

Does Timing of Dialysis in Patients with ESRD and Acute Myocardial Infarcts Affect Morbidity or Mortality?

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Background and objectives: Patients with ESRD have an increased incidence of coronary events with a relatively higher risk for mortality after acute myocardial infarction (AMI). We evaluated whether it is safer to delay dialysis in AMI or if delay poses separate risks.

Design, setting, participants, & measurements: We conducted a retrospective review of 131 long-term hemodialysis patients who had AMI and were admitted between 1997 and 2005 at three New York City municipal hospitals. Patients were separated into three groups on the basis of time between cardiac symptoms and first dialysis (<24 h, 24 to 48 h, and >48 h).

Results: A total of 17 (13%) patients died, 10 (59%) of whom had either hypotension or an arrhythmia during their first cardiac care unit dialysis. Although these groups were comparable in acuity and cardiac status, there were no findings of increased morbidity (26, 36, and 20%, respectively) or mortality (11, 18, and 13%, respectively), despite differences in the timing of each group's dialysis. We found that previous cardiac disease, predialysis K⁺, ΔK⁺ after dialysis, and APACHE scores were significantly higher in patients with peridialysis morbidity.

Conclusions: We conclude that there is no increased morbidity with early dialysis in AMI, but rather close attention needs to be paid to the rate of decrease in serum potassium in patients with ESRD and their level of acuity when undergoing dialysis.

Clin J Am Soc Nephrol ●●: ●●●-●●●, 2009. doi: 10.2215/CJN.04470908

Patients with ESRD have an increased incidence of coronary events and a relatively higher risk for mortality after acute myocardial infarction (AMI) (1,2). In fact, cardiac disease is the major cause of death in American hemodialysis (HD) patients, accounting for 43% of all-cause mortality between 2001 and 2003 (3). As a result, this population has between a 10- and 20-fold increased incidence of cardiac-related death compared with the general population (4). This includes patients with sudden cardiac death, an event that has been postulated to be due to potassium (K⁺) changes related to the dialysis schedule (5), and remains the most common form of cardiovascular death in patients with ESRD (6,7). These observations illustrate that beyond issues of coronary ischemia, the dialysis patient may also be subjected to electrolyte abnormalities that indirectly add to the risk for cardiac-related death. Considering such risks, cardiologists and nephrologists have been plagued with the question of how safe the dialysis procedure is during an AMI. In the acutely damaged myocardium, electrolyte fluxes such as K⁺, as well as osmolar and volume fluxes, may potentiate arrhythmias and their consequent hemodynamic insults. Arrhythmic mechanisms account for 58 and

64% of the cardiac deaths in peritoneal dialysis and HD, respectively (6).

The issue of the optimal timing of HD after an acute cardiac event has still not been clearly answered. The customary practice has been to err on the side of delaying HD. We sought to determine the potential sequelae of early or late dialysis in the setting of an AMI and how this may affect overall morbidity and mortality.

Materials and Methods

We reviewed the charts of all patients who had ESRD, were on HD, had the diagnosis of AMI, and were admitted to the cardiac care unit (CCU) between 1997 and 2005 to the following New York City municipal hospitals: Elmhurst and Queens Hospital Centers-Mount Sinai School of Medicine (both in Queens, NY) and Jacobi Medical Center-Albert Einstein College of Medicine (Bronx, NY). These institutions care for a relatively underserved urban population. Diagnosis was made by the cardiology staff on the basis of creatine phosphokinase (CPK), troponin levels, and electrocardiogram (ECG) evaluations. All of the patients had diagnostic codes for AMI on discharge (2). Existing cardiac pathology was identified in the chart by the findings of previous AMI, positive stress test, cardiac catheterization, or echocardiogram identifying segmental hypokinesis. Patients who required dialysis for acute renal failure were excluded. All laboratory data reported in this study reflect values on admission ± SEM or just before the initiating dialysis event when noted ± SEM. APACHE II scores (8) were calculated using admission laboratory values.

Charts and dialysis flow sheets were reviewed, and data regarding admission laboratory examinations, the first dialysis event, interdialytic

Received September 4, 2008. Accepted May 25, 2009.

Published online ahead of print. Publication date available at www.cjasn.org.

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hypotension (BP <90 systolic or >30 mmHg decrease in systolic BP during dialysis), net ultrafiltration, peridialysis arrhythmias, and echocardiograms that occurred in the first 48 h were recorded. Peak troponin and CPK levels were recorded as highest overall and highest predialysis levels. ECGs were reviewed by the authors; where ST elevation myocardial infarction (STEMI) was noted, it pertains to the computer-generated assessment reviewed by the cardiology department.

