Association of intermittent versus continuous hemodialysis modalities with mortality in the setting of acute stroke among patients with end-stage renal disease

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ABSTRACT
Patients with end-stage renal disease (ESRD) are 8–10 times more likely to suffer from a stroke compared with the general public. Despite this risk, there are minimal data elucidating which hemodialysis modality is best for patients with ESRD following a stroke, and guidelines for their management are lacking. We retrospectively queried the US Renal Data System administrative database for all-cause mortality in ESRD stroke patients who received either intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT). Acute ischemic stroke and hemorrhagic stroke were identified using the International Classification of Diseases 9th Revision (ICD-9)/ICD-10 codes, and hemodialysis modality was determined using Healthcare Common Procedure Coding System (HCPCS) codes. Time to death from the first stroke diagnosis was the outcome of interest. Cox proportional hazards modeling was used, and associations were expressed as adjusted HRs. From the inclusion cohort of 87,910 patients, 92.9% of patients received IHD while 7.1% of patients received CRRT. After controlling for age, race, sex, ethnicity, and common stroke risk factors such as hypertension, diabetes, tobacco use, atrial fibrillation, and hyperlipidemia, those who were placed on CRRT within 7 days of a stroke had an increased risk of death compared with those placed on IHD (HR=1.28, 95% CI 1.25 to 1.32). It is possible that ESRD stroke patients who received CRRT are more critically ill. However, even when the cohort was limited to only those patients in the intensive care unit and additional risk factors for mortality were controlled for, CRRT was still associated with an increased risk of death (HR=1.32, 95% CI 1.27 to 1.37). Therefore, further prospective clinical trials are warranted to address these findings.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with end-stage renal disease (ESRD) are at a significantly increased risk of having a stroke compared with the general public, and these patients have a poor prognosis following their stroke diagnosis.
⇒ There are limited data regarding optimal dialysis treatment for these patients following their stroke.

WHAT THIS STUDY ADDS

⇒ Patients placed on continuous renal replacement therapy (CRRT) within 7 days of a stroke, who accounted for 7% of the 87,741 included patients, had an increased risk of death compared with those placed on intermittent hemodialysis (HR=1.28, 95% CI 1.25 to 1.32).
⇒ Even among only those patients with ESRD and stroke admitted to the intensive care unit, CRRT was associated with an increased risk of death (HR=1.32, 95% CI 1.27 to 1.37).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ CRRT was not associated with improved mortality in this large-scale retrospective study, although database limitations emphasize the need for further study, ideally using a prospective design, to determine the best hemodialysis modality for these high-risk patients.

INTRODUCTION
End-stage renal disease (ESRD) is a major risk factor for the occurrence of a stroke. It is estimated that patients with ESRD are 8–10 times more likely to suffer from a stroke compared with the general public.[1] In addition, Nayak-Rao and Shenoy found that case fatality rates of patients who had a stroke and chronic kidney disease (CKD) reached almost 90%, emphasizing the high mortality associated with this patient population.[1] Patients with CKD who suffer an ischemic stroke are at a higher risk of neurological deterioration, poor functional outcome, and mortality,[2]

along with a greater risk for hemorrhagic transformation,[3] compared with patients who had a stroke without CKD. In a prospective cohort study of 128 patients who developed a hemorrhagic stroke, those with moderate to severe CKD had a 2.3 times greater hematoma volume and a greater than 4 times risk for 1-year mortality compared with patients with no reduced kidney function.[4] Thus, outcomes are poor among patients with CKD irrespective of the type of stroke and are even worse among patients with ESRD.[5]

Regardless of the type of stroke from which patients with ESRD suffer, the need for dialysis remains constant. The 2 most prevalent treatment modalities for patients with ESRD who suffer from a stroke are continuous renal replacement therapy (CRRT), in which dialysis is conducted continuously at a slow rate over several days without interruption, or intermittent hemodialysis (IHD), a more standard form of dialysis that usually occurs over a 3–4 hour session.[6] There is currently limited clinical evidence supporting the use of 1 modality over the other for these patients.[7] However, it is presumed that CRRT is a better treatment than standard hemodialysis for patients who have had a stroke, as CRRT's reduced rate of solute removal over longer periods of time is associated with greater stability in cerebral perfusion pressure and fewer intracranial pressure surges following acute neurological injuries.[6 8 9] IHD, alternatively, involves more rapid removal of waste products which could potentially worsen intracranial pressure and cerebral edema in patients who have had a stroke. Such an exacerbation of increased intracranial pressure is thought to be due to both cerebral vasodilation secondary to a drop in blood pressure, in addition to rapid solute removal causing an osmolar gradient between the brain and blood compartments.[8 10] These proposed mechanisms have been used to justify the use of CRRT over standard hemodialysis in hemodynamically unstable patients with ESRD who suffer a stroke; however, there are currently little data on actual outcomes of these treatments.

