Prophylactic Dialysis in Patients With Renal Dysfunction Undergoing On-Pump Coronary Artery Bypass Surgery

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Background. Preoperative creatinine values higher than 2.5 mg/dL are associated with markedly increased risk for both mortality and morbidity in patients undergoing coronary artery bypass surgery. We aimed to determine the effects of prophylactic perioperative hemodialysis on operative outcome in patients with nondialysis-dependent moderate renal dysfunction.

Methods. Forty-four adult patients with creatinine levels greater than 2.5 mg/dL but not requiring dialysis underwent coronary artery bypass surgery with cardiopulmonary bypass. The patients were randomly divided into two groups. In group 1 (dialysis group, 21 patients), perioperative prophylactic hemodialysis was performed in all patients. Group 2 (23 patients) was taken as a control group and hemodialysis was performed only if postoperative acute renal failure was diagnosed.

Results. The hospital mortality was 4.8% (1 patient) in the dialysis group, and 30.4% (7 patients) in the control group ($p = 0.048$). Postoperative acute renal failure requiring hemodialysis was seen in 1 patient (4.8%) in the dialysis group and in 8 patients (34.8%) in the control group ($p = 0.023$). Thirty-three postoperative complications were observed in the control group for an early morbidity of 52.2% (12 patients) and 13 complications occurred in 8 patients in the dialysis group (38.1%). The average length of the intensive care unit and postoperative hospital stay were shorter in the dialysis group than in the control group ($p = 0.005$ and $p = 0.023$, respectively).

Conclusions. Preoperative creatinine levels higher than 2.5 mg/dL, increase the risk of mortality and the development of acute renal failure and prolong the length of hospital stay after on-pump coronary artery bypass surgery. Perioperative prophylactic hemodialysis decreases both operative mortality and morbidity in these high-risk patients.

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Patients with chronic renal failure often have multiple comorbid disorders such as hypertension, diabetes mellitus, and coronary artery disease. Coronary artery disease is a major cause of mortality and morbidity in patients with renal dysfunction [1]. The presence of impaired renal function results in several physiologic abnormalities that could contribute to adverse operative outcome [2, 3]. Many reports have described the results of coronary artery bypass surgery in patients with end-stage renal disease [4, 5]. However, there have been limited number of reports about the outcome of patients with mild to moderate renal failure not on dialysis [6–9]. These studies have demonstrated preoperative nondialysis-dependent renal insufficiency as a risk factor for the development of acute renal failure and mortality after cardiac surgery. In a previous study, we showed that mild elevation of creatinine (1.6 to 2.5 mg/dL) adds moderate risk, but preoperative values higher than 2.5 mg/dL are associated with markedly increased risk of postoperative dialysis, prolonged hospital stay and in-hospital mortality [7]. Several preventive measures like low-dose dopamine infusion, mannitol administration, maintenance of high perfusion pressure during cardiopulmonary bypass (CPB), attempts to deliver pulsatile perfusion, intraoperative ultrafiltration, and cautious monitoring of fluid-electrolyte balance during the perioperative period were recommended to prevent postoperative acute renal failure [6, 7, 10].

We proposed that earlier intervention such as prophylactic preoperative hemodialysis may reduce mortality and morbidity after cardiac surgery in this group of patients. To address this issue we have started using prophylactic perioperative hemodialysis in patients with nondialysis-dependent moderate (serum creatinine ≥ 2.5 mg/dL) renal dysfunction undergoing coronary artery bypass surgery using CPB. The aim of this study was to investigate the impact of prophylactic perioperative hemodialysis on the operative outcome in these patients.

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Table 1. Patient Demographics and Preoperative Variables

	Dialysis Group n (%)	Control Group n (%)
Number of patients	21	23
Sex		
Male	16 (76.2)	19 (82.6)
Female	5 (23.8)	4 (17.4)
Age (year)	58.10 ± 11.84[a]	54.30 ± 11.06
BSA (m^2)	1.75 ± 0.16	1.78 ± 0.17
LVEF (%)	44.10 ± 9.34	46.95 ± 8.08
Creatinine level (mg/dL)	3.46 ± 0.80	3.25 ± 0.79
BUN level (mg/dL)	62.62 ± 20.75	51.61 ± 12.51
Potassium level (mEq/L)	4.89 ± 0.64	4.72 ± 0.56

[a] Data are means ± SD.

