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Farsad Afshinnia, Alex Straight, Qi Li, Yelena Slinin, Robert N. Foley & Areef Ishani

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CLINICAL STUDY

Trends in Dialysis Modality for Individuals with Acute Kidney Injury

Farsad Afshinnia
St. Joseph's Hospital, HealthEast Care System, University of Minnesota, School of Public Health, St. Paul, Minnesota, USA

Alex Straight
Division of Hypertension and Renal Diseases, University of Minnesota, Minneapolis, Minnesota, USA

Qi Li
Center for Chronic Disease Research, Minneapolis, Minnesota, USA

Yelena Slinin
Department of Medicine, Minneapolis VA Medical Center, University of Minnesota, School of Medicine, Minneapolis, Minnesota, USA

Robert N. Foley
Center for Chronic Disease Research, Minneapolis, Minnesota, USA

Areef Ishani
Department of Medicine, Minneapolis VA Medical Center, University of Minnesota, School of Medicine, Minneapolis, Minnesota, USA

Backgrounds. There are no national level data on types of dialysis in use for acute kidney injury (AKI). We aimed to assess trends in dialysis modality for AKI and mortality associated with each modality from 1998 to 2005. *Methods*. Using data from the 5% Medicare cohort, we identified individuals with AKI requiring dialysis. Individuals with preexisting end-stage renal disease were excluded. Intermittent hemodialysis (IHD), daily intermittent hemodialysis, and continuous renal replacement therapy (CRRT) were defined using Current Procedure Terminology codes. Mortality was defined as death during 30 days after the first dialysis session. *Results*. Between 1998 and 2005, there were a total of 18,249 patients identified with AKI requiring renal replacement therapy. CRRT was increasingly used for AKI, with 9.9% of patients in 1998 to 18.3% by 2005. Proportion of daily dialysis decreased during this period, while use of IHD remained stable at approximately 68%. Overall 30-day mortality declined from 44.4% in 1998 to 40.2% in 2005. Crude mortality for CRRT was highest in all years (51.0–61.8%), followed by daily (38.2–49.9%) and IHD groups (35.8–43.4%). Multinomial logistic regression analysis showed that white race, presence of sepsis, atherosclerotic heart diseases, peripheral vascular diseases, dysrhythmia, gastrointestinal and liver diseases, and any year after 2000 were independently associated with higher odds of using CRRT after adjusting for other variables. *Conclusion*. The proportion of patients using CRRT has increased over time. Mortality associated with IHD has decreased from 1998 to 2005. Mortality associated with different dialysis modalities is likely the result of severity of illness.

Keywords kidney failure, acute, mortality, renal replacement therapy

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Address correspondence to Farsad Afshinnia, MD, 2750 Cedar Avenue S, #205, Minneapolis, MN 55407, USA; Tel.: (612) 208-0942; Fax: (651) 326-3706; E-mail: afshi001@umn.edu

INTRODUCTION

Acute kidney injury (AKI) is a common problem in critically ill patients and occurs in 5–30% of patients admitted to intensive care units.[1,2] AKI has been demonstrated to be an independent predictor of mortality.[3–5] Mortality rates following an episode of AKI have ranged

between 40–80% among those in intensive care units.[1,5,6] Historically, there have been controversies in the management of renal replacement therapy (RRT) in the setting of AKI in regard to its indication, use of intermittent or continuous techniques, and optimum treatment regimen.[7,8] These controversies have resulted in different practice patterns around the globe in the use continuous and intermittent dialysis at different rates in such patients. While intermittent hemodialysis (IHD) was the dominant mode of dialysis during the late 1990s for critically ill patients in the United States,[9] this has not been the case in other countries. In the United Kingdom, up to 65% of AKI patients are treated with continuous veno-venous hemofiltration as first line therapy.[10] Similarly, continuous renal replacement therapy (CRRT) is the dominant form of RRT for AKI in Australia.[11] In the most recent survey of 130 practitioners from 27 sites in the United States, IHD and CRRT were used in 57 and 36% of patients with AKI needing dialysis, respectively.[12]