Data are presented as a function of time, in hours, beginning at the onset of cardiac symptoms such as chest pain or emergency department admission and the first dialysis event in the CCU: <24 versus 24 to 48 versus >48 h. The data retrieved were also analyzed comparing patients who demonstrated peridialysis morbidity (hypotension and/or arrhythmias) and those who did not. Any of these events that occurred during the dialysis and/or up to 6 h later were considered dialysis-related morbidity. Postdialysis K⁺ concentrations were drawn <8 h after dialysis. Mortality reflects death during the AMI admission.

The evaluation of data among different groups was performed using χ^2 test for dichotomous data and either *t* test (for two groups) or one-way ANOVA (for more than two groups) for continuous data (9). Statistical analysis was performed using Sigma Stat 1.0 (Jandal Corp., Corte Madera, CA).

Results

A total of 131 patients were identified as having ESRD that required long-term HD at the time of their AMI. All of the patients were admitted through the emergency department and received intermittent HD as their renal replacement therapy. The average age was 59.5 yr, 59% had a history of diabetes, and 32% had previous cardiac disease. In total, 35 (27%) patients had a morbid event, either hypotension (29 [23%] patients) or arrhythmia (seven [6%] patients); one patient had both. Arrhythmias consisted of either brady- or tachycardias (both supraventricular and ventricular) but not simple ectopy. A total of 17 (13%) patients died, 10 (59%) of whom had some morbid event during their first CCU dialysis.

A total of 66 (51%) patients received dialysis within the first 24 h of their cardiac event; the remaining were split evenly between the other two periods (Table 1). The three divided groups were similar as to albumin levels and APACHE score but not as to age, congestion on chest x-ray, chest pain on presentation, history of diabetes, or previous cardiac disease (Table 1). The third dialysis group (>48 h) was significantly

older compared with the other two groups. All cardiac parameters (CPK, troponin levels, STEMI, and ejection fraction [EF] by echocardiogram) were similar among the groups (Table 2, Figure 1), except for the incidence of left ventricular hypertrophy (LVH). CPK is presented as both peak within the first 3 d and highest value before dialysis. The CPK and troponin values presented by either method pose difficulties in interpretation because both time and dialysis will affect peak levels.

There were no significant differences between the groups in net ultrafiltration volumes or the peridialysis laboratory examinations except for the admission serum K⁺. This was significantly elevated in the group undergoing dialysis in the first 24 h (Table 3). Despite differences in the timing of dialysis, there were no findings of increased morbidity (26, 36, and 20%, respectively; Figure 2) or mortality (11, 18, and 13%, respectively; Figure 2).

When evaluating our total patient population comparing those with morbidity in the peridialysis period with those without, there were no differences in age, the incidence of chest pain, diabetes, or congestive heart failure (Table 4); however, APACHE scores and history of previous AMI (Table 4) were significantly greater in the morbidity group, whereas the presence of STEMI approached significance (Table 5). Other cardiac parameters measured were not significantly different (Table 5, Figure 3).

Predialysis K⁺ and the Δ K⁺ (Table 6) were found to be significantly higher in the group with peridialysis morbidity. Again, net ultrafiltration was essentially equal; however, these differences did not seem to influence mortality. Admission serum albumin levels approached significance (Table 4).

Discussion

The safety of patients who undergo maintenance dialysis early in the course of an AMI has always raised concerns for complications such as arrhythmias and hypotension. This concern has led to delay of maintenance dialysis to a "later" and "safer" point in the course of the AMI. Ifudu *et al.* (10) reviewed 35 patients with ESRD and AMI and found a significant increase in intradialytic hypotension in such patients. They found the following risk factors for hemodynamic instability: Previous myocardial infarction, inferior myocardial wall involve-

Table 1. Admission findings^a

Parameter	Time: Symptoms to HD			P
	<24 h (n = 66)	24 to 48 h (n = 34)	>48 h (n = 31)	
Age (yr; mean \pm SEM)	58.0 \pm 1.9	56.0 \pm 2.5	65.4 \pm 2.4	0.035
Previous AMI/cardiac disease (%)	38	56	52	<0.005
Diabetes (%)	49	70	43	<0.05
Chest pain (%)	68	68	29	<0.001
CXR congestion (%)	67	32	61	<0.005
APACHE score (mean \pm SEM)	14.7 \pm 0.6	16.1 \pm 0.8	16.5 \pm 1.0	NS
Albumin (mg/dl; mean \pm SEM)	3.30 \pm 0.09	3.30 \pm 0.12	3.10 \pm 0.13	NS

^aAMI, acute myocardial infarction; CXR, chest x-ray.