While CRRT may be mechanistically beneficial in limiting cerebral edema following a stroke, there are external factors that may impact the use of 1 dialysis modality over the other. For instance, it is worth noting that CRRT requires the placement of a catheter for vascular access to conduct this form of dialysis in the subset of patients with ESRD who do not already have a catheter in place. IHD, on the other hand, can be started more rapidly since it does not require a catheter for the initiation of dialysis; any pre-existing vascular access, such as a graft or fistula, may be used. In addition, the medical setting appears to be an important factor in determining the dialysis modality used and subsequent mortality outcomes of these patients following a stroke. Reductions in mortality associated with CRRT have been shown to be dependent on the medical teams' familiarity and expertise with conducting this form of dialysis.[11 12]

Few, if any, large-scale studies have examined mortality in patients with ESRD who suffer a stroke and are placed on CRRT or IHD. In this current retrospective study of a claims database (the US Renal Data System or USRDS), associations between dialysis modality and all-cause mortality were examined among patients with ESRD in the setting of acute stroke across a large subject sample size.

MATERIALS AND METHODS

Population

All patients aged 18–100 years with ESRD who had a stroke (acute ischemic stroke and hemorrhagic stroke), and started dialysis between 2004 and 2015, were identified by the International Classification of Diseases 9th Revision (ICD-9) and ICD-10 codes using hospital, detailed inpatient, or physician/supplier claims in the USRDS database.[13] Acute ischemic stroke was identified using ICD-9/ICD-10 codes of 433.X and 434.X/I63.X, and hemorrhagic stroke was identified using 430.X, 431.X, 432.X/I61.X, and I62.X (online supplemental tables 1 and 2). The stroke must have occurred between January 1, 2004 and August 31, 2015 to allow for at least 4 months of follow-up after the stroke. Subjects with missing age, race, sex, or ethnicity were excluded. Subjects without a Healthcare Common Procedure Coding System (HCPCS) code of 90935, 90937, 90945, or 90 947 were also excluded, as the purpose of the study was to compare continuous renal replacement (HCPCS 90945 and 90947) with standard hemodialysis (HCPCS 90935 and 90937). Subjects who died on the date of the stroke were excluded as they contributed no follow-up time for determination of the main independent variable (n=169 total). The date of the first stroke occurrence was used when defining the outcome and occurrence of risk factors.

Outcome

Time to death from the first stroke occurrence was the outcome of interest. Those who did not die were considered as censored observations in the analysis and their follow-up time was defined as the time from the first stroke to December 31, 2015.

Main independent variable

The main independent variable was CRRT following the stroke. Four HCPCS procedure codes (90935, 90937, 90945, or 90947) occurring within 7 days following the first stroke diagnosis were extracted from the detailed inpatient and physician/supplier claims and used to define the CRRT status. Subjects with a code of 90945 or 90947 were defined as having CRRT and those with a code of 90935 or 90937 were defined as having standard IHD.

Other risk factors or covariates of interest

Demographic variables of interest from the Centers for Medicare & Medicaid Services (CMS) Medical Evidence Form 2728 included age at stroke (calculated from date of birth to age at first stroke), race, sex, and ethnicity. Other risk factors or covariates of interest were determined by ICD-9 or ICD-10 codes in hospital, detailed inpatient, or physician/supplier claims in the USRDS data sets and include essential hypertension, diabetes, tobacco use, atrial fibrillation, and hyperlipidemia (online supplemental tables 1 and 2). All diagnoses were determined as having occurred before the first stroke occurrence. In a second analysis attempting to account for the severity of the stroke as well as other risk factors for mortality, the data were reanalyzed but the cohort was limited to those admitted to the intensive care unit (ICU), determined by identifying those with an ICU hospitalization on the day of their stroke diagnosis.

