ORIGINAL INVESTIGATION

Management of Acute Kidney Injury in the Intensive Care Unit

A Cost-effectiveness Analysis of Daily vs Alternate-Day Hemodialysis

*Amar A. Desai, MD, MPH; Jacqueline Baras, BA; Benjamin B. Berk, MD, MS; Aya Nakajima, MBA;
Alan M. Garber, MD, PhD; Douglas Owens, MD, MS; Glenn M. Chertow, MD, MPH*

Background: Although evidence suggests that a higher hemodialysis dose and/or frequency may be associated with improved outcomes, the cost-effectiveness of a daily hemodialysis strategy for critically ill patients with acute kidney injury (AKI) is unknown.

Methods: We developed a Markov model of the cost, quality of life, survival, and incremental cost-effectiveness of daily hemodialysis, compared with alternate-day hemodialysis, for patients with AKI in the intensive care unit (ICU). We employed a societal perspective with a lifetime analytic time horizon. We modeled the efficacy of daily hemodialysis as a reduction in the relative risk of death on the basis of data reported in the 2004 clinical trial published by Schiffl et al. We performed 1- and 2-way sensitivity analyses across cost, efficacy, and utility input variables. The main outcome measure was cost per quality-adjusted life-year (QALY).

Results: In the base case for a 60-year-old man, daily hemodialysis was projected to add 2.14 QALYs and \$10 924 in cost. We found that the cost-effectiveness of daily hemodialysis compared with alternate-day hemodialysis was \$5084 per QALY gained. The incremental cost-effectiveness ratio became less favorable (>\$50 000 per QALY gained) when the maintenance hemodialysis rate of the daily hemodialysis group was varied to more than 27% and when the difference in 14-day postdischarge mortality between the alternatives was varied to less than 0.5%.

Conclusion: Daily hemodialysis is a cost-effective strategy compared with alternate-day hemodialysis for patients with severe AKI in the ICU.

Arch Intern Med. 2008;168(16):1761-1767

Author Affiliations: Division of Nephrology (Drs Desai and Chertow), Center for Health Policy and Primary Care and Outcomes Research (Drs Desai, Garber, and Owens), School of Medicine (Ms Baras and Dr Berk), and Graduate School of Business (Ms Nakajima), Stanford University, Stanford, California; and Department of Medicine, Veterans Affairs Palo Alto Health Care System, Palo Alto, California (Drs Garber and Owens).

THE CARE OF CRITICALLY ILL patients is technically complex and resource intensive, consuming a disproportionate share of limited health care resources. Acute kidney injury (AKI) occurs frequently in patients in the intensive care unit (ICU) with increasing incidence in recent years.[1,2] The rise in the incidence of AKI will further strain an intricate health care system charged with allocating resource-intensive interventions including hemodialysis.

Evidence-based management strategies for persons with severe AKI are not currently available; for example, the optimal timing, modality, dose and frequency of hemodialysis are unknown. Randomized clinical trials comparing alternate-day hemodialysis with continuous dialytic techniques (continuous renal replacement therapy [CRRT]) have yielded mixed results; most studies have been quite small with heterogeneous study samples, and meta-analyses have likewise been inconclusive. Economic analyses have also been challenging to conduct, owing to alternative methods of accounting for alternate-day hemodialysis and CRRT, and the paucity of utility data in the acute care setting.

More recent studies have focused on dose and frequency of hemodialysis in critically ill patients with AKI. Ronco et al[3] demonstrated prolonged survival for subjects randomized to higher hemofiltration flow rates (35 and 45 mL/kg/h, relative to 20 mL/kg/h). Schiffl et al[4] showed higher survival rates and a shorter time to renal recovery in subjects randomized to alternate-day hemodialysis 6 times/wk (daily hemodialysis) compared with subjects randomized to alternate-day hemodialysis 3 times/wk (alternate-day hemodialysis).

