–1136.
7. Biebuyck JF, Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1060.
8. Carriere S. Factors affecting renal cortical blood flow: a review. *Can J Physiol Pharmacol*. 1975;53:1–20.
9. Kien ND, Moore PG, Jaffe RS. Cardiovascular function during induced hypotension by fenoldopam or sodium nitorprusside in anesthetized dogs. *Anesth Analg*. 1992;74:72–78.
10. Safi HJ, Harlin SA, Miller CC, et al. Predictive factors for acute renal failure in thoracic and thoracoabdominal aortic aneurysm surgery. *J Vasc Surg*. 1996;24:338–345.
11. Novis BK, Roizen MF, Aronson S, Thisted RA. Association of preoperative risk factors with postoperative acute renal failure. *Anesth Analg*. 1994;78:143–149.
12. Lokhandwala MF, Amenta F. Anatomical distribution and function of dopamine receptors in the kidney. *FASEB J*. 1991;5:3023–3030.
13. Frishman WH, Hotchkiss H. Selective and nonselective dopamine receptor agonists: an innovative approach to cardiovascular disease treatment. *Am Heart J*. 1996;132:861–870.
14. Perdue PW, Balser JR, Lipsett PA, Breslow MJ. "Renal dose" dopamine in surgical patients: dogma or science? *Ann Surg*. 1998;227:470–473.
15. Singer I, Epstein M. Potential of dopamine A-1 agonists in the management of acute renal failure. *Am J Kidney Dis*. 1998;31:743–755.
16. McCrory C, Cunningham AJ. Low-dose dopamine: will there ever be a scientific rationale? [editorial]. *Br J Anaesth*. 1997;78:350–351.
17. Garwood S, Hines R, Harris S. Does dopamine exacerbate renal ischemia? *Anesth Analg*. 1999;88:SCA9.
8. Brooks DP, Drutz DJ, Ruffolo RR Jr. Prevention and complete reversal of cyclosporine A-induced renal vasoconstriction and nephrotoxicity in the rat by fenoldopam. *J Pharmacol Exp Ther*. 1990;254:375–379.
19. Jorkasky DK, Audet P, Shusterman N, et al. Fenoldopam reverses cyclosporine-induced renal vasoconstriction in kidney transplant recipients. *Am J Kidney Dis*. 1992;19:567–572.
20. Garwood S, Hines R. Perioperative renal preservation: dopexamine and fenoldopam: new agents to augment renal performance. *Semin Anesth*. 1998;17:308–318.
21. Mathur VS, Carey RM, O'Connell DP. Renal and systemic hemodynamic effects of very low dose fenoldopam in normotensive subjects. *Anesth Analg*. 1999;88:SCA85.
22. Chiolero R, Borgeat A, Fisher A. Postoperative arrhythmias and risk factors after open heart surgery. *Thorac Cardiovasc Surg*. 1991;39:81–84.
23. Germann R, Hasibeder W, Haisjackl M, et al. Dopamine-1 receptor stimulation and mucosal tissue oxygenation in the porcine jejunum. *Crit Care Me*d. 1995;23:1560–1566.
24. Shi Y, Zalewski A, Bravette B. Selective dopamine-1 receptor agonist augments regional myocardial blood flow: comparison of fenoldopam and dopamine. *Am Heart J*. 1992;124:418–423.
25. Hill AJ, Feneck RO, Walesby RK. A comparison of fenoldopam and nitroprusside in the control of hypertension following coronary artery surgery. *J Cardiothorac Vasc Anesth*. 1993;7:279–284.