Variable	Level	Overall
Mortality, n (%)	Died	77,340 (88.2)
	Alive	10,401 (11.9)
Time in years to death/follow-up, mean (SD)		1.6 (2.0)
Dialysis modality, n (%)	CRRT	6250 (7.1)
	IHD	81,491 (92.9)

Table 1 Descriptive statistics overall among patients with ESRD and stroke

CRRT, continuous renal replacement therapy; ESRD, end-stage renal disease; IHD, intermittent hemodialysis.

Additional comorbidities associated with mortality were also controlled; these included essential hypertension, diabetes, tobacco use, atrial fibrillation, hyperlipidemia, obesity, alcohol use, malnutrition, and all diagnoses in the Charlson Comorbidity Index, excluding having a cardiovascular event or renal disease.

Statistical methods

All statistical analyses were performed using SAS V.9.4 and statistical significance was assessed using a significance level of 0.05. Descriptive statistics were determined overall by CRRT status and by mortality. Simple logistic regression models with CRRT as the outcome variable were used to examine potential confounders of demographic and clinical risk factors. A Kaplan-Meier survival curve was determined for CRRT on time to death and a log rank test was used to examine preliminary differences in survival between those who had CRRT versus IHD following a stroke. Cox proportional hazards (CPH) models were used to examine the relationship between CRRT status and mortality controlling for demographic and clinical risk factors in both the initial population and the cohort limited to those admitted to the ICU. Each variable was first examined in a simple CPH model on mortality, and the assumption of proportional hazards was assessed using the -log(log(Survival)) plot due to the large sample size. Then a multivariable CPH model on time to death using CRRT status and all other demographic and clinical risk factors was constructed. Each demographic or clinical risk factor was then removed from the model one at a time; if it was not statistically significant and did not change the model fit, this factor was not included but otherwise it was re-entered into the model. Model fit was examined using the Akaike's information criterion and the Bayes information criterion. Both final CPH models on time to death consisted of CRRT status, any statistically significant demographic or clinical risk factor, or any demographic or clinical risk factor that was not statistically significant but was needed in the model to improve the model fit.

RESULTS

In the USRDS between 2004 and 2015, there were 87,910 patients who had a stroke identified. Subjects who died on the date of the stroke were excluded (n=169). Of the 87,741 subjects included in the analysis, 80% (n=69,996) had an acute ischemic stroke, 10% (n=8998) had a hemorrhagic stroke, and 10% (n=8748) had both an acute ischemic stroke and a hemorrhagic stroke. Table 1 gives the descriptive statistics overall. Median time to death or follow-up was 0.86 years (IQR 0.18–2.41). Table 2 gives demographic and clinical risk factors overall and by dialysis modality. Eighty-eight per cent of the subjects died and 7% were on CRRT within 7 days following their first stroke. The average age of all stroke subjects was 69 years, 50% were female, 32% were black, 5% were other race, and 12% were of Hispanic ethnicity. Those who used tobacco or had hyperlipidemia were more likely to be on CRRT within

Table 2 Demographic and clinical risk factors overall and by dialysis modality among patients with ESRD and stroke

Variable	Level	Overall	Dialysis modality				
			CRRT	IHD	OR	95% CI	P value
Age at first stroke, mean (SD)		69.0 (12.5)	65.7 (13.0)	69.3 (12.5)	0.98	0.977 to 0.981	<0.0001
Sex, n (%)	Female	43,776 (49.9)	2998 (48.0)	40,778 (50.0)	0.92	0.87 to 0.97	0.0016
	Male	43,965 (50.1)	3252 (52.0)	40,713 (50.0)	1.00		
Race, n (%)	Black	27,750 (31.6)	1519 (24.3)	26,231 (32.2)	0.67	0.63 to 0.71	<0.0001
	Other	4122 (4.7)	281 (4.5)	3841 (4.7)	0.85	0.75 to 0.96	
	White	55,869 (63.7)	4450 (71.2)	51,419 (63.1)	1.00		
Ethnicity, n (%)	Hispanic	10,742 (12.2)	560 (9.0)	10,182 (12.5)	0.69	0.63 to 0.75	<0.0001
	Non-Hispanic	76,999 (87.8)	5690 (91.0)	71,309 (87.5)	1.00		
Essential hypertension, n (%)	Yes	63,953 (72.9)	4289 (68.6)	59,664 (73.2)	0.80	0.76 to 0.85	<0.0001
	No	23,788 (27.1)	1961 (31.4)	21,827 (26.8)	1.00		
Diabetes, n (%)	Yes	62,034 (70.7)	4187 (67.0)	57,847 (71.0)	0.83	0.79 to 0.88	<0.0001
	No	25,707 (29.3)	2063 (33.0)	23,644 (29.0)	1.00		
Tobacco, n (%)	Yes	20,040 (22.8)	1574 (25.2)	18,466 (22.7)	1.15	1.08 to 1.22	<0.0001
	No	67,701 (77.2)	4676 (74.8)	63,025 (77.3)	1.00		
Atrial fibrillation, n (%)	Yes	20,727 (23.6)	1224 (19.6)	19,503 (23.9)	0.77	0.73 to 0.83	<0.0001
	No	67,014 (76.4)	5026 (80.4)	61,988 (76.1)	1.00		
Hyperlipidemia, n (%)	Yes	51,525 (58.7)	3967 (63.5)	47,558 (58.4)	1.224	1.18 to 1.31	<0.0001
	No	36,216 (41.3)	2283 (36.5)	33,933 (41.6)	1.00		