In this economic evaluation, we explore the cost-effectiveness of a daily hemodialysis strategy compared with a conventional, alternate-day hemodialysis strategy for the treatment of AKI in critically ill patients. Our analysis is based on data from the prospective clinical trial conducted by Schiffl et al[4] in 2002. We hypoth-

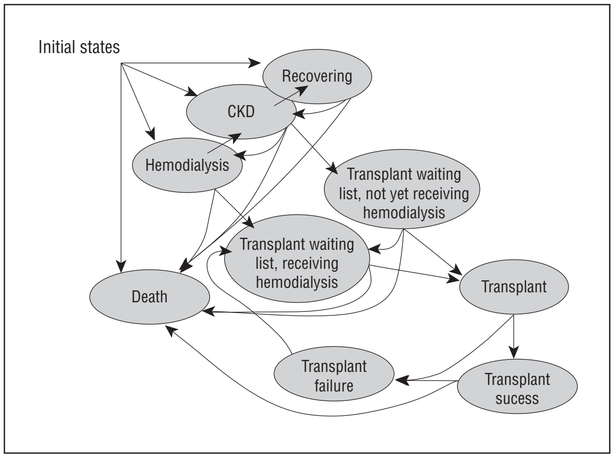

Figure 1. Schematic representation of the decision model showing a Markov state diagram of posthospitalization course for patients with acute renal failure who received daily or alternate-day hemodialysis in the intensive care unit. Circles indicate various health states; arrows, transitions between the various states. CKD indicates chronic kidney disease.

esized that hemodialysis received 6 times/wk would be a cost-effective intervention relative to other management strategies in modern ICU care.

METHODS

OVERVIEW

We developed a decision-analytic model to evaluate quality-adjusted life-years (QALYs) and costs of daily hemodialysis vs alternate-day hemodialysis in the ICU setting for patients with severe AKI. The model describes events that occur during a hospitalization for AKI and events after discharge for surviving patients. Outcomes include life expectancy, quality-adjusted life expectancy, and relevant medical and nonmedical costs assessed from a societal perspective. We used TreeAge Pro Healthcare software (version 2006; TreeAge Software, Williamstown, Massachusetts) to develop our model and perform statistical analyses.

PATIENT POPULATION

Most cases of severe AKI are caused by acute tubular necrosis. For our decision model base case, the patient is a 60-year-old man without prior known chronic kidney disease (CKD), admitted to an ICU with AKI requiring hemodialysis. Efficacy estimates are based on results of a prospective trial with nonrandom, alternating assignment. The mortality rate, according to the intention-to-treat analysis, was 28% for daily hemodialysis and 46% for alternate-day hemodialysis.

DECISION MODEL

The main simulated intervention relates to the frequency of hemodialysis: 6 vs 3 times/wk. There is no published evidence suggesting that CRRT or slow, low-efficiency hemodialysis (SLED) enhances survival or reduces AKI-associated morbidity.[5] Because CRRT is generally more expensive than hemodialysis, it is strictly dominated in this setting.[6] We excluded CRRT and SLED from analysis in our study and focused on the issue of frequency of hemodialysis.

A Markov model was used to simulate the post-AKI hospitalization course of these patients (**Figure 1**). Initial states include in-hospital death, postdischarge CKD without maintenance hemodialysis, postdischarge CKD with maintenance hemodialysis, and postdischarge recovery without evidence of CKD. The model also represents progression to the transplant waiting list (with and without maintenance hemodialysis), posttransplant success and failure, and postdischarge death. The cycle length was 1 year, and the model was run for 40 cycles.

DATA SOURCES

Transition probabilities were obtained from the ICU, AKI, CKD, and maintenance hemodialysis literature (**Table 1**). Limited data were available beyond 14-day postdischarge mortality from the study by Schiffl et al[4] to differentiate outcomes between the 2 alternative interventions. Aggregate post-AKI or CKD data were therefore used, with differences in other outcomes resulting from the initial differences in mortality.

COSTS

All costs were reported in US dollars adjusted to 2006 values using the medical care component of the Consumer Price Index.[22] Inpatient costs of care included the actual direct costs of ICU stay, hospital non-ICU stay, and the cost of hemodialysis. The cost for hemodialysis was based on cost data accounting figures from a local university medical center and the biomedical literature. Other inpatient costs were estimated based on figures presented in recent economic analyses.[20,21] Annual costs for hemodialysis, CKD, and transplant were based on 2006 US Renal Data System (USRDS) data and represent aggregate costs for inpatient and outpatient services for each group.[13]

LIFE EXPECTANCY

Age-specific mortality rates from the Centers for Disease Control and Prevention were used for patients who recovered normal kidney function. The 2006 USRDS data[20] were used for life expectancy estimates for persons undergoing hemodialysis and following the transplant. Mortality and hospitalization rates for persons with CKD were estimated based on the results of a prospective cohort study.[23]

ASSUMPTIONS

Several assumptions were made for our decision model. For each of these assumptions, we performed sensitivity analyses to determine whether the assumption was relevant to the cost-effectiveness of the alternatives and for what ranges of values a particular alternative was more cost-effective. For example, it was unclear whether the observed short-term benefit in subjects randomized to daily hemodialysis in the study by Schiffl et al[4] persisted, resulting in divergent survival curves for the 2 populations, or whether the benefit occurred only during the acute hospitalization. In our base case, the benefit from daily hemodialysis was restricted to the period of acute hospitalization; after discharge, the mortality rates in the daily and alternate-day hemodialysis groups were similar. We performed a sensitivity analysis on the long-term benefit of each intervention to determine how the cost-effectiveness would vary in each scenario.