Fisher's exact test or independent-samples Student *t* test, as appropriate: no significant differences between groups.

BSA = body surface area; BUN = blood urea nitrogen; LVEF = left ventricular ejection fraction.

Table 2. Associated Coexisting Disorders and Coronary Risk Factors

	Dialysis Group n (%)	Control Group n (%)
Hypertension	16 (76.2)	15 (65.2)
Smoking	13 (61.9)	15 (65.2)
DM	14 (66.7)	13 (56.5)
Hyperlipidemia	11 (52.4)	12 (52.2)
Prior MI	14 (66.7)	13 (56.5)
History of CHF	5 (23.8)	6 (26.1)
COPD	1 (4.8)	2 (8.7)
CVD	2 (9.5)	1 (4.3)
Prior nephrectomy	3 (14.3)	1 (4.3)
Prior renal Tx	1 (4.8)	0 (0)

Fisher's exact test or χ^2 test, as appropriate: no significant differences between groups.

CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CVD = cerebrovascular disease; DM = diabetes mellitus; MI = myocardial infarction; Tx = transplantation.

Patients and Methods

Between September 1999 and August 2001 a total of 44 patients with preoperative creatinine levels greater than 2.5 mg/dL but not requiring dialysis underwent primary elective coronary artery bypass grafting (CABG) by using CPB in our clinic. Thirty-five patients were male and 9 were female with a mean age of 56.11 ± 11.47 years (range 30 to 72). The patients were prospectively allocated into two groups. Randomization was carried out according to the last digits of the medical record number of the patients.

Group 1 was the dialysis group (21 patients) and preoperative prophylactic hemodialysis was performed in all patients. Group 2 (23 patients) was taken as a control group and hemodialysis was performed only if postoperative acute renal failure was seen. Our Institutional Review Board approved the study and written informed consent was obtained from all patients after explanation of the potential risks and benefits of the study.

Patients demographics and preoperative variables are listed in Table 1. The most common coronary risk factors were systemic hypertension (31 patients, 70.5%), cigarette smoking (28 patients, 63.6%), diabetes mellitus (27 patients, 61.4%), and hyperlipidemia (23 patients, 52.3%). Coexisting disorders and coronary risk factors are showed in Table 2.

Preoperatively the hemodialysis catheter was placed through the right internal jugular vein through percutaneous cannulation in all dialysis group patients. These patients were scheduled to receive hemodialysis twice within 72 hours before the operation. Conventional hemodialysis was performed using a volume-controlled dialysis machine (AK 200 S; Gambro, Lund, Sweden), bicarbonate dialysate, and a polyamine S membrane hollow-fiber low-flux dialyzer (Polyflux L; Gambro, Lund, Sweden). The bicarbonate dialysate contained 137 mEq/L sodium, 2.0 mEq/L potassium, 3.0 mEq/L calcium, and 33 mEq/L bicarbonate. Dialysate temperature was set at 36°C. Dialysate flow rates were set at 500 mL/min whereas blood flow rates were 250 to 350 mL/min. The duration of hemodialysis sessions was 4 to 5 hours.

In the dialysis group postoperative prophylactic hemodialysis was performed based on the observation of the serum creatinine level within 48 hours after the operation. If the serum creatinine level was higher than the preoperative value by 10% or more the hemodialysis was performed. In the control group, postoperative dialysis was instituted whenever 50% increase in serum creatinine from base line was observed or patient exhibited inadequate urine output less than 400 mL for 24 hours despite correction of hemodynamic status and diuretic therapy especially if fluid overload, hyperkalemia, or metabolic acidosis was also present.

All operations were performed through a median sternotomy incision. Cardiopulmonary bypass was established through standard aortocaval cannulation using a roller pump and hollow-fiber membrane oxygenator at moderate hypothermia (28°C to 30°C), with pump flow rates of 2.0 to 2.5 $L \cdot min^{-1} \cdot m^{-2}$ to maintain perfusion pressure about 65 mm Hg. During bypass the hematocrit was maintained between 20% and 25%. After aortic cross clamping, all patients received intermittent cold blood cardioplegia. Cardioplegia was delivered either in an antegrade fashion through the aortic root or coronary ostium or in a retrograde fashion through the coronary sinus. Topical hypothermia with cold saline solution was used in all operations. Distal anastomoses were performed during a period of aortic cross clamping and proximal anastomoses were performed with partial aortic clamping during rewarming. To improve renal perfusion dopamine infusion (3 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was started before bypass. All patients in both group underwent isolated primary elective CABG. Radial artery was not harvested with the assumption that it may be used for creation of arteriovenous fistula for hemodialysis in the future.