Table 2. Admission: Cardiac status and parameters^a

Parameter	Time: Symptoms to HD			P
	<24 h (n = 66)	24 to 48 h (n = 34)	>48 h (n = 31)	
LVH (%)	95	82	70	<0.005
STEMI (%)	11	9	13	NS
Echo EF (%)	50.1 ± 1.7	54.4 ± 2.9	45.8 ± 3.2	NS
CPK peak (U/L; mean ± SEM)	267 ± 36	420 ± 111	610 ± 214	NS
CPK before HD (U/L; mean ± SEM)	226 ± 38	310 ± 104	435 ± 142	NS
Peak troponin (μg/L; mean ± SEM)	31.0 ± 15.0	11.0 ± 3.8	19.0 ± 9.6	NS

^aCPK, creatine phosphokinase; EF, ejection fraction; HD, hemodialysis; LVH, left ventricular fraction; STEMI, ST elevation myocardial infarction.

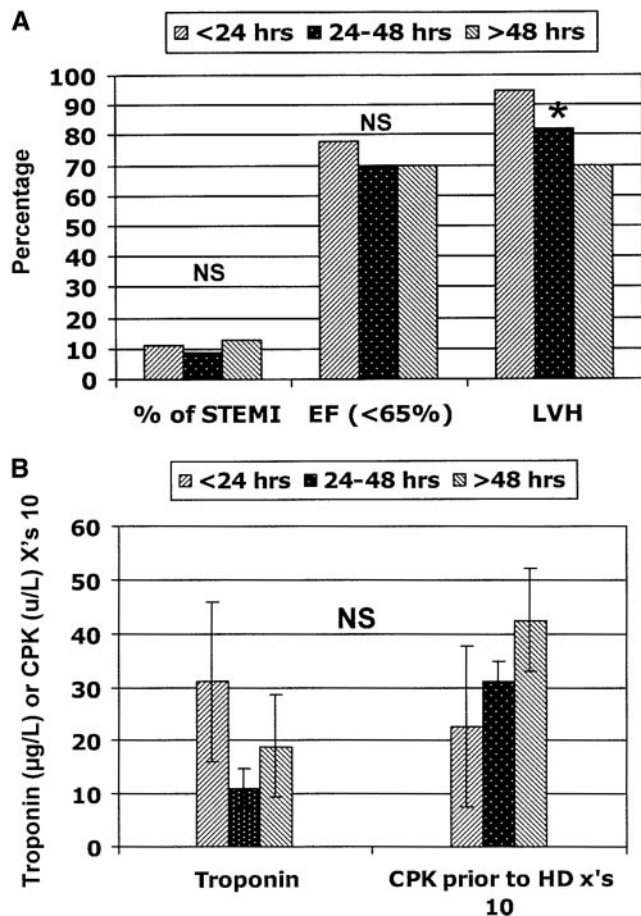


Figure 1. Cardiac injury. (A) There was no significant difference in the patient groups as to ST elevation myocardial infarction (STEMI) or percentage of ejection fraction (EF). Left ventricular hypertrophy (LVH) was significantly different among the groups. **P* < 0.005. (B) There was no significant difference in peak creatine phosphokinase (CPK; before hemodialysis [HD]) or troponin levels among the groups. NS, nonsignificant *P* value.

ment, advanced age (>68 yr), a low diastolic BP (<60 mmHg) at onset of HD, and a low predialysis serum albumin level (≤3.6 g/dl). This study did not assess the benefit of delaying

dialysis. Similar to Ifudu *et al.*, we identified previous AMI (*P* = 0.0085) and low albumin levels (approached significance, *P* = 0.063) as risks for complications during dialysis. Furthermore, patients with higher APACHE scores were more likely to have hemodynamic issues and arrhythmias (Table 4).