We made assumptions about the incidence of CKD and maintenance hemodialysis after AKI. Because, to our knowledge, no published studies distinguish outcomes other than mortality for daily vs alternate-day hemodialysis, our base case model used identical proportional rates of CKD and maintenance hemodialysis after discharge. In addition, no data exist that distinguish among persons with CKD secondary to AKI from any other

Table 1. Input Variables and Range Tested in the Sensitivity Analysis

Variable	Base Case	Sensitivity Analysis, Range	Source
Starting age of population, y	60	45-75	Schiffl et al[4]
In-hospital probabilities, %			
Death following alternate-day hemodialysis	46	15-70	Schiffl et al[4]
Death following daily hemodialysis	28	15-70	Schiffl et al[4]
Full renal recovery (normal kidney function) following alternate-day hemodialysis	28	5-50	Morgera et al,[7] Bagshaw et al,[8] Schiffl[9]
Full renal recovery (normal kidney function) following daily hemodialysis	39	5-50	Morgera et al,[7] Bagshaw et al,[8] Schiffl[9]
Discharge with hemodialysis following alternate-day hemodialysis	5	0-10	Morgera et al,[7] Bagshaw et al,[8] Korkeila et al,[10] Schiffl[9]
Discharge with hemodialysis following daily hemodialysis	5	0-10	Morgera et al,[7] Bagshaw et al,[8] Korkeila et al,[10] Schiffl[9]
Discharge with chronic kidney disease following alternate-day hemodialysis	21	10-40	Morgera et al,[7] Bagshaw et al,[8] Korkeila et al,[10] Schiffl[9]
Discharge with chronic kidney disease following daily hemodialysis	28	10-40	Morgera et al,[7] Bagshaw et al,[8] Korkeila et al,[10] Schiffl[9]
Renal transplant probabilities, %			
Preemptive renal transplant	0.01	0-0.03	Abou Ayache et al,[11] Coresh et al[12]
Hemodialysis to renal transplant	3	2-4	US Renal Data System,[13] US Organ Procurement and Transplantation Network[14]
Perioperative death	1	0-5	Miller[15]
Graft failure	9	0-15	US Renal Data System,[13] US Organ Procurement and Transplantation Network[14]
Posttransplant success	90	85-95	US Renal Data System,[13] US Organ Procurement and Transplantation Network[14]
Utilities, time trade-off			
Chronic kidney disease	0.87	0-1	Gorodetskaya et al,[16] Maor et al[17]
Hemodialysis	0.783	0-1	Gorodetskaya et al,[16] Arnesen and Trommald,[18] Matas and Schnitzler[19]
Postrenal transplant failure	0.783	0-1	Gorodetskaya et al,[16] Arnesen and Trommald,[18] Matas and Schnitzler[19]
Renal transplant success	0.913	0-1	Matas and Schnitzler[19]
In-hospital costs, 2006 US $			
ICU per day	2000	1500-3000	Golan et al,[20] Burchardi and Schneider[21]
Non-ICU per day	1200	600-2000	Golan et al,[20] Burchardi and Schneider[21]
Alternate-day hemodialysis costs per total stay[a]	43 921	40 000-50 000	Golan et al,[20] Burchardi and Schneider[21]
Daily hemodialysis costs per total stay[a]	46 043	40 000-50 000	Golan et al,[20] Burchardi and Schneider[21]
Alternate-day hemodialysis per treatment	300		UCSF[b]
Annual costs, 2006 US $			
Chronic kidney disease	7653	7000-8000	US Renal Data System[13]
Outpatient hemodialysis	72 695	65 857-78 012	US Renal Data System[13]
Renal transplant costs, 2006 US $			
Initial cost (hospitalization)	105	100 000-200 000	US Renal Data System[13]
Annual costs subsequent to transplant success	19 187	10 000-30 000	US Renal Data System[13]
Costs during the first year of graft failure	22 001	10 000-30 000	US Renal Data System[13]
Discount rate, %	3	0-5	
Time frame, y	40	25-55	

Abbreviation: ICU, intensive care unit.