CRRT, continuous renal replacement therapy; ESRD, end-stage renal disease; IHD, intermittent hemodialysis.

Table 3 Final CPH model results among patients with ESRD and stroke

		Final CPH model		
Variable	**Level**	**HR**	**95% CI**	**P value**
Main independent variable				
Dialysis modality	CRRT	1.28	1.25 to 1.32	<0.0001
	IHD	1.00		
Demographic and clinical risk factors				
Age at first stroke		1.019	1.018 to 1.020	<0.0001
Sex	Female	0.98	0.97 to 0.99	0.0257
	Male	1.00		
Race	Black	0.84	0.83 to 0.86	<0.0001
	Other	0.88	0.85 to 0.91	
	White	1.00		
Ethnicity	Hispanic	0.86	0.84 to 0.88	<0.0001
	Non-Hispanic	1.00		
Essential hypertension	Yes	1.04	1.02 to 1.05	0.0002
	No	1.00		
Diabetes	Yes	1.15	1.13 to 1.17	<0.0001
	No	1.00		
Tobacco	Yes	1.16	1.14 to 1.18	<0.0001
	No	1.00		
Atrial fibrillation	Yes	1.30	1.28 to 1.33	<0.0001
	No	1.00		
Hyperlipidemia	Yes	0.93	0.92 to 0.95	<0.0001
	No	1.00		

CPH, Cox proportional hazards; CRRT, continuous renal replacement therapy; ESRD, end-stage renal disease; IHD, intermittent hemodialysis.

7 days of a stroke compared with those without these characteristics. Those who were older, female, black or other race, of Hispanic ethnicity, or had essential hypertension, diabetes, or atrial fibrillation were less likely to be on CRRT within 7 days of a stroke.

Table 3 gives the results of the final multivariable CPH model. Figure 1 gives the Kaplan-Meier survival curve for those placed and not placed on CRRT within 7 days of a stroke. Online supplemental table 3 shows the results of the simple logistic regression models on CRRT. In the simple CPH models, those on CRRT within 7 days of their stroke had an increased risk for death compared with those not on CRRT (HR=1.20, 95% CI 1.17 to 1.23). In the final multivariable model, all variables were statistically significantly associated with mortality. Controlling for age, race, sex, ethnicity, essential hypertension, diabetes, tobacco use, atrial fibrillation and hyperlipidemia, those who were placed on CRRT within 7 days of a stroke had an increased risk of death compared with those not placed on CRRT (HR=1.28, 95% CI 1.25 to 1.32). Age, essential hypertension, diabetes, tobacco use, and atrial fibrillation were associated with an increased risk of death, while female sex, black or other race compared with white race, Hispanic ethnicity, and hyperlipidemia were associated with a decreased risk of death. Figure 2 illustrates a forest plot for the final multivariable CPH model of CRRT on mortality controlling for other demographic and clinical risk factors.

In an attempt to account for the severity of the stroke and other comorbidities in these patients, a second analysis was performed in which the cohort was limited to those admitted to the ICU; additional risk factors associated with mortality were also controlled for as shown in online supplemental table 4. Of the 87,910 patients who had a stroke, there were 37,802 who had an ICU stay. Of the 37,802 subjects included in the analysis, 74% (n=27,857) had an acute ischemic stroke and 26% (n=9945) had a hemorrhagic stroke. Of these 37,802 individuals, 3127 received CRRT and 34,675 IHD. Additional characteristics of the CRRT dialysis population are shown in online supplemental table 5. Online supplemental table 6 shows the characteristics of the subjects who survived versus those who did not, and online supplemental figure 1 illustrates the Kaplan-Meier curves for survival in those on CRRT versus IHD.