A number of new randomized controlled trials have challenged differing survival benefits for various RRT modalities. Until recently, it had been suggested that greater dialysis clearance either by CRRT or daily hemodialysis[8,13] was associated with improved patient survival compared to conventional dialysis patterns. More recently, in 2008, the Acute Renal Failure Trial Network (ATN) showed no decreased mortality, improved recovery of kidney function, or reduced rate of nonrenal organ failure in intensive renal support in critically ill patients as compared to a less intensive therapy.[14] Given the overall practice variation for RRT, we aimed to determine the changing trends of different modalities of RRT in use for AKI in Medicare beneficiaries from 1998 to 2005 in the United States, as well as describing the trend in 30-day in-hospital mortality observed with each modality of RRT over the same time period.

MATERIALS AND METHODS

Cohort Construction

We constructed a cohort using random samples of Medicare beneficiaries. The sample population is obtained from Medicare 5% Part B. Medicare Part B is a provider/supplier claim-based insurance database with a yearly database available since the early 1990s. The 5% Part B is established by random sampling of 5% of the entire general Medicare population. The data is gathered from all medical centers nationwide through a centralized database established on provider-based claims, reflecting diagnoses and procedures during duration of care, and is representative of the Medicare population.[15] The final cohort included all hospitalized individuals between 1998 and 2005 with Medicare as their primary insurance source who underwent acute renal replacement therapy. Participants were required to have Medicare as their primary insurance source. Demographic and co-morbid information was extracted from the hospital discharge summary.

Defining Renal Replacement Modality

Using the Medicare 5% Part B files, the following modalities of renal replacement therapy were identified: continuous renal replacement therapy (CRRT) (90945 and 90947), intermittent hemodialysis (IHD) (90935 and 90937), and peritoneal dialysis (PD) (90945 or 90947 with CPT code 49420 identifying the placement of a peritoneal catheter present within 14 days). Daily hemodialysis (DHD) was considered to have occurred if three or more consecutive days of dialysis were provided, with Sundays excluded. Individuals with evidence of end-stage kidney disease (defined as registration in the ESRD registry) prior to hospital admission were excluded from the final cohort. Additionally, individuals registered in the ESRD program within five days of their hospital admission date were considered to have ESRD and excluded from the final cohort. Each hospitalization with an AKI episode was considered a separate event. Additionally, if during a single hospital admission, an individual had a gap between dialysis sessions of greater than 30 days, each period of dialysis was considered a separate episode of AKI and counted separately. Mortality was defined as death from any cause during the first 30 days of starting dialysis.

Statistical Analysis

Descriptive statistics of mean, absolute, and relative frequencies are used to present the data. Chi-square was used to compare categorical variables between groups. Analysis of variance with Tukey post hoc analysis was applied to compare the continuous variables across different groups. Multinomial logistic regression analysis was used to determine independent variables associated with modality of dialysis. Due to the large sample size and achieving statistical significance for small differences, clinical significance was additionally defined as the base of judging the differences. Analyses were done by SAS software version 9.01.

RESULTS

Between 1998 and 2005, there were total of 19642 events in 18249 patients identified as AKI requiring renal

Table 1
Baseline characteristics and underlying medical problems of patients with AKI needing renal replacement theapy for each event of AKI from 1998 to 2005