[a] Total stay: 10 days, ICU; 15 days, non-ICU; hemodialysis treatment over span of 15 days.

[b] Internal data from University of California, San Francisco (UCSF).

CKD population. Estimates for rates of progression, mortality, and costs in our model were from the general CKD population.

For transplant patients, we modeled "waiting for transplant" by directing a specific subset of the CKD and the population with end-stage renal disease (ESRD) to transplant during each cycle, where they waited for 5 years in the base case. Posttransplant patients accrued the same annual costs as nontransplant patients, except for initial costs for transitioning to transplant success (cost of transplant) or to transplant failure (cost of graft rescue attempt). We assumed that all patients with transplant failure transitioned back to maintenance hemodialysis. The key differences among transplant and nontransplant patients were in mortality rates and transplant failure (hemodialysis) rates. Retransplant rates were equal to first-transplant rates in the base case.

Other assumptions were made in cost and utility estimates. For cost differences between the daily and alternate-day hemodialysis strategies, we considered only costs stemming from the doubling of hemodialysis sessions per week. That is, we assumed that the cost per hemodialysis episode was the same for each group. We did not include costs such as increasing staff, purchasing additional hemodialysis machines, or otherwise in-

Table 2. Base Case Results of Cost-effectiveness Analysis of Management of AKI in the ICU

ARF Hemodialysis Strategy	Cost, $[a]	Incremental Cost, $	Effectiveness, QALY	Incremental Effectiveness, QALY	Incremental Cost-effectiveness Ratio, $/QALY
Alternate-day hemodialysis	82 267.62	10 924.18	5.89	2.14	5083.90
Daily hemodialysis	93 191.80		8.03		

Abbreviations: AKI, acute kidney injury; ARF, acute renal failure; ICU, intensive care unit; QALY, quality-adjusted life-year.

[a] Calculated in 2006 US dollars.

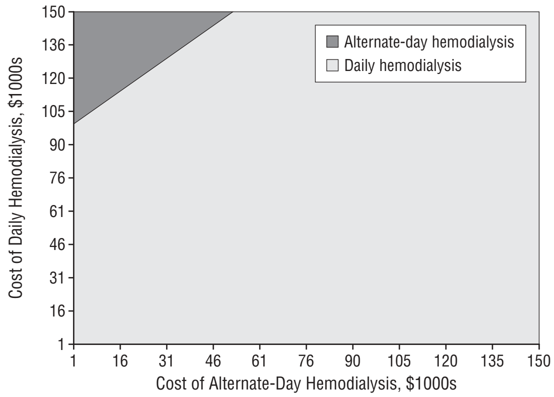

Figure 2. Two-way sensitivity analysis of in-hospital costs for daily vs alternate-day hemodialysis. The shaded regions represent the ranges in which each alternative dominates, using a threshold of $50 000 per quality-adjusted life-year.

creasing hospital capacity for hemodialysis. Sensitivity analysis for the cost differential was performed to determine the threshold at which additional costs would change which alternative was more cost-effective. We used time trade-off (TTO) utility measures for all states in our model. We used mean utility values in our base case and performed a sensitivity analysis.

RESULTS

BASE CASE ANALYSIS

Table 1 provides the input variables used in our model. In the base case for a 60-year-old man, daily hemodialysis was associated with an incremental cost of $5084/QALY gained compared with alternate-day hemodialysis (**Table 2**). Daily hemodialysis was projected to add 2.14 QALYs and $10 924 in cost. The positive incremental cost-effectiveness ratio (ICER) reflects the costs of more frequent hemodialysis during acute hospitalization and prolonged survival (and therefore increased costs) associated with a larger proportion of patients alive with CKD after discharge.

For the base case cohort, our model showed that patients are absent from the hemodialysis health state by approximately year 9 in both intervention alternatives. Because the costs of hemodialysis represents the greatest proportion of posthospitalization costs other than those of the transplant (nearly $68 000/year in the base case), this similarity in maintenance hemodialysis requirements between the groups likely explains the small overall cost difference between the alternatives (<$11 000).