In assessing the safety of HD early in the course of an AMI, our study suggests that time does not seem to have any negative outcomes. Most (55%) of the patients actually received dialysis relatively early, within the first 24 h of their symptoms. Compared with the other two timed groups, all were similar as to APACHE scores as well as measured parameters that assess cardiac injury and function (EF, STEMI, CPK, and troponin levels). The similarity of these groups and the lack of significant differences in morbidity or mortality suggest that timing of dialysis *per se* does not play a role in outcomes; however, given differences as to clinical presentation and comorbid history, this cannot be stated with certainty.

Not being a randomized study, selection to time of dialysis may have had some clinical bias. For instance, the higher incidence of congestion and K⁺ levels in the 24-h dialysis group likely contributed to the decision for earlier dialysis in that group. Conversely, the older age seen in the >48 h group may suggest a bias to delay on the basis of age and presumed stability; however, the lack of APACHE score difference does not support the presence of physiologic or clinical instability. Unfortunately, data regarding the last dialysis before admission were not available; therefore, what role this played in the timing selection is not known. A recent dialysis session could have made the nephrologists' decision to postpone dialysis more comfortable.

Perhaps our most intriguing findings are the significant differences in the predialysis and the ΔK⁺ when comparing patients who had peridialysis morbidity with those who did not (Table 6). In the outpatient population, predialysis K⁺ levels, either too low or too high (<4 or >5.6), carry an increased risk for morbidity and/or mortality (11). Hyperkalemia in dialysis patients is a common problem seen in 5 to 10% of patients per month and accounting for a mortality rate of 3.1 per 1000 patient-years (12). It has been hypothesized that the increase in sudden death after the 3-d delay between outpatient dialysis events may have its source in high K⁺ levels accrued during

Table 3. Peridialysis data^a

Parameter	Time: Symptoms to HD			P
	<24 h (n = 66)	24 to 48 h (n = 34)	>48 h (n = 31)	
Creatinine (mg/dl; mean ± SEM)	7.10 ± 0.41	8.00 ± 0.51	6.90 ± 0.49	NS
Predialysis K ⁺ (mEq/dl; mean ± SEM)	5.28 ± 0.10	4.98 ± 0.16	4.78 ± 0.17	0.05
DK ⁺ (mean ± SEM)	1.07 ± 0.11	1.00 ± 0.15	1.12 ± 0.17	NS
UF volume (L; mean ± SEM)	2.34 ± 0.21	2.80 ± 0.36	2.40 ± 0.31	NS
Morbidity (%)	26	36	20	NS
Mortality (%)	11	18	13	NS
Morbidity and mortality combined (%)	34	42	30	NS

^aK⁺, potassium; UF, ultrafiltration.

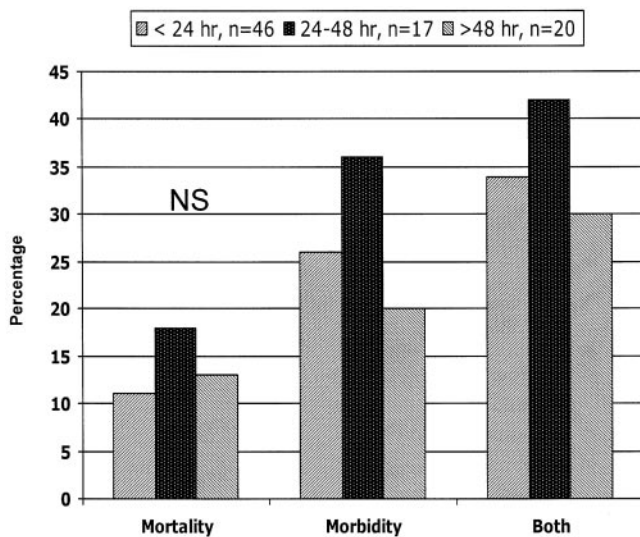


Figure 2. Percentage of morbidity and mortality. There was no significant difference comparing the individual complications as to time to first dialysis.

this period (13). Physiologically, this is not unexpected given the importance of K⁺ in maintaining the heart's resting membrane potential as well as its conductivity (12).

Although often cited as a likely contributing factor to cardiac arrhythmias in patients with ESRD, surprisingly little in the scientific literature has directly evaluated K⁺ and/or K⁺ shifts in the setting of AMI. This concern, however, has led to attempts to support intracellular myocardial K⁺ in patients who have had AMI and are not on dialysis, through the use of glucose-insulin-K⁺ infusions. These studies have had mixed clinical outcomes (14,15).