	Year							
Variables	1998	1999	2000	2001	2002	2003	2004	2005
N	2018	2247	2228	2381	2566	2652	2750	2800
Mean age (yrs)	73.1	73.5	73.1	72.9	72.9	73.0	72.8	72.5
Mean admission-RRT interval (days)	15.7	15.0	15.1	16.6	16.9	16.0	17.0	14.6
Male sex (%)	53.8	52.5	54.6	54.3	54.2	54.3	55.6	55.9
Black race (%)	14.9	15.1	14.6	16.4	17.8	16.3	16.2	15.6
White race (%)	79.0	77.3	78.9	76.7	75.0	77.0	76.6	77.4
Others (%)	6.1	7.6	6.5	6.8	7.2	6.7	7.2	7.0
Sepsis (%)	32.5	34.4	32.3	35.4	39.8	38.9	41.3	41.8
ASHD (%)	48.3	48.2	48.8	47.9	46.3	45.1	45.8	42.8
CHF (%)	63.7	62.0	65.5	62.9	63.4	63.8	61.5	61.1
Stroke (%)	15.1	14.7	15.4	14.4	16.0	14.9	15.5	13.3
PVD (%)	26.7	24.5	24.7	26.4	25.2	25.9	25.9	26.3
GI (%)	17.7	17.1	17.5	18.0	16.1	16.3	15.9	14.6
Liver (%)	5.7	6.0	6.4	8.2	7.5	7.5	8.7	10.4
Dysrrhythmia (%)	47.8	49.3	51.8	52.2	53.2	52.1	51.7	50.4
Cancer (%)	11.1	12.8	12.7	12.5	14.3	12.7	14.4	13.7
Diabetes (%)	35.1	34.3	37.0	39.4	39.4	38.5	38.8	39.9
HTN (%)	54.4	54.6	58.1	57.4	60.9	60.3	61.5	61.9
Anemia (%)	38.5	38.5	38.9	40.4	40.3	42.8	45.3	45.5

Abbreviations: RRT = renal replacement therapy, ASHD = atherosclerotic heart disease, CHF = congestive heart failure, PVD = peripheral vascular disease, GI = gastrointestinal diseases, HTN = hypertension.

replacement therapy. Table 1 shows the characteristics of the patients who were hospitalized and underwent RRT for AKI. Overall, the mean age ranged between 72.5 to 73.5 years over the study period. There has also been a mild predilection toward male sex (52.5–55.9%), which increased slightly over time. Mean duration between hospital admissions until initiation of RRT has slightly increased from 15.7 days in 1998 to 17 days in 2004, and decreased to 14.6 days in 2005. African-Americans were more commonly represented in the final cohort (14.9–16.4%) compared with the 2000 U.S. census (12.9%).[16] The most prevalent underlying co-morbidities were hypertension, congestive heart failure (CHF), dysrhythmia, atherosclerotic heart disease (ASHD), and sepsis with prevalence in 2005 of 61.9%, 61.1%, 50.4%, 42.8%, and 41.8%, respectively. Over time, there has been a significant decrease in prevalence of ASHD from 1998 to 2005, but there has been a significant increase in the trend of sepsis, diabetes, hypertension, anemia, and liver diseases over the same time period. Table 2 shows the univariate comparison of baseline characteristics by modality of dialysis. Accordingly, mean duration between hospital admissions until initiation of RRT was significantly higher in the CRRT and DHD groups as compared to the IHD group. Black patients were more likely to be treated with IHD compared to CRRT. Conversely, white patients had greater use of CRRT compared to IHD. Individuals treated with CRRT were more likely to have sepsis, ASHD, liver disease, and dysrhythmia, and less likely to have diabetes, hypertension, and anemia compared to those on intermittent dialyses. Table 3 shows the variables independently associated with DHD and CRRT after adjusting for baseline characteristics. Accordingly, the odds of using CRRT as compared to IHD has progressively increased independent of other comorbidities since 2000, while the odds of using DHD as compared to IHD have decreased since 2003. Black and other races are significantly less likely than white patients to use DHD or CRRT. The presence of sepsis, CHF, stroke, peripheral vascular diseases, gastrointestinal diseases, liver diseases, dysrhythmia, cancer, and anemia are associated with higher odds of using DHD than IHD, independent of age, sex, race, year of practice, and other comorbidities. Similarly, presence of sepsis, ASHD, peripheral vascular diseases, gastrointestinal diseases, liver diseases, and dysrhythmia are independently associated with higher odds of using CRRT than IHD, while patients with stroke, diabetes, hypertension, and anemia were more likely to be on IHD than CRRT.