SENSITIVITY ANALYSIS

Sensitivity analysis, using ranges derived from the literature and expert opinion, showed that several variables strongly influenced the ICER. These included AKI initial recovery rates, in-hospital AKI costs, chronic hemodialysis-associated mortality rates, CKD health state utilities for both alternatives, and CKD mortality in the alternate-day hemodialysis group. We performed 1- and 2-way sensitivity analyses on the cost, utility, and transition probability variables that had the greatest impact. Several important findings emerged, all suggesting a robust ICER for the daily hemodialysis strategy. First, we found in-hospital AKI costs were not material to the cost-effectiveness. The ICER was less than $50 000/QALY for all cost values in a 1-way sensitivity analysis. When costs for both alternatives were varied in a 2-way analysis, the ICER was greater than $50 000/QALY only when the cost of daily hemodialysis exceeded the cost of alternate-day hemodialysis by $105 000 (**Figure 2**).

Second, the cost of maintenance (chronic) hemodialysis was the main driver of overall costs in the model. However, because the maintenance hemodialysis rates were so similar and small in both intervention groups, the ICER was not sensitive to even large changes in the costs of maintenance hemodialysis. One-way sensitivity analysis showed that changes in maintenance hemodialysis costs from $36 000 to $140 000 per year resulted in less than a $2000/QALY change in the ICER.

Maintenance hemodialysis *rates*, however, had a large effect on the ICER. In our base case, the daily hemodialysis survival advantage was allocated to the recovery (51%), CKD (39%), and maintenance hemodialysis (9%) health states in the same proportion as in the alternate-day hemodialysis group. If, however, the daily hemodialysis survivors are allocated disproportionately to costly long-term maintenance hemodialysis (>20% of the total daily hemodialysis group or >27% of the survivors, while adjusting the CKD and full renal recovery to keep the same initial proportions), cost-effectiveness becomes less favorable (**Figure 3**). Finally, sensitivity analysis shows that the daily hemodialysis strategy is highly cost-effective even when the difference in 14-day postdischarge mortality between daily hemodialysis and alternate-day hemodialysis is within 0.5% (**Figure 4**).

Sensitivity analysis around age at the time of hospitalization, discount rate, and utility estimates had little influence on the cost-effectiveness. The ICER varied from just over $4500/QALY to just under $6500/QALY because the initial age varied from 45 to 75 years. The results of our analysis are insensitive to discount rates ranging between 0% and 5%.

Because our base case assumed that the benefit from a daily hemodialysis strategy occurred during the period of hospitalization, we performed additional modeling assuming a continued benefit after discharge. We modeled 3 scenarios: 40% mortality benefit for patients in CKD and hemodialysis health states for the daily hemodialysis group at every age; 40% reduction in CKD and hemodialysis incidence (continued morbidity benefit) for the daily hemodialysis group at every age; and both. In the continued mortality benefit scenario, the cost-effectiveness is less favorable at $10 000/QALY, whereas it becomes more favorable ($2500/QALY) in the continued morbidity benefit scenario in which lower incidence translates into lower prevalence at each age. In the scenario in which there are continued mortality and morbidity benefits, the cost-effectiveness becomes less favorable than the base case at $7000/QALY.

COMMENT

We assessed the cost-effectiveness of daily compared with alternate-day hemodialysis for critically ill patients with AKI. Our analysis suggests that daily hemodialysis is associated with a favorable incremental cost per QALY compared with alternate-day hemodialysis. The results of our analysis are robust and hold under most assumptions, even if the difference in mortality rates between groups is much smaller than what was observed in a recent clinical trial.[4]

Although daily hemodialysis would require additional inpatient resources, our analysis showed that these inpatient costs did not have a notable effect on the overall cost-effectiveness. Hemodialysis costs could increase the ICER substantially if the excess patients who survived in the daily hemodialysis group disproportionately required maintenance hemodialysis. Although a sicker patient population may have higher risk of developing ESRD after an episode of AKI, there is no evidence to suggest that patients who receive daily hemodialysis are at higher risk for ESRD.

Our analysis confirms that a life-saving technology such as hemodialysis can result in considerable downstream costs that influence cost-effectiveness results. Although our base case assumed that the benefit patients received from daily hemodialysis did not persist beyond their hospital stay, a more optimistic scenario in which survival was improved on a longer-term basis would result in more individuals living with CKD and ESRD and therefore a cost-effectiveness modestly less favorable than in our base case analysis. As the incidence of AKI increases, and if survival rates improve with therapeutic advances (such as daily hemodialysis), we may see increased numbers of patients with impaired kidney function. This paradoxical effect may have important implications for overall resource utilization.