As suggested in our study, initiating dialysis early in AMI may have been pressured by concomitant hyperkalemia in the first group. Lowering the dialysate bath K⁺ concentration does result in its enhanced removal (16), and this prompts the use of such baths for patients with hyperkalemia. This of course would result in relatively large K⁺ swings, possibly risking arrhythmia. Indeed, as demonstrated by Morrison *et al.* (17), using 2-mEq/L K⁺ baths resulted in complex ventricular ar-

rhythmias that improved when the K⁺ baths were increased to 3.5 mEq/L. In a separate study of outpatient dialysis, the avoidance of high interdialytic K⁺ gradients also resulted in less arrhythmia as measured by ectopy (18). Perhaps more impressive was a review of 400 cardiac arrests that occurred in dialysis facilities (19) that demonstrated that 17.1% of patients who sustained cardiac arrest underwent dialysis with 0- or 1-mEq/L K⁺ baths as compared with 8.8% in those who did not have cardiac arrests ($P < 0.0001$).

These studies suggest that steep dialysate bath gradients may lead to cardiac events possibly through the effects on resting membrane potentials. In the setting of an injured, ischemic myocardium, this effect may be exaggerated. In fact, studies have shown that the prolonged QT intervals seen during dialysis were attributed to K⁺ removal (20,21). In our study, the final K⁺ levels and the net ultrafiltration were similar between groups, suggesting that the rate of decline in K⁺ concentration was the significant factor in morbidity, not the final level attained. Indeed, we identified an incidence of arrhythmias of 5% in the first 48 h of admission. This is higher than what is seen in patients without ESRD during AMI, although only 20% had diabetes in this study (22); therefore, the initiation of dialysis during the AMI period imparts both positive and negative effects to the pathophysiology of the patient. Obviously, the maintenance of electrolytes, acid-base status, and the treatment of uremia are necessities. Clearance of solute may need further attention in such stressed and likely catabolic situations. Further research may suggest that more dialysis is necessary during an AMI rather than less. For instance, it has been shown that oxidant stress, as measured by redox states, is improved after dialysis (23). If so, then heightened dialysis may play a role in limiting infarct size by limiting the formation of reactive oxygen species, further inflammation, and consequent injury.

This must be balanced with the increased risk for hemodynamic events and arrhythmias during AMI. This is especially so because intradialytic hypotension is the most common complication during dialysis and occurs in >25% of outpatient HD patients (24). In our study, we found that that 35 (27%) of the 128 patients had morbid events during and immediately after the first dialysis session of their AMI admission. A total of 23% were hypotensive episodes. Because we are looking at only one

Table 4. Admission data based on peridialysis morbidity^a

Parameter	No Morbidity (n = 95)	Morbidity (n = 36)	P
Age (yr; mean ± SEM)	58.9 ± 1.5	61.1 ± 2.6	NS
Diabetes (%)	51	60	NS
Previous MI/CAD (%)	37	67	<0.005
CHF (%)	57	60	NS
Chest pain (%)	52	66	NS
APACHE score (mean ± SEM)	14.700 ± 0.498	17.700 ± 0.810	0.002
Albumin (mg/dl; mean ± SEM)	3.33 ± 0.07	3.07 ± 0.13	0.063

^aCAD, coronary artery disease; CHF, congestive heart failure.

Table 5. Cardiac status separated by peridialysis morbidity

Parameter	No Morbidity (n = 95)	Morbidity (n = 36)	P
STEMI (%)	9	20	0.075
EF (%)	50.6 ± 1.6	48.7 ± 2.9	NS
LVH	82/93 (8%)	28/35 (0%)	NS
Peak troponin (μg/L; mean ± SEM)	29.1 ± 19.0	55.0 ± 26.0	NS
CPK peak (U/L; mean ± SEM)	401 ± 77	350 ± 99	NS
CPK before HD (U/L; mean ± SEM)	272 ± 54	366 ± 96	NS