Table 2
Distribution of patients' characteristics and underlying medical problems by modalities of dialysis in each event of AKI from 1998 to 2005

Variables	Dialysis modality		
	CRRT	DHD	IHD
N	2717	3536	13351
Mean age (yrs)	70.8‡	72.9†	73.4
Mean admission-RRT interval (days)	19.0‡	18.8‡	14.4
Male sex (%)	1581 (58.2)‡	1980 (56.0)†	7129 (53.4)
Race:			
Black race (%)	302 (11.1)‡	506 (14.3)‡	2323 (17.4)
White race (%)	2271 (83.6)	2807 (79.4)	10040 (75.2)
Others (%)	144 (5.3)	223 (6.3)	988 (7.4)
Sepsis (%)	1359 (50.0)	1529 (43.2)	4443 (33.3)
ASHD (%)	1388 (51.1)‡	1694 (47.9)†	6021 (45.1)
CHF (%)	1687 (62.1)	2376 (67.2)‡	8264 (61.9)
Stroke (%)	345 (12.7)†	601 (17.0)†	1976 (14.8)
PVD (%)	807 (29.7)‡	994 (28.1)‡	3244 (24.3)
GI (%)	489 (18.0)†	661 (18.7)‡	2083 (15.6)
Liver (%)	364 (13.4)‡	276 (7.8)†	868 (6.5)
Dysrrhythmia (%)	1668 (61.4)‡	1931 (54.6)‡	6435 (48.2)
Cancer (%)	323 (11.9)	492 (13.9)	1749 (13.1)
Diabetes (%)	774 (28.5)‡	1418 (40.1)	5260 (39.4)
HTN (%)	1117 (41.1)‡	2192 (62.0)	8238 (61.7)
Anemia (%)	888 (32.7)‡	1630 (46.1)‡	5621 (42.1)

†p value < 0.01, comparison with IHD.
‡p value < 0.001, comparison with IHD.
Abbreviations: RRT = renal replacement therapy, CRRT = continuous renal replacement therapy, DHD = daily intermittent dialysis, IHD = intermittent hemodialysis, ASHD = atherosclerotic heart disease, CHF = congestive heart failure, PVD = peripheral vascular disease, GI = gastrointestinal diseases, HTN = hypertension.

Table 3 also shows that odds ratio of sepsis, dysrhythmia, and liver diseases is higher in CRRT than DHD, suggesting that the individuals with more hemodynamic instability were more likely to be put on CRRT.

The median number of days from the first date of dialysis to hospital discharge was 9.5 days (inter-quartile range of 4 to 20 days). Overall, the median number of dialysis sessions for each event of AKI was 3 (inter-quartile range of 1 to 6). Ninety-five percent of patients had fewer than 18 dialysis sessions. The median of dialysis sessions for patients on CRRT, DHD, IHD, and PD was 4, 5, 2, and 5 sessions (inter-quartile ranges of 1 to 9, 3 to 9, 1 to 4 and 2 to 7), respectively. Figure 1 demonstrates that IHD was the most frequently used modality of dialysis, followed by DHD, CRRT, and PD. Over time, the rate of CRRT use increased from 9.9% to 18.3% from 1998 to 2005, while the rate of DHD decreased from 20.4% to 15.3% during the same time period. The rate of IHD was fairly stable during this period at about 68.0%.

The overall 30-day mortality was 44.4% in 1998 and has remained stable until 2002. Since then, the 30 day mortality has gradually declined to 40.2% in 2005. Figure 2 shows the 30-day mortality by modalities of dialysis in patients with AKI from 1998 to 2005. Accordingly, the highest mortality was associated with CRRT (51.0–61.8%), followed by DHD (38.2–49.9%) and IHD (35.8–43.4%). Mortality with continuous dialysis appeared to increase initially until 2000, but it was followed by a steady decline though 2004. The overall mortality trend appears to be decreasing as a result of decrease in mortality observed among individuals treated with intermittent dialyses.