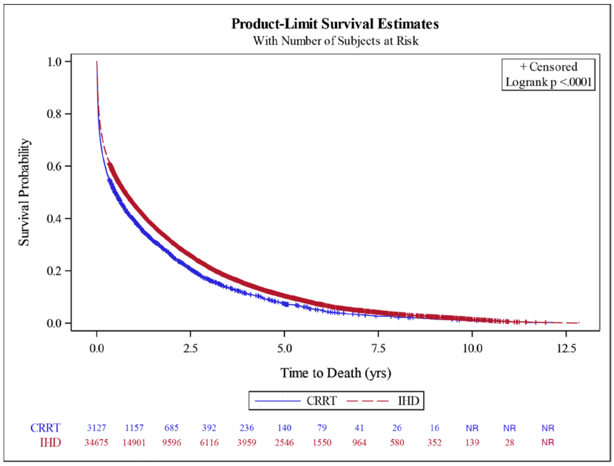

Figure 1 Survival of patients with end-stage renal disease (ESRD) and stroke receiving continuous renal replacement therapy (CRRT) or intermittent hemodialysis (IHD). Kaplan-Meier curves showing survival estimates of both the continuous renal replacement therapy group and the IHD group over time following stroke diagnosis. NR, not reported, per US Renal Data System (USRDS) regulations that observations of 10 or less must be suppressed.

In this analysis of patients with ESRD and stroke in the ICU, after controlling for demographic and clinical risk factors in the final multivariable model, those who were placed on CRRT within 7 days of a stroke had an increased risk of death compared with those not placed on CRRT (HR=1.32, 95% CI 1.27 to 1.37). As described in the Materials and Methods section, variables which were removed from the final CPH multivariable model due to lack of significance included sex, essential hypertension, obesity, alcohol use, and connective tissue disease. All remaining variables in the final model were significant as shown in figure 3. These include age, hemorrhagic stroke, diabetes, tobacco use, atrial fibrillation, hyperlipidemia, malnutrition, myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, pulmonary disease, peptic ulcer disease, mild to moderate liver disease, paraplegia, non-metastatic and metastatic cancer, severe liver disease, and HIV, all of which were associated with an increased risk of death. In contrast, black or other race compared with white race, Hispanic ethnicity, and hyperlipidemia were associated with a decreased risk of death.

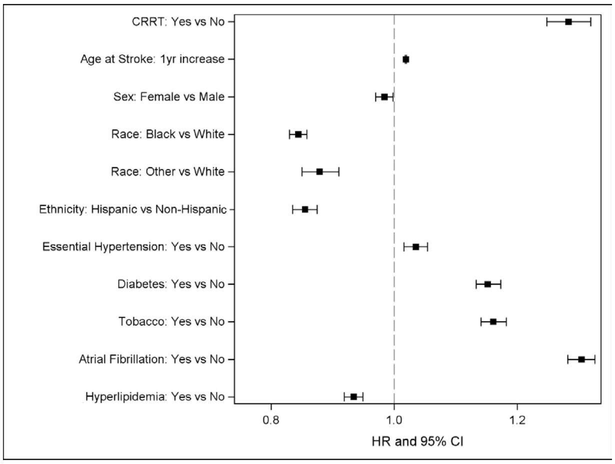

Figure 2 Final Cox proportional hazards (CPH) model for dialysis modality and other risk factors on mortality. Forest plot showing the final CPH model results expressed as HRs and 95% CIs. Results include continuous renal replacement therapy (CRRT) compared with intermittent hemodialysis (IHD) in addition to other demographic and clinical risk factors and their impact on mortality.

DISCUSSION

This retrospective study based on administrative claims data found in the initial analysis an association between worse all-cause mortality in patients who had ESRD and a stroke and received CRRT for treatment as compared with patients who had ESRD and a stroke and received IHD (HR=1.28, 95% CI 1.25 to 1.32), after controlling for the most common risk factors associated with stroke including essential hypertension, diabetes, tobacco use, atrial fibrillation, and hyperlipidemia. These findings were perhaps unexpected considering the proposed mechanisms supporting the use of CRRT to limit intracranial pressure surges and cerebral edema following a stroke. Our results also emphasize possible underutilization of CRRT in patients with ESRD who had an acute stroke, since only 7.1% (n=6250) of patients with ESRD and stroke (and 8.3%, n=3127, of ICU-admitted patients who had a stroke and ESRD) were found to have received this procedure.