In this study serum creatinine was chosen for detection

Table 3. Operative Variables

	Dialysis Group	Control Group
Operation time (min)	150.42 ± 31.56[a]	148.21 ± 26.41
CPB (min)	66.33 ± 24.23	73.51 ± 27.85
Cross-clamp time (min)	44.14 ± 19.66	50.56 ± 19.51
Graft number	3.14 ± 0.35	3.08 ± 0.84
Mediastinal drainage (mL)	587.76 ± 148.71	725.65 ± 381.33
Blood-blood product (unit)	2.19 ± 1.24	2.56 ± 1.70

[a] Data are means ± SD.

Independent-samples Student *t* test: no significant differences between groups.

CPB = cardiopulmonary bypass.

of renal dysfunction. Frequent measurements of serum creatinine level were done in the early postoperative period to monitor progress in acute renal failure. The highest preoperative serum creatinine level within 1 week before operation was taken as the preoperative creatinine level. The postoperative creatinine level was taken as the highest value in the first month after the operation. Postoperative renal failure was defined as urine output of less than 400 mL in a 24-hour period, a 50% increase in serum creatinine from base line, or need for dialysis. Operative mortality was defined as any death that occurred within 30 days of the operation or during the same hospitalization. Any deaths occurred after the patient was discharged from the hospital but within 30 days of the procedure were included in the description of operative mortality unless the cause is clearly unrelated to the operation.

Statistical Analysis

All statistical analys3s were performed with SPSS for Windows statistical package release 7.5 (SPSS, Chicago, IL). Descriptive statistics were expressed as mean values ± standard deviation or as percentages. Once the homogeneity was confirmed with the Levene test, an independent-samples *t* test was used to compare the noncategoric or continuous variables. Comparison between groups for categorical variables was made by χ-^{2} test and Fisher's exact test was used if the sample size was smaller. A paired-samples *t* test was used to compare blood creatinine, blood urea nitrogen (BUN) and potassium levels before and after the operation within each group and before and after preoperative prophylactic hemodialysis within the dialysis group. Statistical significance was assumed if the *p* value was less than 0.05.

Results

Preoperative patient demographics and preoperative variables except BUN level did not show any statistical significance between the dialysis and control groups (Table 1). The mean preoperative creatinine level of both groups were similar and higher than 3.0 mg/dL. The mean preoperative BUN level in the dialysis group was significantly higher than in the control group (62.62 ± 20.75 mg/dL versus 51.61 ± 12.51 mg/dL, $p = 0.043$). In the dialysis group after the two sets of preoperative prophylactic hemodialysis serum creatinine, BUN and potassium levels were decreased significantly (3.46 ± 0.80 mg/dL versus 2.39 ± 0.50 mg/dL for creatinine, $p = 0.0001$; 62.62 ± 20.74 mg/dL versus 36.24 ± 13.24 mg/dL for BUN, $p = 0.0001$; and 4.89 ± 0.64 mEq/L versus 3.97 ± 0.58 mEq/L for potassium, $p = 0.0001$).

Prevalence of comorbidities and coronary risk factors such as hypertension, diabetes mellitus, and hyperlipidemia in both groups of patients were similar (Table 2). There were no significant differences in operative variables between the groups (Table 3). Eight patients died in the hospital for an overall 30-day mortality of 18.2%. The in-hospital mortality rates for patients in the dialysis group and control group were 1(4.8%) and 7(30.4%), respectively ($p = 0.048$). The causes and the timing of postoperative deaths are presented in Table 4. Forty-six postoperative complications observed in 20 patients for an early morbidity of 45.4%. Thirty-three postoperative complications were seen in the control group for an early morbidity of 52.2% (12 patients) whereas 13 complications were seen in 8 patients in the dialysis group (38.1%; Table 5). There was no complication directly related to the prophylactic hemodialysis in the dialysis group.