DISCUSSION

Overall, the number of AKI events started on renal replacement therapy increased from 1998 through 2005. In general, during this time period the prevalence of sepsis,

Table 3
Components of multinomial logistic regression analysis showing variables independently associated with DHD and CRRT when compared with IHD modality after adjustment in individuals with AKI from 1998 to 2005

Variables	OR (CRRT vs. IHD)	95% CI of OR (CRRT vs. IHD)	OR (DHD vs. IHD)	95% CI of OR (DHD vs. IHD)	*p* value
Year					< 0.0001
1998 (reference)	1.00		1.00		
1999	1.03	0.84 to 1.27	0.94	0.81 to 1.10	
2000	1.31	1.07 to 1.60	0.93	0.80 to 1.09	
2001	1.43	1.17 to 1.74	0.93	0.80 to 1.08	
2002	1.75	1.44 to 2.11	0.93	0.80 to 1.08	
2003	1.55	1.28 to 1.88	0.89	0.76 to 1.03	
2004	1.78	1.47 to 2.14	0.84	0.72 to 0.97	
2005	2.17	1.80 to 2.61	0.78	0.67 to 0.91	
Age (yrs)	0.98	0.97 to 0.98	0.99	0.99 to 0.99	< 0.0001
Female sex	0.95	0.87 to 1.04	0.91	0.84 to 0.98	< 0.05
Race:					< 0.0001
Black vs. white	0.67	0.59 to 0.77	0.78	0.70 to 0.87	
Others vs. white	0.73	0.61 to 0.89	0.81	0.69 to 0.94	
Sepsis	1.71	1.56 to 1.87	1.39	1.24 to 1.51	< 0.0001
ASHD	1.30	1.18 to 1.43	0.98	0.90 to 1.06	< 0.0001
CHF	0.97	0.87 to 1.06	1.15	1.06 to 1.25	< 0.005
Stroke	0.88	0.77 to 1.00	1.11	1.00 to 1.23	< 0.01
PVD	1.35	1.22 to 1.49	1.15	1.05 to 1.25	< 0.0001
GI	1.18	1.06 to 1.33	1.13	1.02 to 1.25	< 0.005
Liver	1.67	1.45 to 1.92	1.18	1.02 to 1.36	< 0.0001
Dysrhythmia	1.60	1.46 to 1.76	1.18	1.09 to 1.28	< 0.0001
Cancer	0.93	0.81 to 1.06	1.13	1.01 to 1.26	< 0.05
Diabetes	0.69	0.63 to 0.76	1.01	0.93 to 1.09	< 0.0001
Anemia	0.71	0.65 to 0.78	1.16	1.07 to 1.25	< 0.0001
HTN	0.49	0.44 to 0.53	1.00	0.92 to 1.08	< 0.0001

Abbreviations: OR = odds ratio, CI = confidence interval, CRRT = continuous renal replacement therapy, DHD = daily intermittent dialysis, IHD = intermittent hemodialysis, ASHD = atherosclerotic heart disease, CHF = congestive heart failure, PVD = peripheral vascular disease, GI = gastrointestinal diseases, HTN = hypertension.

diabetes, hypertension, anemia, and liver diseases increased, while the prevalence of gastrointestinal disorders and atherosclerotic heart diseases declined in patients with AKI needing dialysis. Over this time period, IHD was the most frequently used dialysis modality for AKI, with a fairly stable proportion of approximately 68% from 1998 to 2005. During this same time period, use of DHD declined from 20.4% to 15.3% while the use of CRRT increased from 9.9% to 18.3%. The overall 30-day all-cause mortality declined from 44.4% in 1998 to 40.2% in 2005. As expected, the highest crude mortality was observed with CRRT, followed by DHD and IHD modality.