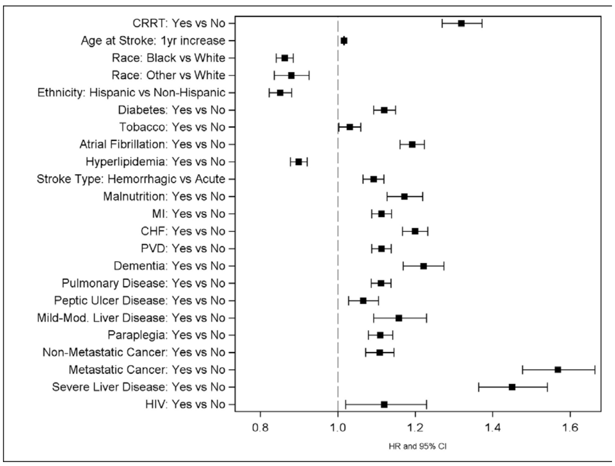

Figure 3 Final Cox proportional hazards (CPH) model for dialysis modality and other risk factors on mortality in patients with ESRD who had a stroke and were admitted to the intensive care unit (ICU). Forest plot showing the final CPH model results for the ICU-admitted cohort expressed as HRs and 95% CIs. Results include continuous renal replacement therapy (CRRT) compared with intermittent hemodialysis (IHD) in addition to other demographic and clinical risk factors and their impact on mortality. CHF, congestive heart failure; MI, myocardial infarction; PVD, peripheral vascular disease.

A possible explanation for the association of increased risk of mortality with CRRT versus IHD could be that clinicians preferentially performed CRRT on more seriously ill patients. Patients may have been placed on CRRT due to factors such as greater hemodynamic instability or a worse prognosis following their stroke. The data in the USRDS are limited by the administrative nature of the database; nevertheless, we attempted to account for the severity of the stroke and other comorbidities by performing a second analysis in which we limited the cohort to only those patients admitted to the ICU. Additional risk factors for mortality were also controlled for in this analysis, but even in this second analysis, CRRT was associated with a greater risk of mortality (HR=1.32, 95% CI 1.27 to 1.37). However, it should be noted that it is still possible that the patients with ESRD who had a stroke and received CRRT were more critically ill than those who were prescribed IHD; the severity of the patient's illness cannot be assessed using the USRDS database, which lacks values such as the Glasgow Coma Score, the Sequential Organ Failure Assessment (SOFA) score, albumin values, markers of malnutrition and/or inflammation, and other parameters that can be used to define the condition of a critically ill patient. Diagnoses were based solely on Current Procedural Terminology (CPT) and ICD codes which fail to take into account the nuances that go into treatment of critically ill patients such as the use of pressors or the neurological status of the patient. Our analysis, therefore, lacks insight into the full clinical picture of patients placed on CRRT, and we cannot exclude the potential difference in stroke severity across groups as a reason for discrepancies in the associations with mortality in these 2 forms of dialysis. Future studies on this topic would benefit from using a database with additional clinical information to provide context for illness severity in the setting of acute stroke. A prospective study design would be ideal to assess outcome differences across dialysis modalities in this patient population. These future studies would more definitively determine if the proposed mechanisms suggesting CRRT as the preferred approach in the setting of acute neurological injury hold true clinically.

An overwhelming majority of patients were treated with standard IHD (92.9%, n=81,491) compared with CRRT (7.1%, n=6250). This was true even in those patients admitted to the ICU, who were presumably more critically ill (8.3%, n=3127 vs 91.7%, n=34,675 for IHD and CRRT, respectively). Despite the large discrepancy in use of IHD versus CRRT, the statistical power of our analysis remains high at 99.2%. Thus, we believe our sample size is sufficient to examine the relationship between CRRT and mortality outcomes. This deficiency in CRRT use may possibly be attributed to lack of access to this modality in many hospitals throughout the country. CRRT is a relatively new form of dialysis that primarily occurs in the ICU setting, requiring the use of specialized equipment and round-the-clock trained staff which may be limited in certain settings. CRRT use varies widely both globally and domestically. Strongly held physician beliefs, patient illness acuity and comorbidities, institution and ICU types, insurance providers, and perceived cost of care have all been cited as factors that ultimately determine the use of CRRT, underscoring the multifactorial nature of choosing a particular dialysis modality in the setting of acute kidney injury.[14]