An analysis of the mean blood creatinine, BUN, and potassium values in the dialysis group patients on admission and postoperative period showed a significant

Table 4. Causes and Timing of Postoperative Deaths

Patient Age/Sex	Group	ARF	LCO	Pulm	MOF	Stroke	TND	RD	POD	DD
57/male	Dialysis	−	+	−	−	−	−	+	+	6
44/male	Control	+	+	+	+	−	−	−	+	7
72/male	Control	+	−	+	−	−	+	−	+	9
60/female	Control	+	+	+	+	−	−	−	+	12
46/male	Control	+	−	+	−	−	−	−	+	13
65/male	Control	−	+	−	−	−	−	+	−	6
62/male	Control	−	+	−	−	+	−	−	−	9
64/female	Control	+	−	+	−	−	+	−	+	10

+ = present; − = absent; ARF = acute renal failure; DD = postoperative day of the death; LCO = low cardiac output; MOF = multiple organ failure; POD = postoperative dialysis; Pulm = pulmonary complication; RD = rhythym disturbances; TND = transient neurological deficit.

Table 5. Postoperative Complications and Results

	Dialysis Group n (%)	Control Group n (%)	p Value[a]
Acute renal failure	1 (4.8)	8 (34.8)	0.023[a]
Low cardiac output	2 (9.5)	5 (21.7)	0.416
Pulmonary complications	1 (4.8)	5 (21.7)	0.188
Wound infection	1 (4.8)	3 (13.0)	0.609
Sepsis and MOF	0 (0)	2 (8.7)	0.489
Gastrointestinal bleeding	1 (4.8)	0 (0)	0.477
Stroke	0 (0)	1 (4.3)	1.0
Transient neurologic deficit	1 (4.8)	4 (17.4)	0.348
Rhythm disturbances	6 (28.6)	3 (13.0)	0.272
Reexploration for bleeding	0 (0)	2 (8.7)	0.489
Cardiac index (L/min/m^2)	2.73 ± 0.38	2.60 ± 0.41	0.285
Creatinine level (mg/dL)	3.07 ± 0.99	4.27 ± 1.06	0.0001[a]
BUN level (mg/dL)	53.71 ± 19.54	65.04 ± 18.80	0.057
Potassium level (mEq/L)	4.31 ± 0.56	5.09 ± 0.69	0.0001[a]
Intensive care unit stay (hours)	39.47 ± 21.87	85.34 ± 68.89	0.005[a]
In-hospital stay (days)	8.90 ± 2.62	11.69 ± 4.78	0.023[a]
In-hospital mortality	1 (4.8)	7 (30.4)	0.048[a]

[a] Fisher's exact test or independent-sample Student t test, as appropriate: significant differences for $p < 0.05$.

Data are means ± SD.

BUN = blood urea nitrogen; MOF = multiple organ failure.

decrease (3.46 ± 0.80 mg/dL versus 3.07 ± 0.99 mg/dL for creatinine, $p = 0.045$; 62.62 ± 20.75 mg/dL versus 53.71 ± 19.54 mg/dL for BUN, $p = 0.022$; and 4.89 ± 0.64 mg/dL versus 4.31 ± 0.56 mg/dL for potassium, $p = 0.01$). Based on observation within 48 hours after the operation postoperative prophylactic hemodialysis was performed in 7 dialysis group patients whose serum creatinine level increased by 10% or more of the preoperative value. Postoperative acute renal failure developed in only 1 of these patients and this patient was discharged with no need for long-term dialysis therapy. In the control group postoperative creatinine and BUN values were found significantly higher than the preoperative values (3.25 ± 0.79 mg/dL versus 4.27 ± 1.06 mg/dL for creatinine, $p = 0.0001$; 51.61 ± 12.51 mg/dL versus 65.04 ± 18.80 mg/dL for BUN, $p = 0.0001$; and 4.72 ± 0.56 mg/dL versus 5.09 ± 0.69 mg/dL for potassium, $p = 0.0075$). An increase in the serum creatinine level after the operation by 20% or greater than the preoperative value was taken as a significant elevation and occurred in 14 patients (60.1%) in the control group. Eight patients in the control group required postoperative dialysis because of persistent oligoanuria, rise in serum creatinine and BUN levels, hyperkalemia, acidosis, and positive fluid balance. Five of them died during the early postoperative period. The development of acute renal failure requiring dialysis between the groups was significantly different ($p = 0.023$).