In a worldwide survey of 54 hospitals from 23 countries, CRRT was the most frequently applied (80%) modality of dialysis in AKI, followed by intermittent (16.9%), PD, and slow continuous ultrafiltration.[1] The overall hospital mortality in this setting was 60.3%. In a survey of 212 units in the United Kingdom (UK) providing RRT in 2003, CRRT was offered by 97%, IHD was provided by 30%, and only 2.4% of the units used IHD as the only modality of RRT.[17] In a similar survey in the UK in 2007, 65% of the units used continuous veno-venous hemofiltration as the first-line therapy, while 31% of the units used continuous veno-venous hemodiafiltration.[10] A major difference of these studies with our report is that the above studies have used facilities surveys assuming homogeneity across different populations. Our results determined the modality of RRT for AKI using claims billing and demonstrate that the greatest use of CRRT occurred in 2005, accounting for 18.3% of RRT for AKI. Although the influence of Ranco and Schiffl's papers[8,13,18] does not seem to have changed the dominant utilization of IHD in critically ill patients in the United States, the increase in the trend of CRRT may be

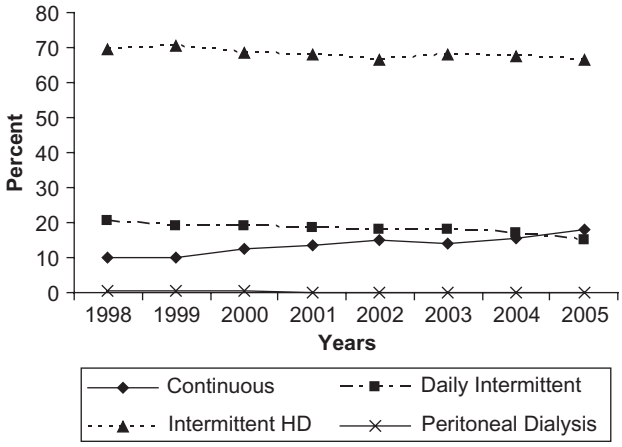

Figure 1. Trend of use of different modalities of dialysis in AKI from 1988 to 2005.

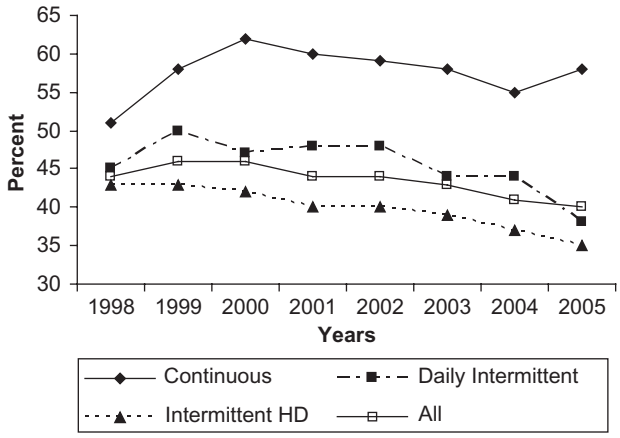

Figure 2. Trend of mortality in AKI by different modalities of dialysis from 1998 to 2005.

a reflection of initiation of continuous modality in a growing subgroup of sicker patients with multiple medical problems, and the decrease in trend of DHD may partially be explained by a fairly reciprocal increase in use of CRRT. Few individuals with AKI requiring RRT utilized PD. This low rate is likely the result of studies suggesting greater mortality with PD compared to IHD, as well as a possible fear of greater infectious, respiratory, and metabolic complications associated with PD, along with the emergence of alternative techniques for RRT among individuals with cardiovascular compromise.[19,20] Mean duration between hospital admissions to initiation of RRT was significantly higher in CRRT and DHD than in IHD. However, it may be a reflection of a prolongation of hospital stay as a result of more severe complications and comorbid conditions that developed in these groups during hospitalization rather than a delay in initiation of RRT.