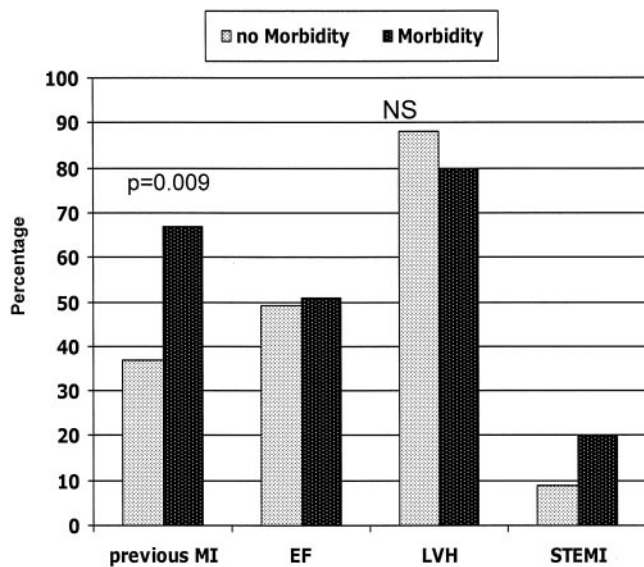


Figure 3. Cardiac status and peridialysis morbidity. Patients with peridialysis morbidity were more likely to have had a previous MI. The EF, the incidence of LVH, and type of AMI (STEMI versus non-STEMI) did not seem to play a role in peridialysis morbidity.

dialysis event in our patients, the 23% incidence that we report is high. Hemodynamic changes during dialysis have multiple causes inclusive of delayed plasma filling from the extravascular space, uremic dysautonomia, activation of cytokines, changes in blood osmolality, release of neurohumoral mediators, altered nitric oxide/endothelin balance, and even LVH

(24). LVH is common in patients with ESRD, as was evident in >80% of our patients. All of these hemodynamic risks may be heightened during the AMI event.

Although our study did not demonstrate that dialysis poses a huge risk during an AMI, it may lead to pathophysiologic detriments that are not initially apparent or readily measured. Given the precarious hemodynamics concerning coronary perfusion and the need to maintain coronary flow, swings in BP may cause continued ischemic damage. This may remain clinically unrecognizable but may increase infarct size and hinder cardiac rehabilitation, possibly limiting future EF. This may explain the 74% 2-yr mortality rate in dialysis patients after an AMI (1), as well as our observation that 59% of the patients with either hypotension or arrhythmia eventually died during the admission. On the whole, this is clearly not an ideal period to be affecting hemodynamics if it can be avoided.

Finally, the history of previous MI and/or coronary artery disease also seems to have an impact on outcomes, which is consistent with previously reported findings regarding sudden death in patients with ESRD (5). Diminished cardiac function and/or mass at the outset are logically expected to be a negative factor even without ESRD. The APACHE score difference illustrates that the patient's acute physiologic status understandably also plays a role in outcomes. Although not necessarily a good predictor of cardiac mortality, we presented this score to assess better the comparability of the groups at the time of their AMI.

Conclusions

Our study does not indicate that timing of dialysis poses a risk. What may be of greater importance is the K⁺ status and its

Table 6. Outcomes based on peridialysis morbidity

Parameter	No Morbidity (n = 93)	Morbidity (n = 35)	P
Creatinine (mg/dl; mean ± SEM)	7.170 ± 0.310	7.610 ± 0.474	NS
UF volume (L/dialysis; mean ± SEM)	2.52 ± 0.17	2.35 ± 0.35	NS
Pre-HD K ⁺ (mEq/L; mean ± SEM)	4.97 ± 0.10	5.39 ± 0.15	0.028
Post-HD K ⁺ (mEq/L; mean ± SEM)	4.10 ± 0.07	4.05 ± 0.11	NS
ΔK ⁺ (mean ± SEM)	0.956 ± 0.090	1.350 ± 0.150	0.021
Death (%)	11	20	NS

treatment and the severity of the patient's condition on admission, as identified by APACHE scores. Patients with a history of MI may also be at risk. Given that this is a retrospective as well as a small study, we cannot make any clear recommendations; however, our findings suggest that rather than delay dialysis, concern should be placed on the degree and rate that K⁺ levels change. Given these findings, it may be advisable to have such patients undergo dialysis with a gradual decline in K values, possibly through sustained low-efficiency daily dialysis or daily dialysis with higher K⁺ baths, but not delay dialysis. Rapid volume and/or electrolyte shifts may pose a theoretical if not clinical risk for sudden cardiac death. Procedures such as sustained low-efficiency daily dialysis may be the proper treatment in patients with ESRD and with AMI, through their slower and more physiologic approach to treatment of electrolyte and volume change. Alternatively, the use of a method that gradually increases the K gradient in intermittent dialysis may avoid complications (18,25). By decreasing episodes of hypotension and arrhythmia, careful dialysis may result in limiting infarct size and improve cardiac rehabilitation and mortality.

Acknowledgments

We thank Amalita LaMalva for clerical work and assistance.

Disclosures

None.

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