Another consideration in terms of the use of CRRT versus IHD is the fact that patients with ESRD who have a graft or fistula, which equates to 19.4% of USRDS patients, require a new vascular access to be placed before CRRT can be initiated.[13] This invasive procedure in an already critically ill patient comes with potential risks including but not limited to arterial puncture, hemothorax, pneumothorax, thrombus formation, and pericardial tamponade, along with the downstream complication of a catheter-related bloodstream infection following line placement.[15–19] Given the low incidence of these complications, it is hard to determine the extent to which catheter placement deters CRRT use for clinicians and may be negligible. Placing a catheter, however, does take time and has the potential to delay treatment of patients following their stroke which may lead to further complications. IHD uses any pre-existing vascular access, including grafts and fistulas, to conduct the dialysis treatment quickly without subjecting the patient to the risks and potential delay associated with placement of a new catheter. These factors, along with potential limited access to CRRT, may help explain why IHD was found to be used to a greater extent than CRRT.

Interestingly, a diagnosis of hyperlipidemia appeared to be protective in both final adjusted models, in contrast to all other common stroke risk factors. Several clinical investigations have found similar results and linked hyperlipidemia in patients who had a stroke to reduced white matter hyperintensity volume, indicating less cerebral small vessel pathology, and ultimately reduced mortality rates.[20 21] Other studies have found high low-density lipoprotein levels to be detrimental to stroke prognosis, emphasizing the importance of the lipoprotein profile as opposed to absolute level.[22] One possible explanation for the protective role of the diagnosis of hyperlipidemia could be the anti-inflammatory effect of statins that many patients with hyperlipidemia are placed on, although we do not have data regarding patient statin use from this database. An additional explanation for this finding is that patients who are diagnosed with hyperlipidemia by their providers are better managed than patients with unidentified, and thus untreated, hyperlipidemia. These hypotheses are conjectural, and the exact relationship between stroke prognosis and hyperlipidemia diagnosis remains in question.

Our analysis has several important limitations. Due to limited access to clinical data through this administrative database, it is hard to determine the extent of selection bias in patients who received CRRT, and it remains possible that those patients placed on CRRT had a more severely ill clinical picture, thus accounting for the increased mortality. Although our second analysis examined only those with an ICU stay at the time of their stroke and controlled for other risk factors associated with mortality, there is no ability to control for other measures of stroke severity such as the Glasgow Coma Score or the SOFA score. We also did not take into consideration the length of time each patient was on dialysis, which could affect mortality outcomes for patients with ESRD since dialysis vintage is associated with increased mortality risk.[23] Our analysis also did not control for type of stroke (eg, ischemic vs hemorrhagic) which could alter mortality outcomes as well. Furthermore, those patients who also use private insurance or the Veterans Affairs healthcare system for treatment may not have complete records in the USRDS, limiting and potentially skewing our sample compared with the entire population of patients with ESRD who had a stroke. In addition, a patient with a stroke originally administered IHD, who then exhibited an acute decompensation within 7 days of the stroke, would be classified as a CRRT patient, although the original modality implemented was IHD. Such a scenario could increase the risk of misclassification bias. It is also important to note that our retrospective descriptive study is only looking at associations between mortality in stroke and dialysis modality and not causation, which would be better assessed with a prospective study design. Despite these limitations, the USRDS, in collaboration with the CMS, the United Network for Organ Sharing, and the ESRD networks, has the most comprehensive and reliable longitudinal data sets on patients with ESRD, allowing a retrospective study design with high power to address clinical questions of interest in a large population.[13] Our study manifests the severe mortality outcomes that this patient population faces, and the large, heterogeneous sample obtained from this database strengthens the external validity of this study, making our results very generalizable.

In conclusion, in this retrospective review of the USRDS database, patients with ESRD who had a stroke and received IHD had decreased all-cause mortality compared with patients who received CRRT, even in those patients admitted to the ICU. However, the administrative claims database used to conduct this study limited the access to the clinical context of each patient, making it difficult to otherwise control for sickness severity across hemodialysis modality groups. Nevertheless, our results raise a question as to the superiority of CRRT, and further prospective clinical trials are clearly warranted to confirm or refute these findings.

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