One previous study[24] explored the cost-effectiveness of hemodialysis vs no hemodialysis in AKI. Hamel et al[24] used data from the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT study), a hospitalized cohort of patients selected for having 1 of several comorbid conditions associated with a life expectancy of approximately 6 months. The authors[24] estimated a mean ICER greater than $128 000/QALY with the strategy of provision of hemodialysis and continued aggressive care vs the strategy of withholding hemodialysis; the ICERs ranged from approximately $62 000 to $274 000 based on non–AKI-related prognostic factors. Although the validity of these analyses was not challenged, the cohort was highly selected, and the results are inapplicable to most clinical settings. Most predictive models in critically ill patients with AKI are not sufficiently accurate tools on which to base the withholding of life-saving interventions; moreover, few models have been cross-validated. Although AKI requiring hemodialysis is a devastating complication, a large proportion of patients do survive, and in the absence of advanced comorbid disease, as in the SUPPORT study, some may survive for decades. Therefore, we believe that a cost-effectiveness analysis of different hemodialysis strategies, rather than a hemodialysis vs no hemodialysis comparison, was most relevant in the modern era.

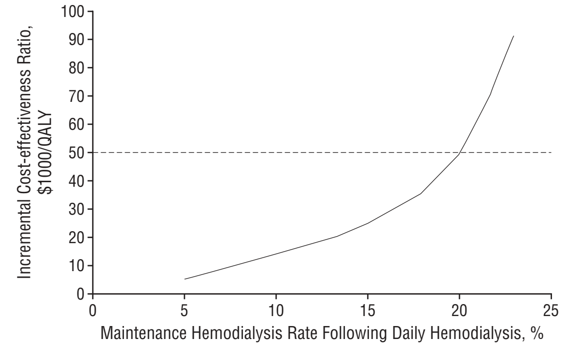

Figure 3. One-way sensitivity analysis of maintenance (chronic) hemodialysis rates for patients following daily hemodialysis. The dashed line indicates the $50 000 per quality-adjusted life-year (QALY) threshold. The solid black curve indicates the cost-effectiveness.

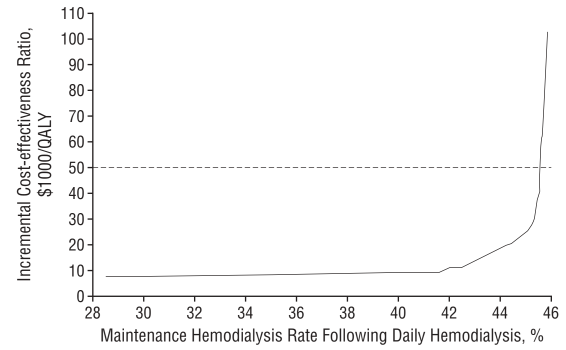

Figure 4. One-way sensitivity analysis of initial mortality rate for patients following daily hemodialysis. The initial mortality rate is the mortality rate 14 days after hospital discharge. The dashed line indicates the $50 000 per quality-adjusted life-year (QALY) threshold. The solid black curve indicates the cost-effectiveness.

Our analysis has several notable strengths. First, the point estimates for efficacy are based on the results of a randomized trial rather than on observational data. Second, a thorough review of the biomedical literature provided reliable ranges for our sensitivity analysis that are appropriate for our study population. Third, the cost-effectiveness of a daily hemodialysis strategy was a robust finding and was insensitive to the influence of most variables. Fourth, our cost estimates for hemodialysis care, transplant, and CKD care are based on actual costs reported in and validated by the USRDS. Finally, Markov models allowed us to incorporate changes in the progression of disease following recovery from AKI, although additional controlled trials with longitudinal follow-up would provide useful prognostic information regarding important complications related to kidney disease.

Our analysis also has several limitations. Our cost-effectiveness analysis was subject to the limitations of the original study from which our decision tree model and base case were drawn.[25] First, Schiffl et al[4] excluded patients initially assigned to continuous renal replacement therapies, leaving what was likely a less ill group to receive hemodialysis. Although the study demonstrated a notable improvement in survival for persons with AKI requiring hemodialysis who were treated 6 times weekly, patients who were not candidates for alternate-day hemodialysis were excluded from the study, so that the results may not be generalizable to all patients with AKI, some of whom have such severe hemodynamic disturbances as to be poor candidates for alternate-day hemodialysis. Second, the delivered dose of hemodialysis was 20% to 30% less than the prescribed dose. Although the target volume-indexed clearance time product Kt/V_{urea} (a standard measurement of hemodialysis dose) was 1.2 per session, the mean delivered Kt/V_{urea} per session was only 0.94 in the alternate-day hemodialysis group and 0.92 in the daily hemodialysis group. As a result, it is possible that the observed difference resulted from relatively ineffective hemodialysis in the conventional therapy (3 times weekly) group, rather than enhanced or optimal hemodialysis in the intensive therapy (6 times weekly) group. Third, the overall mortality rate for the ICU population in the study by Schiffl et al[4] was less than expected, perhaps indicating a selected population. Finally, because we focused our inquiry on the frequency of hemodialysis, our results cannot be extrapolated to other dialytic therapies such as CRRT and SLED, which were not applied in the study by Schiffl et al[4] or considered in our analyses.