There was no significant difference in the average length of preoperative hospital stay between the groups (9.28 ± 4.14 days versus 8.47 ± 1.80 days, $p = 0.418$). However, the average lengths of stay in the cardiac intensive care unit (ICU) for patients in the dialysis and control groups were 39.47 ± 21.87 hours and 85.34 ± 68.89 hours, respectively ($p = 0.005$). Accordingly, there was significant difference in the average length of postoperative in-hospital stay between the groups (8.90 ± 2.62 days in the dialysis group versus 11.69 ± 4.78 days in the control group, $p = 0.023$).

Comment

Cardiac and renal function are intimately related, with each having significant influences on the other. The risk of cardiovascular disease such as left ventricular hypertrophy, congestive heart failure, ischemic heart disease, and peripheral vascular disease in patients with dialysis- or nondialysis-dependent renal failure appears to be far greater than in the general population. Both coronary risk factors such as hypertension, smoking, diabetes and hyperlipidemia and uremia-specific risk factors such as decline in kidney function, anemia, and hyperparathyroidism contribute to the prevalence of these disorders in patients with renal failure [1, 11, 12]. The kidneys play a major role in the maintenance of extracellular fluid volume and peripheral vascular resistance. Owing to poor water clearance and excessive interstitial fluid, a history of congestive heart failure is frequently observed in patients with impaired renal function. Not as unexpectedly, a high number of risk factors mentioned above was noted in our study population and hypertension was seen most commonly.

Although it is influenced by body surface area and body water mass, serum creatinine is still the most readily available biochemical marker of renal function. Mild elevations of serum creatinine may reflect a significant impairment of renal function. We used serum creatinine levels as an indicator of renal function.

As a result of advances in medical treatment, aggressive thrombolytic therapy, and angiographic interventions a large number of high-risk patients with chronic renal failure are being referred for cardiac operation. Development of myocardial protection techniques and improvements in perioperative management have reduced the risk of CABG despite an increasing proportion of these high-risk patients. Regardless of the improvements in perioperative management the reported mortality for end-stage renal failure patients is clearly high, ranging from 8% to 31% [4, 5, 13, 14]. In these reports morbidity ranged from 29% to 66%. A limited number of studies that involved patients with nondialysis-dependent renal dysfunction have shown that the mortality ranged from 5% to 19% and the morbidity ranged from 29% to 80% [6–9, 15]. According to the database of the Society of Thoracic Surgeons, operative mortality of isolated CABG is about 3.0% [16]. These comparisons apparently demonstrated the risk of coronary artery bypass surgery in patients with renal dysfunction. The risks of mortality and morbidity were considerably higher in patients with preoperative creatinine levels greater than 2.5 mg/dL [15]. In a previous study we found that the mortality of these high-risk population was as high as 33% [7]. We and others also demonstrated that in patients with creatinine levels greater than 2.5 mg/dL mortality and morbidity were markedly increased especially when postoperative renal failure was severe enough to require dialysis [7, 17]. Postoperative renal failure is a complicated situation that has many consequences on the other organ systems, such as bleeding diathesis and susceptibility to infection. The development of acute postoperative renal failure after cardiac operations is the result of hemodynamic factors or toxic insults to the kidneys or both. There are many interactions between renal function and fluid balance during CPB. Moderate transient impairment of renal function occurs after nearly 30% of open heart operations [18]. Adverse systemic effects of renal dysfunction were augmented by the use of CPB, which is known to cause fluid shifts, electrolyte imbalances, and whole body inflammation. The negative effects of CPB on renal function may be due to several factors such as nonpulsatile flow, inadequate renal perfusion, or nephrotoxic products. The preoperative blood volume and body fluid compositions may have significant effects on the fluid balance during CPB. Fluid tends to accumulate in the extracellular, interstitial space during bypass. The amount of fluid accumulation during CPB may be a major determinant of the postoperative need for diuretic, osmotic, and oncotic agents. The elimination of excessive interstitial fluid postoperatively greatly depends upon renal function and intact renal function is essential to elimination of the retained fluid. Patients with creatinine levels more than 2.5 mg/dL seem more susceptible to the adverse effects of CPB because they are likely to have a higher proportion of functionally borderline glomeruli, which potentially are more susceptible to deterioration of their function when exposed to the insults of an operation. Since renal dysfunction often adversely affects the postoperative recovery after CPB, the question arises: how should these patients be managed in the most appropriate way?