Our results also suggest that males utilize RRT for AKI to a greater extent than females, a finding in agreement with Medicare beneficiaries' sex distribution from 1992 to 2001[21] as well as with Nationwide Inpatient Sample database from 1988 to 2002.[22] Similarly, distribution of race is almost identical to these studies.[21,22] Increases in the trend of diabetes, hypertension, anemia, and liver diseases over time may be a reflection of change in the spectrum of AKI, including its etiology and comorbid conditions, as well as a change in physicians practice pattern regarding willingness to initiate RRT in a wider spectrum of disease entities. Patients on CRRT had a significantly higher prevalence of sepsis, liver diseases, dysrhythmia, and ASHD. High prevalence of these comorbidities might have contributed to the severity of their acute illnesses, leading to greater hemodynamic instability and a higher rate of initiation of continuous modality.

The highest mortality observed in this study in patients on CRRT is in agreement with other observational studies in which use of CRRT in AKI was associated with a higher mortality rate, likely due to higher severity of underlying illnesses leading to selection of this modality.[19,31–33] A similar concept may explain the relatively higher mortality rate observed in patients on DHD as compared to those on IHD. The comparable outcomes of IHD and CRRT in randomized trials[23–30] suggest that the higher mortality observed with CRRT in our report is a reflection of severity of underlying diseases and comorbidities rather than complication of dialysis modalities.

Our results demonstrate a decrease in the 30-day in-hospital mortality among individuals with AKI requiring RRT. This observation is in agreement with other observational studies in which a decreased mortality and an increase in incident of AKI over time have been reported.[21,22] It seems that the severity of illness in critically ill patients on continuous modality contributes to a relatively high and stable rate of mortality observed in this group, while patients on intermittent dialysis had a steady decreased rate of mortality over years. Various explanations for the increased incidence and decreased mortality of AKI include but are not limited to change in sensitivity and specificity of ICD-9 codes over time (although in AKI needing RRT, change in coding may not be a significant factor as compared to patients not on dialysis), initiation of RRT for less severe forms of AKI, change in the spectrum of AKI including its etiology and co-morbidities, and finally improved general and supportive care.[22,34–36]

The strength of this study is its large sample size, use of multiple years, and use of data from across the United States. There are also numerous limitations to this study. First, it includes only individuals with Medicare as their

primary insurance source. However, the elderly constitute the segment of the population with the greatest incidence of AKI. Additionally, it has been demonstrated by others[22,34–36] that coding practices for AKI may have changed over time. Although a sensitivity of coding for AKI as low as 15%[21] has been argued to contributed in underestimation of the incidence of AKI and overestimation of the outcome, this argument may not be equally relevant in patients who underwent RRT, because it is unlikely that a physician would bill for a procedure not provided (Medicare fraud) or not bill for a procedure that is provided (economic incentive to bill appropriately). Also, because our study is simply observational, our estimates of 30 day mortality are highly biased by underlying severity of illness, in that the sickest individuals are most likely to have had CRRT as compared to IHD. As such, the trends over time are more informative within a modality as opposed to compared different modalities. The rate of Sustained Low-Efficiency Dialysis (SLED) is not separately captured in our analysis, as this modality is billed in a similar manner to CRRT; however this modality is likely to be rarely used.[14] Finally, the lack of a universal indication for initiation of dialysis could alter the incidence of AKI requiring RRT, and the resulting 30 day mortality.

CONCLUSION

The most frequently used modality of dialysis in Medicare beneficiaries with AKI from 1998 to 2005 has been IHD, but CRRT has been gaining in frequency of use. The highest mortality is associated with CRRT use and is likely a result of severity of disease. Overall, the 30-day mortality rate in AKI has decreased over time, possibly because of better supportive care or the initiation of dialysis in less severe forms of AKI.

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The authors declare that they do not have any conflict of interest.

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