In addition, some aspects of our methods and several of the assumptions that were made could be construed as potential limitations. For example, we assumed a mean length of hospital stay based on various studies, in which patients were on average sicker than those in the sample randomized in the study by Schiffl et al.[4] Traditionally, most studies of AKI have focused on short-term outcomes assessed at hospital discharge.[26] Fewer studies have reported on the longer-term prognosis after AKI in terms of survival, quality of life, and recovery of kidney function. Longer-term outcomes of persons who survive episodes of severe AKI have not been well characterized.

Compared with other therapeutic options for critically ill patients such as drotrecogin alfa, daily hemodialysis is a relatively cost-effective strategy. A daily hemodialysis strategy may result in some increased resource outlays by hospitals (new hemodialysis machines, increased nursing or labor costs), which were not modeled in our analysis. However, the low ICER suggests that a daily hemodialysis strategy would be a rational use of resources in the ICU setting. Additional studies that stratify patients on severity of illness may provide important information for targeting daily hemodialysis strategies to those who would benefit the most. If future randomized trials demonstrate benefit for other, more expensive dialytic alternatives, such as CRRT and SLED, it would be important to compare cost-effectiveness with these alternatives with daily and conventional hemodialysis. The Acute Renal Failure Trials Network study,[27] a randomized trial of 6 times weekly vs 3 times weekly hemodialysis or high- vs conventional-dose CRRT or SLED, should help to clarify the relative effects of hemodialysis frequency among those subjects assigned to hemodialysis. Cost analyses have also been planned for this study.

Applying the results of cost-effectiveness analysis conducted from a societal perspective can be difficult for physicians and administrators who must work within a limited budget. The high costs of critical illness make it important to consider economic outcomes alongside clinical outcomes in deciding how to utilize limited resources. Although continuous dialytic therapies hold promise, current evidence is mixed with unclear benefits to warrant the considerable upfront costs and staff training to initiate such a program. A daily hemodialysis strategy provides a cost-effective option for managing AKI in critically ill patients that can be readily implemented in most hospitals that already provide hemodialysis services.

Accepted for Publication: March 10, 2008.

Correspondence: Amar A. Desai, MD, MPH, Division of Nephrology, Stanford University School of Medicine, 780 Welch Rd, Ste 106, Palo Alto, CA 94304 (desai_amar@hotmail.com).

Author Contributions: *Study concept and design:* Desai, Baras, Berk, Nakajima, Owens, and Chertow. *Acquisition of data:* Desai, Baras, Berk, Nakajima, and Chertow. *Analysis and interpretation of data:* Desai, Baras, Berk, Nakajima, Garber, Owens, and Chertow. *Drafting of the manuscript:* Desai, Baras, Berk, Nakajima, and Chertow. *Critical revision of the manuscript for important intellectual content:* Desai, Baras, Garber, Owens, and Chertow. *Statistical analysis:* Desai, Berk, Nakajima, Garber, and Chertow. *Obtained funding:* Garber. *Administrative, technical, and material support:* Desai, Baras, and Nakajima. *Study supervision:* Garber, Owens, and Chertow.

Financial Disclosure: None reported.

Funding/Support: Dr Desai was supported by a training grant from the Agency for Healthcare Research and Quality (AHRQ). Dr Chertow was supported by grant R33 DK067645 and also supported in part by the Department of Veterans Affairs.