Cardiopulmonary bypass does not seem to exert lasting deleterious effects on renal function. The reduction of renal functions mostly is a temporary and reversible event. Thus intensive renal preservation during perioperative period seems to provide sufficient renal protection. To alleviate the effects of CPB on renal functions, low-dose dopamine, furosemide, and mannitol were recommended during or after the cardiac operations [10, 19]. These agents have synergistic effects and they protect renal function by increasing renal blood flow, increasing glomerular filtration, and reducing injury after ischemia [10]. Nevertheless high mortality and morbidity in this group of patients despite routine use of low-dose dopamine, early simultaneous infusion of mannitol-furosemide, and aggressive measurements to assure adequate hydration and urine output perioperatively obligated us to investigate specific prophylactic maneuvers that could potentially improve surgical outcome.

We hypothesized that with the appropriate use of prophylactic hemodialysis before and after the operation and close monitoring of the patient's hemodynamic and electrolyte status, improved surgical outcome could be achieved. This is the first clinical study in CABG patients showing a reduction in mortality and morbidity with the use of prophylactic perioperative hemodialysis.

Hemodialyis is designed to accomplish three objectives. It may remove solutes, alter the electrolyte concentration of the extracellular fluid, and remove different amounts of extracellular fluid. An invasive study in both dialysis and predialysis patients showed that left ventricular end-diastolic pressure was elevated at rest and during exercise with impaired left ventricular stroke work in response to exercise, indicating cardiac performance may be abnormal even relatively early in the development of renal failure [20]. Hemodialysis induces many beneficial changes in uremic patients, several of which could favorably affect contractility. Among the most likely causes for improved contractility with dialysis are the removal of uremic toxins and increases in the plasma ionized calcium and bicarbonate concentrations [21].

Management of fluid balance and electrolyte concentrations is essential during postoperative period. Assessment of tissue perfusion, measurements of daily weights, blood pressure, pulse rate, and central venous pressure are mandatory for correct management. Volume replacement must be according to the urine output. Fluid restriction more than necessary may cause acute renal failure. The conduct of dialysis in the early postoperative period may be complicated by abrupt changes in cardiopulmonary and hemodynamic function despite current improvements in dialysis techniques. Acute changes in blood volume, fluid, and electrolytes, and alterations in blood components and complement activation may adversely affect clinical outcome. Potassium imbalance must be avoided because elevated and reduced levels are associated with life-threatening arrhythmias, especially after ischemia. In our study rhythm disturbances were the most common causes of morbidity in the dialysis group. Abrupt changes in serum potassium level might be responsible for the high incidence of dysrhythmia.

In the control group the postoperative course was complicated in most cases. When postoperative acute renal failure requiring dialysis developed in these patients morbidity and mortality were markedly increased despite institution of dialysis and maximum ICU support. Owing to impaired water clearance, postoperative pulmonary congestion was often observed in control patients. The metabolism of anesthetic agents in these patients is delayed and the effect of anesthesia might be prolonged. These factors might result in a delay in extubation. All patients who required prolonged ventilatory support because of respiratory failure were in the control group.

All pulmonary complications and transient neurologic dysfunctions in the control group were seen in patients with acute renal failure requiring dialysis. Because major morbidity that requires ICU stay was higher in the control group, their average length of postoperative hospitalization was significantly longer than for the dialysis group patients.

Conclusions

Although the mechanism was not elucidated by this study, the finding that prophylactic perioperative hemodialysis has reduced postoperative mortality and morbidity suggests that one may identify high-risk renal patients and begin early intervention. Accelerated renal recovery can be achieved with the combination of perioperative prophylactic dialysis with the use of renal dose dopamine and mannitol-furosemide infusion in these challenging cases.

It remains to be determined whether routine application of prophylactic hemodialysis is a practical and cost-beneficial procedure in patients with nondialysis-dependent moderate renal dysfunction.

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