REFERENCES

1. Waikar SS, Curhan GC, Wald R, et al. Declining mortality in patients with acute renal failure, 1988 to 2002. *J Am Soc Nephrol*. 2006;17(4):1143-1150.
2. Ali T, Khan I, Simpson W, et al. Incidence and outcomes in acute kidney injury: a comprehensive population based study. *J Am Soc Nephrol*. 2007;18(4):1292-1298.
3. Ronco C, Bellomo R, Homel P, et al. Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomized trial. *Lancet*. 2000;356(9223):26-30.
4. Schiffl H, Lang SM, Fischer R. Daily hemodialysis and the outcome of acute renal failure. *N Engl J Med*. 2002;346(5):305-310.
5. Noble JS, Simpson K, Allison ME. Long-term quality of life and hospital mortality in patients treated with intermittent or continuous hemodialysis for acute renal and respiratory failure. *Ren Fail*. 2006;28(4):323-330.
6. Manns B, Doig CJ, Lee H, et al. Cost of acute renal failure requiring dialysis in the intensive care unit: clinical and resource implications of renal recovery. *Crit Care Med*. 2003;31(2):449-455.
7. Morgera S, Kraft AK, Siebert G, et al. Long-term outcomes in acute renal failure patients treated with continuous renal replacement therapies. *Am J Kidney Dis*. 2002;40(2):275-279.
8. Bagshaw SM, Laupland KB, Doig CJ, et al. Prognosis for long-term survival and renal recovery in critically ill patients with severe acute renal failure: a population-based study. *Crit Care*. 2005;9(6):R700-R709.
9. Schiffl H. Renal recovery from acute tubular necrosis requiring renal replacement therapy: a prospective study in critically ill patients. *Nephrol Dial Transplant*. 2006;21(5):1248-1252.
10. Korkeila M, Ruokonen E, Takala J. Costs of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. *Intensive Care Med*. 2000;26(12):1824-1831.
11. Abou Ayache R, Bridoux F, Pessione F, et al. Preemptive renal transplantation in adults. *Transplant Proc*. 2005;37(6):2817-2818.
12. Coresh J, Astor BC, Greene T, et al. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis*. 2003;41(1):1-12.
13. US Renal Data System. *USRDS 2006 Annual Data Report: Atlas of End-Stage Renal Disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2006.
14. 2005 Annual Report of the US Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. US Organ Procurement and Transplantation Network and Scientific Registry of Transplant Recipients Web site. http://www.optn.org/AR2005/default.htm. Accessed October 15, 2006.
15. Miller RD. *Risks Related to Surgery: Miller's Anesthesia*. 6th ed. New York, NY: Elsevier Churchill Livingstone; 2005:914-915.
16. Gorodetskaya I, Zenios S, McCulloch CE, et al. Health-related quality of life and estimates of utility in chronic kidney disease. *Kidney Int*. 2005;68(6):2801-2808.
17. Maor Y, King M, Olmer L, et al. A comparison of three measures: the time trade-off technique, global health-related quality of life and the SF-36 in dialysis patients. *J Clin Epidemiol*. 2001;54(6):565-570.
18. Arnesen T, Trommald M. Roughly right or precisely wrong? systematic review of quality-of-life weights elicited with the time trade-off method. *J Health Serv Res Policy*. 2004;9(1):43-50.
19. Matas AJ, Schnitzler M. Payment for living donor (vendor) kidneys: a cost-effectiveness analysis. *Am J Transplant*. 2004;4(2):216-221.
20. Golan Y, Wolf MP, Pauker SG, et al. Empirical anti-Candida therapy among selected patients in the intensive care unit: a cost-effectiveness analysis. *Ann Intern Med*. 2005;143(12):857-869.
21. Burchardi H, Schneider H. Economic aspects of severe sepsis: a review of intensive care unit costs, cost of illness, and cost effectiveness of therapy. *Pharmacoeconomics*. 2004;22(12):793-813.
22. Archived Consumer Price Index News Releases. Bureau of Labor Statistics Web site. http://www.bls.gov/cpi/home.htm#data. Accessed October 5, 2006.
23. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risk of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351(13):1296-1305.
24. Hamel MB, Phillips RS, Davis RB, et al; SUPPORT Investigators. Outcomes and cost-effectiveness of initiating dialysis and continuing aggressive care in seriously ill hospitalized adults: Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). *Ann Intern Med*. 1997;127(3):195-202.
25. Bonventre JV. Daily hemodialysis: will treatment each day improve the outcome in patients with acute renal failure? *N Engl J Med*. 2002;346(5):362-364.
26. Bagshaw SM. The long-term outcome after acute renal failure. *Curr Opin Crit Care*. 2006;12(6):561-566.
27. Palevsky PM, O'Connor T, Zhang JH, Star RA, Smith MW. Design of the VA/NIH Acute Renal Failure Trial Network (ATN) Study: intensive versus conventional renal support in acute renal failure. *Clin Trials*. 2005;2(5):423-435.